Determinants of congenital anomalies in Afghanistan

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Afghanistan

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Determinant of congenital anomalies in Afghanistan

A thesis submitted in partial fulfilment of the requirement for the degree of Master of Public Health

by

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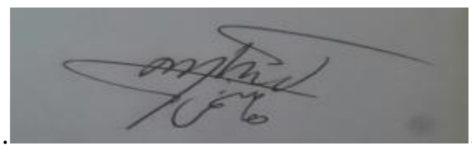
Afghanistan

Declaration:

Where other people's work has been used (either from a printed source, the internet or any other source) this has been carefully acknowledged and referenced in accordance with the departmental requirement.

The thesis 'Determinants of congenital anomalies in Afghanistan' is my own work.

Signature ……………………………………………………

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I am thankful to my advisor and back stopper for their continuous support during my thesis.

I really appreciated the support and motivation from my wife Dr. Saliha Hashimi in this tough period, she always kept her smile, despite being in difficult situation and alone in last one year.

Dedication

I dedicated this thesis to my parents, my brother Dr.Said Olfat Hashimi, who guided and supported me during my tough time and to my wife Dr.Saliha Hashimi without her support and motivation it was not possible to achieve this goal.

Abstract

Said Mujahid Hashimi, Afghanistan

Background: As under-five mortality due to communicable disease has declined in Afghanistan over the last 15 years, congenital anomalies are emerging among the main (residual) causes of under-five mortality, and therefore it is time to focus on this hidden public health problem. So far no systematic study has been conducted on the determinants of congenital anomalies in Afghanistan.

Main Objective and methodology: Main objective is to explore the burden and social determinants of congenital anomalies in Afghanistan and provide recommendation for policy makers. A literature review of published and unpublished articles related to congenital anomalies was conducted, with searched through databases (VU Amsterdam, and PubMed), and search engines (Google and Google Scholar)

Findings: There is scarcity of data about congenital anomalies in Afghanistan; most data are based on modeling and estimations. Prevalence of congenital anomalies in Afghanistan is 74.9/1000 live births. congenital anomalies contribute to 6% of neonatal mortality and is fourth cause of DALYs, annually an average of 2600 children are born with Down syndrome, 835 with congenital rubella syndrome and 2292 with NTDs, and an estimated total of 64,000 children may be born with genetic or partially genetic disorders. Prevalence of consanguinity in Afghanistan is 40- 49% and an estimated 32.9% of congenital anomalies may be attributed to consanguinity; while, advanced maternal age may contribute to 20% of congenital anomalies, followed by high fertility rate, insufficient supplementation of folic acid, congenital infections and insufficient health services.

Socio cultural, traditional, socio economic and religious preferences influence these determinants and are the root causes for high consanguineous marriages, underused of ANC, family planning and increased exposure to environmental teratogens.

Although some interventions exist in current reproductive and child health programs, there is no explicit strategy for control of congenital anomalies in Afghanistan to address congenital anomalies.

Conclusion: Congenital anomalies make an important and relatively increasing contribution to under five mortality. It is necessary to increase awareness about importance of congenital anomalies and the fact that this burden can be reduced through a set of integrated and cost effective interventions, stimulate research and develop a national congenital anomalies control program.

Keywords: Afghanistan, congenital anomalies, birth defects, risk factors, determinants, causes

Word count: 13136

Glossary

Term	Explanation
Teratogens	Anything that affects embryo/ fetus and may cause congenital anomalies
Gastroschisis	A congenital anomaly that affect abdominal wall and with incomplete fusion of abdominal part of intestine is coming out from opening
Cretinism	a congenital disease due to iodine deficiency that leads deficiency of thyroid hormone ; physical deformity, dwarfism, and mental retardation, and goiter are prominent features
Gray(Gy) &Rads	These are measuring unit used for absorbed dose of ionizing radiation, 0.01 Gy is equal to 1 rads
Cataract	It is clouding of eyes lens, leading to vision impairments that could be acquired or congenital
TORCH	It is an abbreviation used for congenital infections and each word present an infection T: toxoplasmosis, R: rubella virus , C: cytomegalovirus, H; Herpes simples O: Others
Oral clefts(cleft lip and cleft palate)	Cleft lip is an opening in the upper lip that may extend into the nose, could be at one side or both side Cleft palate is an opening in the roof of mouth which may be complete or incomplete
South African Rand (ZAR)	local currency unit for south Africa
Unmet need for family planning	"Women with unmet need are those who are fecund and sexually active but are not using any method of contraception, and report not wanting any more children or wanting to delay the next child."Defined by WHO
Patau Syndrome	It is a rare chromosomal disorder also known as trisomy 13, in which additional copy of chromosome 13 is seen in all or some body cells, these patients have, cleft lip, cleft palate heart, eyes anomalies And other congenital anomalies
Edwards' Syndrome	It is a rare chromosomal disorder also known as trisomy 18, in which additional copy of chromosome 18 is seen in all or some body cells, patients usually have anomalies of heart and other organs
Klinefelter syndrome	It is a chrosomal disorder of the X and Y chromosomes, these patient have one extra X chromosome (47, XXY), Klinefelter syndrome results , hypospadias, micropenis and prominent female feature in a male is seen in these patients

Abbreviations

ANC	Antenatal Care
ACE	Angiotensin converting Enzyme Inhibitor
BHC	Basic Health Centre
BPHS	Basic Package for Health Services
CHC	Comprehensive Health Centre
CHD	Congenital Heart Disease
CSO	Central Statistics Organization
CRS	Congenital Rubella Syndrome
CEA	Cost Effectiveness Analysis
CMV	Cytomegalo Virus
DH	District Hospital
DALYs	Disability Adjusted Life Years
EPHS	Essential Package of Health Services
EU	European Union
FDA	Food and Drug Administration
HIV	Human Immunodeficiency Virus
HP	Health Posts
HSC	Health Sub-Centre
HEDP	High Education Development Project
HSV	Herpes Simplex Virus
HMIS	Health Management Information System
IMR	Infant Mortality Rate
ISAF	International Security Assistance Force
IHD	Ischemic Heart Disease
IS	Islamic State
KMU	Kabul Medical University
LMICs	Low Middle Income countries
LRI	Lower respiratory infections
MOD	March of Dimes
MoPH	Ministry of Public Health
MoHE	Ministry of Higher Education
NMR	Neonatal Mortality Rate

MR	Measles, Rubella
MMR	Mumps, Measles, Rubella
NTD	Neural Tube Defect
NGO	Non government organization
NHP	National Health Policy
OR	Odds Ratio
PNC	Post Natal Care
PPP	Purchasing Power Parity
UK	United Kingdom
USAID	US Agency for International Aid
PAF	Population Attributable Fraction
RCT	Randomize Control Trail
RR	Risk Ratio
SDGs	Sustainable Development Goals
STD	Sexually Transmitted Disease
WHO	World Health organization
WFP	World Food Program
ZAR	South African Rand (local currency)

Introduction

I am an Afghan medical doctor and have been working as a paediatrician in Maiwand teaching hospital in Kabul since 2002. During this period I witnessed many children dying from congenital anomalies. There was no diagnostic facilities for these children and our diagnosis was based on clinical examination. I opened the first echocardiography department in the hospital and started my practice and looking after children suffering from cardiac congenital anomalies. During my practice, I encountered many children with different types of congenital anomalies.

Congenital anomalies was a topic of discussion during our daily and weekly meetings we always talked about the causes and how to diagnose and treat these children. But unfortunately there was insufficient information about magnitude and risk factors of congenital anomalies in Afghanistan and my mind was always stuck on medical causes of these anomalies, mostly we thought about the genetic base of these anomalies and ignored other determinants.

When I decided to change my field from clinical practice to public health and joined the master of public health program in KIT. It was during this course for the first time I understood that a lot can be done to prevent disease through public health measures compared to medical treatment. It was during our module of social determinants of health that I realized the importance of other nonmedical factors in the occurrence of disease and the role of public health interventions for disease prevention, then I decided to work on determinants of congenital anomalies in Afghanistan.

According to the report from March of Dimes (2006), the prevalence of congenital anomalies in Afghanistan is 74.9/1000 live births, and it is the 4^{th} main cause of DALYs and contributes to 6 % of neonatal deaths. Meanwhile, the relative contribution, to under-fives mortality, infant and neonatal mortality, will increase because other causes, such as respiratory infections, malnutrition, diarrheal disease are diminishing in Afghanistan. Unfortunately analysis of causes and underlying factors of congenital anomalies has not been conducted in Afghanistan till now. Therefore exploring and analysing the magnitude, and determinants of congenital anomalies, will help in the strategic directions of the ministry of public health (MoPH) and other relevant stakeholders, to reduce the under-five mortality and specially neonatal mortality and achieve sustainable development goals (SDGs).

In this thesis chapter one is about the country background and chapter two, a short introduction to congenital anomalies. In chapter three the problem statement (magnitude of congenital anomalies), justification and methodology will be discussed. Chapter four will discuss social determinants of congenital anomalies, based on an adapted conceptual framework and chapter five analyzes the current policies and strategies, regarding congenital anomalies and evidence based interventions, that address the key determinants of congenital anomalies. Finally the conclusion and some recommendations are discussed in chapter six.

I expect that this document helps the ministry of public health (MoPH) in Afghanistan, as a leader of the health sector and other stakeholders, to review the causes and underlying factors of congenital anomalies in the country and to formulate appropriate health policies and strategies concerning congenital anomalies.

Chapter 1

1. Country background

1.1. Geography

Afghanistan is a land-locked country in South-Central Asia, with a total land area of 647,500 square kilometers. Kabul is the capital city of Afghanistan. The country has borders with six different countries, namely, Pakistan, Iran, Tajikistan, Uzbekistan, Turkmenistan, and China. Afghanistan has 34 provinces and each province has several districts (398 administrative districts). Districts are further divided into smaller units called villages and municipalities (1). 80% Of the land is covered by mountains and deserts and only 2% by jungles (2). Islam is the formal religion of the country and 99.8% of populations are Muslims. Pashtu, Dari and Uzbeki are formal languages (1).

1.2. Population

Total population of Afghanistan in 2016 is 29.7 million. 51 % are men and 49% women. 28.2 million are settled populations and the remaining part are nomads; 21.1 million (74.8%) live in rural areas and 7.1 million (25.2 %) in urban areas (1). According to age distribution, the majority of the population is young with 47 % of the population is under age of 15 and 3% are over the age of 65 years. 57% of male and 31% of female population are age 6 and over have ever attended the school. Net school attendance ratio (NAR) in primary school is 69% for boys and 50% of girls age 7-12 (3). The literacy rate is very low, only 15% women and 49% of men can read and write. The average annual population growth rate, between 2010 and 2015, is about 3.1% (4), total fertility rate is 5.3 children per woman, the general fertility rate per year is 175/1000 women of reproductive age, and the crude birth rate is 37/1000 population/year. The average household size is 8 persons per house(3).

Overall 65% of the population has access to improved drinking water. One fourth of households has an improved toilet facility. 67% of households use some type of solid fuel for cooking. 83% Households in urban areas use liquefied petroleum or natural gas, while 83% of rural households use wood, animal dung or grass for cooking (3).

1.3. Political situation

More than three decades of war and political instability have damaged the socio-economic infrastructure of the country. 10 years of holy war (Jihad) against the Russian army in the 70s and 80s, the internal war between different Jihadist groups in the 90s and then the Taliban era destroyed the infrastructure of the country. After the collapse of the Taliban in 2001 and the deployment of the International security assistance forces (ISAF) a new presidential republic government was established, a new constitution was endorsed and for the first time president and member of parliaments were elected through general elections (5). The current Afghanistan unity government came to power in 2014, lead by Mohammad Ashraf Ghani and is a relatively stable government, but insecurity, the threat of the Taliban and Islamic

State(IS), poverty, unemployment, dependency on foreign aids and corruption are big challenges for the current government(5).

1.4. Economy: Afghanistan is amongst the poorest and least developed countries in the world and ranked 169 out of 188 countries(6). Afghanistan is a low income country, gross domestic product(GDP) is $634 per capita, health expenditure is I$166 purchasing power parity(PPP) which is equal to US $55 per capita, 39.6% of the population is poor(3)(6). The economy has been improving after the collapse of the Taliban, establishment of a new government, foreign donations and investments. According to the report of the World Bank, the economy of Afghanistan expanded on average 5% from 2011 to 2015. But due to insecurity and political instability, lack of foreign investment and reduction of foreign donations the gross product growth has dropped from 14% in 2010 to 1.3% in 2014 (7).

2. Health system

Lack of human resources for health, a weak and devastating health infrastructure, insufficient health facilities, lack of national health policy and the worst health indicators were the main challenges of the ministry of public health (MoPH) after the collapse of the Taliban in 2001 (8)(9). Maternal mortality was 1600/100,000 live birth and under-five mortality was 257/1000 live birth /year in 2001 (8).

To tackle the problems and deliver basic health services to the whole country and especially for the most vulnerable population, MoPH developed a basic package of health services (BPHS) in 2002 and an essential package of health service (EPHS) in 2005. The main components of BPHS are new born care, child health care, nutrition, control of communicable disease, mental health, disability and provision of essential drugs (10). Apart from this MoPH developed a contracting out model in which NGOs, under an agreement with MoPH became responsible for the delivery of health services and implementation of BPHS and EPHS in the country(11).

2.1. National health strategies and policies: An interim health policy and strategy was developed between 2002 and 2004 followed by development of a national health policy for 2005-2009 and now a broad national health strategic plan for 2012-2020 and a national health policy for 2016-2020 are in place. Delivering health services through BPHS and EPHS mostly depend on donors such as USAID, European union (EU), and World Bank and these donors have a potential influence on the health care system and health policies in Afghanistan (8)(12). Despite achievements in the last decade, in reducing under-five mortality to 55/1,000 live births and maternal mortality to 396/100,000 live births/year in 2015 (7). Shortages of professional health providers, access to health services and high out of pocket expenditures (73.3%) are still prominent problems (7)(13). 87% Of the population are living within two hour distance by any means of transport from a health facility (13).

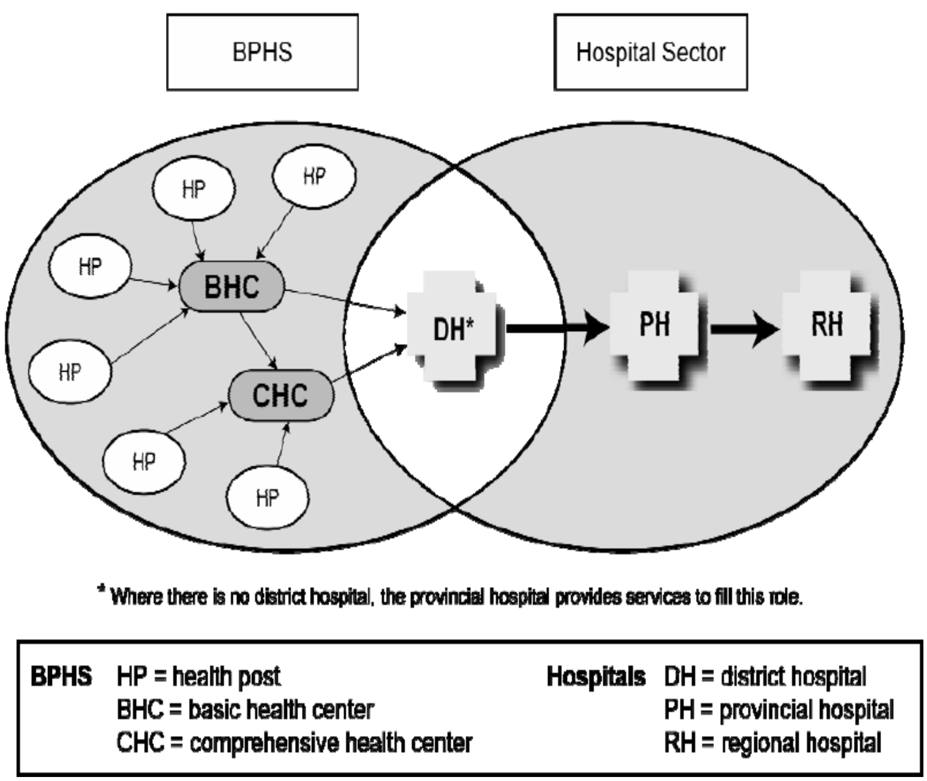
One of the core components of the national health policy (NHP) 2015-2020 is to address malnutrition in Afghanistan and MoPH developed a national public nutrition policy, nutrition action network and national nutritional strategy in line with the NHP to address the problem of malnutrition(7). One of the main components of these policies is food fortification, which is also an effective intervention to prevent congenital anomalies. Three areas prioritized by the national public nutrition policy for food fortification are, salt iodization, oil fortification with Vitamins A and D and Wheat flour fortification with iron, vitamin A, B12, zinc and folic acid (14).

2.1.1 Response to congenital anomalies in Afghanistan: Although child health is on the priority of the MoPH and numerous programs throughout the country are implementing to decrease under-five mortality. But there is no explicit national strategy and policy to control congenital anomalies, which is among the main causes of under-five mortality.

The national congenital anomalies surveillance system, which is crucial for developing policy and strategy, has not been established yet, the mechanism for death registration and the cause of death information does not exist. Precise data about causes and determinants of congenital anomalies is not available.

2.2. Structure of health care Service delivery: Afghanistan has almost a similar structure of a health system which exists in most of the LMICs (15) figure 1. According to the MoPH, the health post (HP), is the first point of contact for health care, followed by a health sub center (HSC), basic health center (BHC), comprehensive health center (CHC), district hospital (DH), provincial and regional and national specialized hospitals. BHPS is implemented by HP, BHC, CHC, and DH. HSC fills the gap between HP and another level of health services (10).

Figure (1): links between various health facilities in Afghanistan



Source: MoPH (2006)

Chapter 2

Congenital Anomalies

2.1. Definition

The development of human beings from conception till birth is a complex process. This development may be affected by several internal and external factors and sometimes results in mal development and congenital anomalies of the foetus. Birth defects, congenital anomalies, and congenital malformations are used synonymously.

Congenital anomalies are defined as structural and functional anomalies present at birth, but some congenital anomalies, such as hearing defects, renal and cardiac anomalies may only be diagnosed later in life (16).

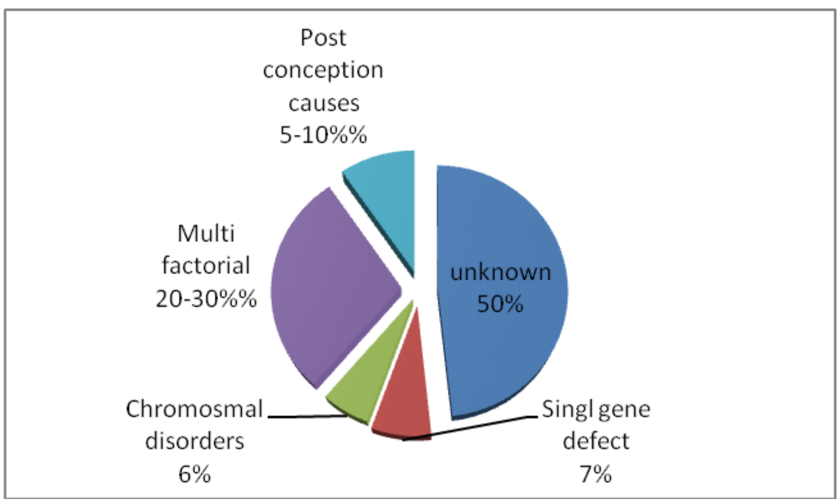
According to the WHO and global reports, on congenital anomalies from March of Dimes, common congenital anomalies are congenital heart defects(CHDs), neural tube defects(NTDs) and Down syndrome (16)(17).

2.2. Causes and determinants

50% of all congenital anomalies are due to unknown causes but there are some known causes in the remaining 50% that are divided into two groups (17).

- Preconception causes and determinants constitute 35-40% of the congenital anomalies
- Post conception causes and determinants constitute 5-10 % of the congenital anomalies

Figure 2: Causes of congenital anomalies



Source: adapted from March of Dimes global report on birth defects (2006)

2.2.1. Preconception causes and determinants: Most of these causes are due to defects in genes or chromosomes, partially genetic anomalies will lead to congenital anomalies in the presence of environmental factors. Preconception causes are subdivided into chromosomal abnormalities (6%), single gene defects (7.5%) and multifactorial(20-30%) (17), Down syndrome and Klinefelter syndrome are examples of chromosomal disorders, thalassemia and hemophilia are example of single gene defects, more than 7000 single gene congenital anomalies are recognized (17). Oral clefts, CHD and limb anomalies are examples of anomalies with multifactorial causes (17).

2.2.2. Post conception causes and determinants

2.2.2.1. Socioeconomic factors: 94% of severe congenital anomalies occur in low- and middle-income countries (16), which is partially due to a higher fertility rate (more children more congenital anomalies) and partially due to increased risk factors such as a low socio economic condition, which may lead to the lack of access to health services, under-nutrition of pregnant women and the exposure of pregnant women to other risky behaviours (16)(17).

2.2.2.2. Parental factors: Mother's age, infections during pregnancy such as rubella, nutritional status (folic acid and other micronutrients), medications such as anti-convulsing drugs, smoking or alcohol consumption during pregnancy, pregnancy-related disease and consanguinity are some important determinants of congenital anomalies related to the parents (17).

2.2.2.3.Environmental factors: Maternal exposure to certain pesticides and chemicals, radiation during pregnancy, working or living near to waste sites and industrial areas may affect development of the foetus, particularly in the presence of other factors (16).

2.2.2.4. Behaviour factors: Individual behaviour such as smoking, use of alcohol, occupation and living conditions, increase the risk of congenital anomalies.

2.2.2.5. Health system factors: prevalence and burden of congenital anomalies are influence by the availability of reproductive, periconceptional and child care services (17).

2.3. The burden of congenital anomalies

According to WHO 303,000 neonatal deaths worldwide were due to congenital anomalies in 2015(18) and ranked 13th in worldwide causes of DALYs (18). Besides among the main causes of under-five mortality, congenital anomalies lead to social stigma, long term disability, decrease productivity and increase economic burden on families, health system, and society (16)(17).

Congenital anomalies were recognized as cause of stillbirths and neonatal mortality in 63rd world health assembly and member states were asked to develop effective congenital anomalies control program and integrate it into to reproductive and child health care services (16).

2.4. Prevention and treatment

Prevention, of some common congenital anomalies, is possible by decreasing or removing its risk factors 70% of congenital anomalies can either be prevented or be partially or completely cured, three types of preventions are in place to decrease the burden of congenital anomalies (16)(17). Details of these interventions are in annex (2).

2.4.1. Primary prevention: These interventions mostly focus on the preconceptional(before and first 8 weeks of pregnancy) period to ensure the birth of the baby without congenital anomalies. Folic acid supplementation, family planning and rubella vaccines are examples of primary interventions (17).

2.4.2. Secondary prevention: These interventions mainly focus on the pregnancy period, where through prenatal diagnosis and genetic screening, congenital anomalies are detected and certain therapeutic options(termination of pregnancy for severe congenital anomalies)are offered, to reduce the number of children with birth defects(17).

2.4.2.Tertiary prevention: These are treatment and rehabilitation of congenital anomalies, such as surgery for oral clefts, hypospadias, congenital heart anomalies and rehabilitation care for children with a long lasting disability.

Box (1): Common interventions for prevention of congenital anomalies (16)

- Ensuring diverse and healthy foods for adolescent girls and mothers before, during and after pregnancy
- Ensuring that mothers and adolescent girls receive adequate folic acid and other multivitamins through diet
- Avoidance of smoking, and alcohol by pregnant mothers
- Prevention of pregnant women (and sometimes women of child-bearing age) from exposure to certain infections that cause congenital anomalies, radiations and environmental hazardous substance
- Appropriate management of diabetes before and during pregnancy
- Risk-benefit analysis of any medication or radiation that is prescribed to pregnant women
- Vaccination against the rubella virus, for children and women
- Increased capacity building of the health staff and other relevant departments about prevention of congenital anomalies
- Screening and treatment for infections such as rubella, varicella and syphilis

Source: WHO (16)

Chapter 3

Problem statement, Justification and methodology

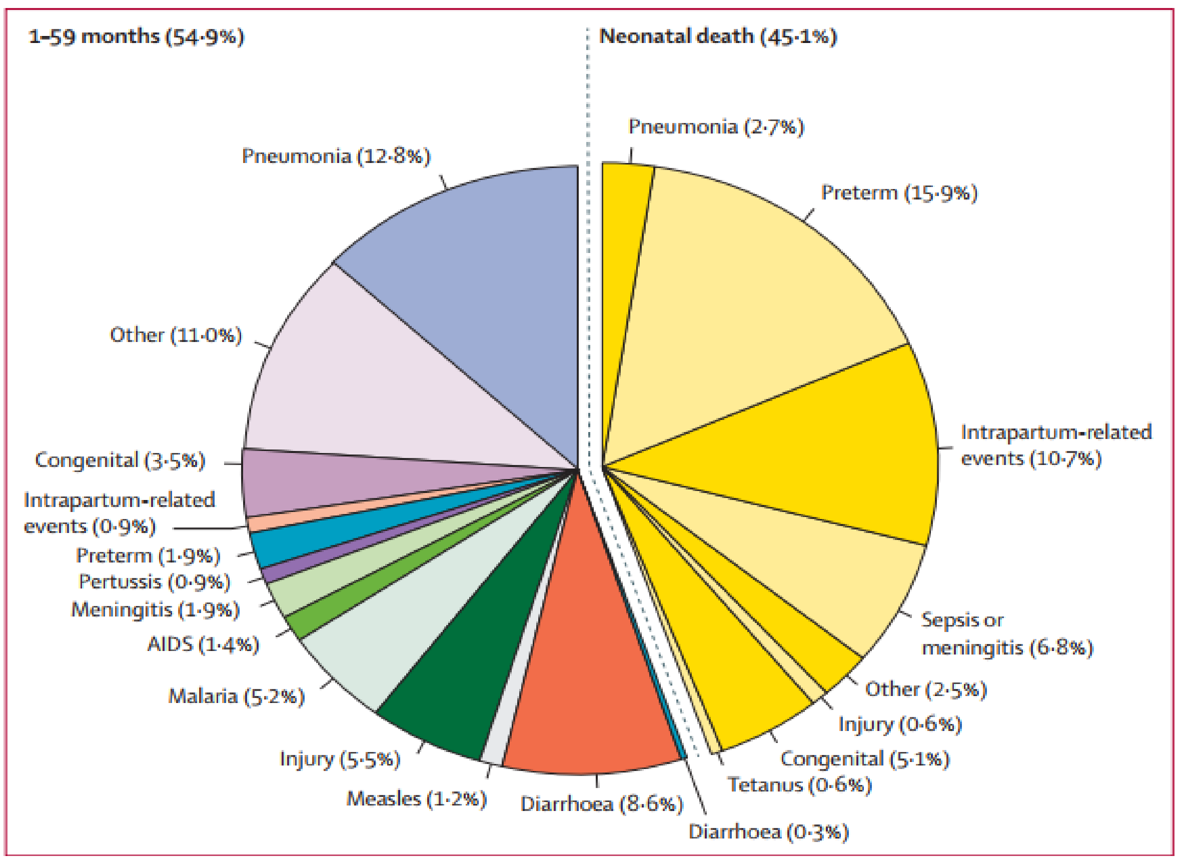
3.1. Problem statement

Annually 7.9 million children (6% of total global births) are born with congenital anomalies due to genetic or partially genetic causes and thousands more are born due to post conception causes such as rubella, alcohol consumption during pregnancy, iodine and folic acid deficiency (17).

5.9 million children died before reaching their fifth birthday in 2015, 45 % of these deaths occur in the neonatal period mainly due to preterm birth (35%), intra partum-related complications (24%), sepsis (17%) and congenital anomalies(10%) (16) figure3. According to the WHO, 2.68 million neonatal deaths in 2015, 303,000 were because of congenital anomalies, 94% of these deaths occur in LMICs (16)(17). In 2015 congenital anomalies contributed to 8.6% of under-five mortality globally(18)

Congenital anomalies are also among the main cause of morbidity and long lasting disability worldwide, every year 3.2 million(1 in 33 infants) children disabilities are related to congenital anomalies (17).

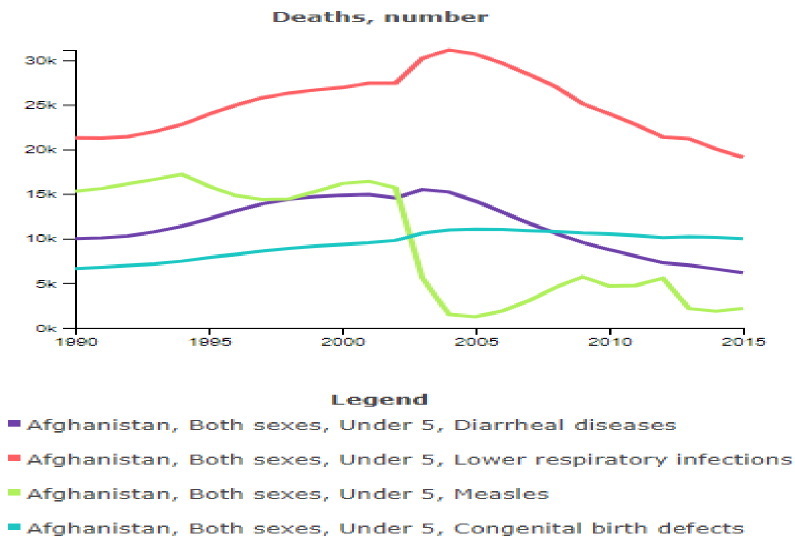
Figure (3): Causes of under-five mortality worldwide (18)



Source: Liu Li et all (2016). Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals.

Because the overall under-five mortality decreased in the last decades from other causes, the relative contribution to under-five mortality, due to congenital anomalies is increasing in developing countries(17).

Figure 4: Trends in number of deaths in under 5 due to diarrheal disease, LRI, measles and congenital anomalies in Afghanistan (28)



Source: Institute of Health metric and evaluation. Global Burden of disease :Afghanistan; 2015. http://ghdx.healthdata.org/gbd-results-tool

In 2015, congenital anomalies ranked 13th cause of DALYs globally and were causing 58,355 thousand DALYs in all ages, while age-standardized rate was 781.1(704.2-869.9)DALYs/100,000 (19). Among congenital anomalies, congenital heart anomalies were causing 343.9 (302.3-383.1)DALYs/100,000 followed by neural tube defects79.9 (61.3-101.2)DALYs/100,000 and Down syndrome32.2 (23.3-44) DALYs/100,000 (l9). Heamoglobinopathies (thalasemia and thalasemia trait, sickle cell disorder and trait, G6PD deficiency and trait) are separately classified by WHO and causes 20,211.2 thousand DALYs worldwide (19). In central Asian countries, congenital anomalies ranked as 7^{th}cause of DALYs (19).

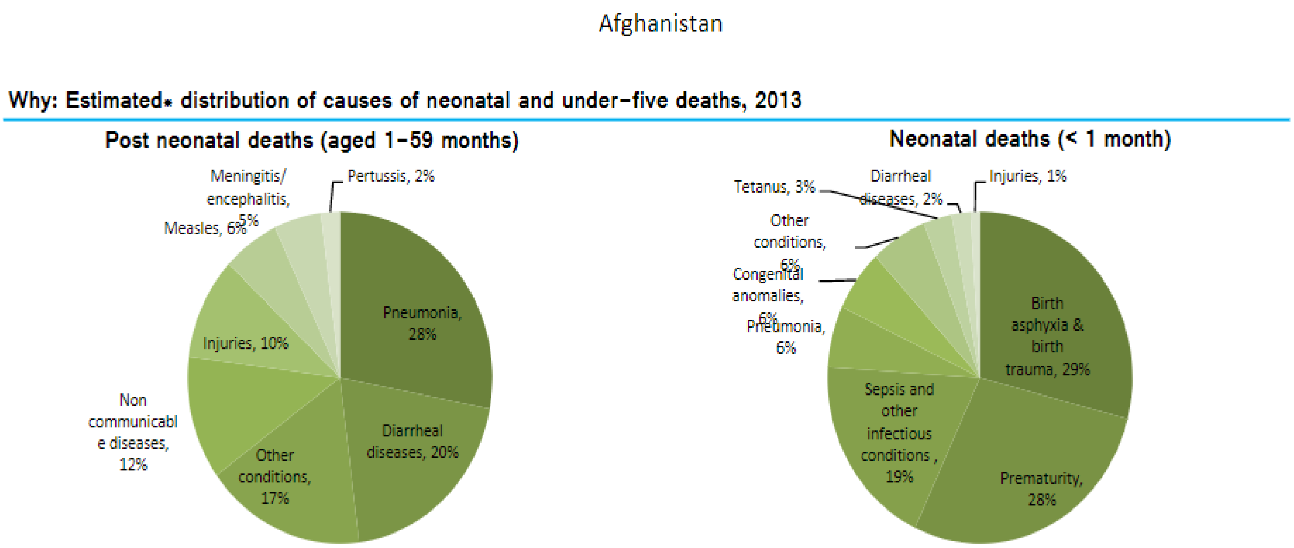
Although congenital anomalies are not in top ten causes of DALYs in Nepal, India and Sri lanka ,but contributes to 9.6 % of neonatal deaths in India, 7.9% in Nepal and 10,9 % in Sri lanka in 2013 (20).

Evidence shows that congenital anomaly is a risk factor for preterm birth, from one million preterm deaths in 2014, 270,000 was due to congenital anomalies (21)(22). This also indicates that contribution of congenital anomalies to under-five mortality may be underestimated, because part of preterm deaths may be due to congenital anomaly which is not taken into account.

Afghanistan still has the worst health indicators in the world and region, the under-five mortality still remains high (55/1,000live birth/year) infant mortality rate (IMR) is 44/1,000/year and neonatal mortality rate (NMR) is 22/1,000 live birth/year (7). 37% of overall deaths occurred in neonatal period and 63% in post neonatal period (34%in 1-11months and 29% 1-4 years) (23).

Main causes of mortality, in the post neonatal period in Afghanistan, is lower respiratory infections(LRI), diarrheal disease, and meningitis, while birth asphyxia, prematurity and sepsis are the leading causes of NMR, followed by congenital anomalies. Congenital anomalies contribute to 6% of neonatal deaths(23) figure 5.

Figure (5): distribution of causes of under-five mortality in Afghanistan (23)



Source: WHO. Eastern mediterranean region. Afghanistan, Neonatal and Child health profile. Department of Maternal, Newborn, Child and Adolescent Health. 2013

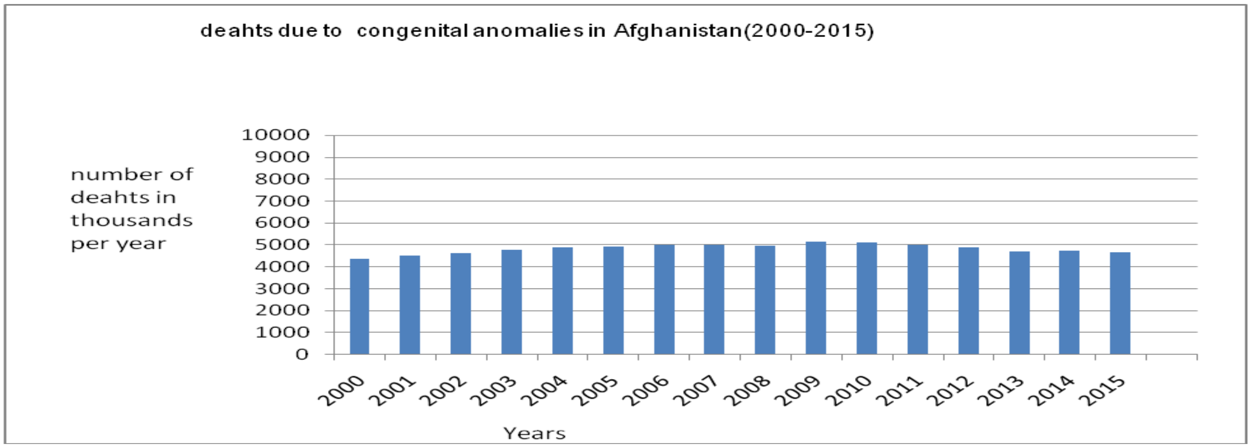
Due to lack of information, about congenital anomalies, the exact prevalence is unknown in Afghanistan. According to a study in one of the hospitals in Kabul, birth prevalence of external structural congenital defects was 68/10,000 live births, NTDs were the most common anomaly 26/10,000 live birth. Mortality was high and 28-39.4% of these children die before leaving the hospital (24). This study is hospital based and only includes external and visible major defects, therefore the study cannot present the exact population prevalence of congenital anomalies. Another study from Afghanistan in a children hospital in 2006 shows that 8% of all newborns admitted, due to any cause, were diagnosed with congenital anomalies(25).

Study in 1982, in the Indira Gandhi children hospital in Afghanistan also shows in 5,279 children admitted from any cause to this hospital 5.5% were diagnosed with congenital anomalies(26). In Afghanistan not every delivery is taken place in hospital and those born in home or private clinics are not reported or registered(3), therefore a hospital based study can not reflect the population prevalence of congenital anomalies.

Report of the March of Dimes (2006) shows that the prevalence of congenital anomalies in Afghanistan is 74.9/1000live birth(17), this is also based on modelled estimation which may underestimate the absolute prevalence of congenital anomalies in Afghanistan.

According to estimations by the WHO, global health observatory(GHO) data, each year, between 4381-5000 under-five children die due to congenital anomalies in Afghanistan (27). Figure 6 below, shows the number of deaths, due to congenital anomalies from 2010 till 2105. I contacted personally with in-charge of health information system in health ministry of Afghanistan and he explained these estimations are based on WHO modelling system, and no surveillance system and data about congenital anomalies exist in MoPH.

Figure (6): trends in deaths due to congenital anomalies in Afghanistan from 2000-2015(27)

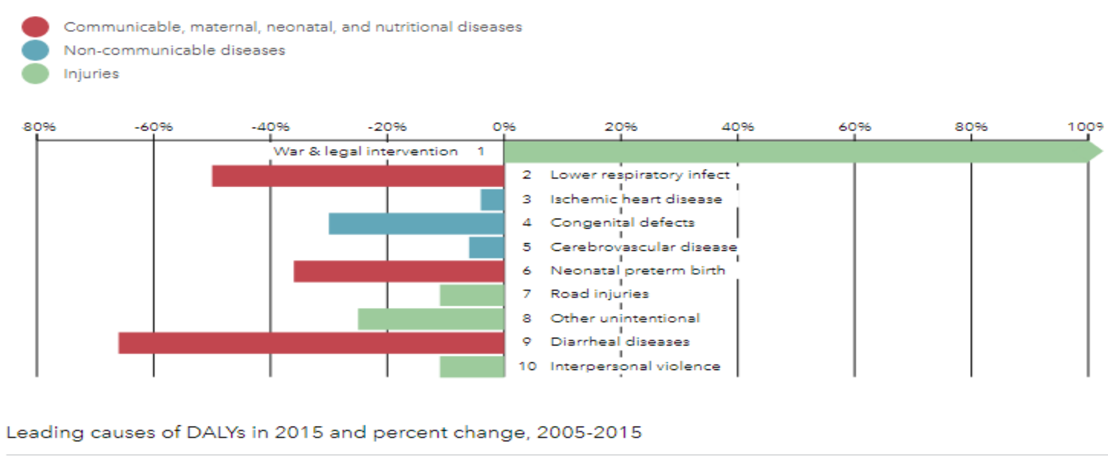


Source: adopted from WHO/GHO (www.who.int/gho/data/node.main.ghe100.2015-by-country)

According to WHO/GHO data, slow progress is seen in reduction of deaths due to congenital anomalies in the last 15 years in Afghanistan (4.7% in 2000 and 4.6% in 2015) (27). This slow progress could be either due to same modelling and estimation method or due to lack of attention to congenital anomalies in the last 15 years.

Besides among the main causes of mortality, congenital anomalies are the 4^{th} cause of DALYs after war, LRI and ischemic heart disease(IHD) in 2015 in Afghanistan(19) figure 7. In 2015 congenital anomalies caused total of 961,864 DALYs in all ages the rate was 2,949.82/100,000 population, three top congenital anomalies were CHD, NTDS, and Down syndrome causing most DALYs (28). These values do not include heamoglobinopathies which also caused 160,682 DALYs separately in 2015 (28).

Figure (7): main causes of DALYs in Afghanistan



Source: institute of health metric and evaluation; available from www.healthdata.org/afghanistan

Although data about congenital anomalies are limited and based on WHO estimations, we may assume that congenital anomalies are among the main causes of under-five mortality and DALYs in Afghanistan.

3.2. Justification

The Sustainable development goal(SDGs) 3.2 aims to reduce under-five mortality to 25/1000 live births/year and newborn mortality to12/1000 live births/year by 2030 (29). Achieving these targets without addressing congenital anomalies is not possible because congenital anomalies contribute to 10% of these deaths worldwide (18).

Congenital anomalies are among the main causes of neonatal and under-five mortality in Afghanistan, Which affects not only the quality of life of the child but also place significant financial and social burden on families and society due to chronic illness and disability. The risk of giving birth to a child, with a congenital anomaly in Afghanistan, is high due to existence of risk factors associated with congenital anomalies compared to other countries.

In addition in Afghanistan, congenital anomalies are under the shadow of other causes of child mortality and morbidities such as respiratory infections, diarrheal disease, measles, low birth weight, under nutrition and therefore studies and programs about congenital anomalies are lacking which have led to the lack of awareness among policy makers about congenital anomalies.

Secondly, most policy makers think that care and prevention of congenital anomalies require expensive diagnostic, surgical and curative interventions that are beyond the health budget of LMICs and fear that focus on congenital anomalies will withdraw resources from other priority programs.

This literature review is conducted to find the burden, main determinants of congenital anomalies and analyze current available policy and intervention for congenital anomalies to provide evidence-informed information for policy makers.

3.3. Overall objective

The main objective of this study is to explore determinants of congenital anomalies in Afghanistan and review current policies in order to make recommendations for policy makers in Afghanistan

3.3.1. Specific Objectives

- To explore the magnitude, trends and determinants of congenital anomalies in the context of Afghanistan
- To review evidence-based policies and strategies that can be employed to address congenital anomalies in resource constrained contexts
- To review current health policies and strategies in Afghanistan related to congenital anomalies
- To provide recommendations for policy and strategy makers about the control of congenital anomalies in Afghanistan

3.4. Methodology

3.4.1. Study design: In order to meet the objectives of this study, a literature review was conducted including journal articles, WHO, world bank websites, MoPH publications and reports, mainly focuses on congenital anomalies in Afghanistan as well as other contexts.

3.4.2. Search strategy: Literature review of published and unpublished articles, related to congenital anomalies, were searched through databases (VU Amsterdam, and PubMed), search engines (Google and Google Scholar). A desk review of grey literature, from relevant institutional websites of MoPH, WHO, UNICEF, World Bank, central statistic organization (CSO) was used. Most articles reviewed in the study, were written in the English language and published after 2000, but some articles are published before 2000 were also included. For some information private contact was also used

3.5. Keywords: Congenital anomalies, Afghanistan, birth defects, congenital malformation, risk factors, genetic disorders cost effective interventions, see annex (1).

3.6. Strength and Limitations: The strength of this study is, it is the first detail study about determinants of congenital anomalies in Afghanistan. The main limitations of this study were lack of absolute and precise data from Afghanistan; most of the data was based on modeling and estimation. The classification of congenital anomalies was confusing; haemoglobinopathies a type of congenital anomaly was classified as a separate category and not include in congenital anomalies by WHO, while March of Dimes has it is own classification system

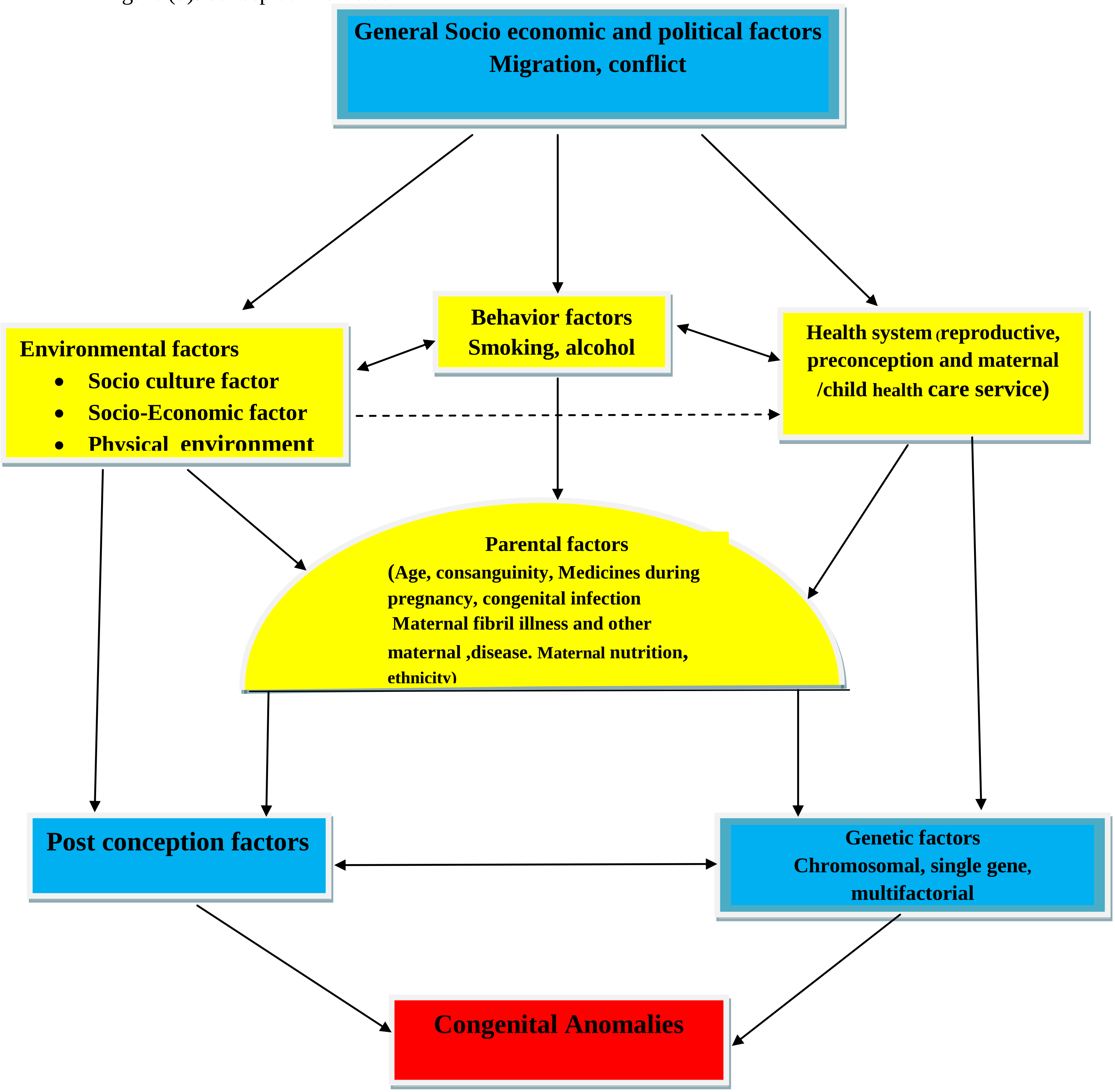
3.7. Conceptual framework

No specific conceptual framework was found to cover all determinants of congenital anomalies, two conceptual framework one from Bangladesh and other from North Carolina were missing some of the main determinants (30)(31).

For a broad picture of determinants of congenital anomalies and how these determinants are influencing each other, the following model was developed by adapting Dahlgren and Whitehead's ecological model for social determinants of health. Dahlgren model shows the relationship between disease, individual and environment. These factors are modifiable and can influence the occurrence of disease in either direction. see annex 4.

The layer of determinants influencing the health and how it finally leads to congenital anomalies, is described in this adapted model and shows links between determinants (The environment surrounding the individual and congenital anomalies). The model shows that the general socio economic and political situation (first outer most layer) influences the behaviour, environmental and health system factors and these factors, besides influencing each other, have direct effects on the parental factors and genetic factors.

Figure (8): conceptual framework



Conceptual framework: adapted from: Dahlgren and Whitehead ecological model. 1991 . See annex 4

Chapter 4

Findings and discussion

This chapter will discuss main findings about determinants of congenital anomalies based on the conceptual framework of figure 8. Parental, behaviour, environmental determinants will be discussed first, because theses determinants are closely linked and influence each other as well as genetic factors. Magnitude and trend of congenital anomalies have been discussed in chapter three.

4.1. Parental Factors

This section will discuss the association of consanguinity, maternal age, paternal age, maternal fibril illness, maternal diabetes, medicines during pregnancy, parents exposure to different chemicals and congenital anomalies.

4.1.1. Consanguinity: Currently 1.1 billion people are living in countries with a high prevalence of consanguineous marriages and 1 in every 3 marriages are between cousins. Consanguineous marriages are common culture in most eastern Mediterranean, North Africa, Indian subcontinent and South America countries(32). Consanguinity is defined as a relationship by marriage between two persons related as second cousin or closer (inbreeding coefficient≥0.0156)(33). Consanguinity doubles the risk of congenital anomalies(16)(17).

A study in United Kingdom (UK) showed that 37% of Pakistani couples were first cousins, the risk of congenital anomalies was double in children born to Pakistani parents (RR 2.19 CI 1.67-2.85). After been controlled for other confounders, 31% of congenital anomalies could be attributed to first cousin marriages, while the relative risk beyond a first cousin marriage was 1.87(34). A study on Pakistani immigrants in Norway, also showed the strong association of first cousin marriages and congenital anomalies in Pakistani parents (RR2.15) and 28% of congenital anomalies were attributed to consanguinity marriages (35).

Consistency was found in studies from several developing and developed countries, specially among Muslim communities between congenital anomalies and consanguineous marriages (36-44). Social preferences, such as strengthen and maintenance of family structure and property, avoidance of financial hardship such as dowry, family tradition and cultural, which see outside marriages as an insult to family, are factors behind a high prevalence of consanguinity in most Muslim countries (33)(44). According to a study in four generations of an Afghan family, 52.3% of children born from consanguineous parents, were suffering from congenital anomalies (45), sample size of this study was too small and was not controlled for other confounders and could not be generalized. In another study in 1983 though, significant association (P>0.05) was found between consanguinity and congenital anomalies in Afghanistan (26), but the study had certain limitations and could be biased due to the presence of other risk factors that have not controlled. Confidence interval was not report in this study.

Cousin marriage is common in Afghanistan, 40-49% of marriages are consanguineous and 25-30% of these marriages are between first cousins (33). A study in several provinces of Afghanistan, shows between 38.2-51.2% marriages are consanguine among them 27.8% were first cousin marriages(46). If we assume consanguinity poses a doubles risk of congenital anomalies(RR 2)and the 49% prevalence of consanguineous marriage in Afghanistan, then the population attributable fraction(PAF)of consanguinity would be 32.9% to congenital anomalies. We may safely conclude that consanguinity is an important determinant of congenital anomalies in Afghanistan.

These are rough estimations, which are based on studies from other countries and therefore it does not reflect the real situation in the context of Afghanistan, but it shows that consanguinity contributes to a majority of genetic and non genetic congenital anomalies in every country, and in Afghanistan with high prevalence of consanguinity it will even contribute to a much higher than other countries.

4.1.2.Maternal age: Risk of specific chromosomal and non-chromosomal congenital anomalies is increasing with the maternal age (16)(17) see annex 6. For example, the risk of Down syndrome at the age of 25 is 1/1340 live births (0,8/1000), which increases to 1/353 (3/1000) live births at the age of 35 and above (47). Several other studies also show the relationship between advanced maternal age and non-chromosomal congenital anomalies of the renal, genitor-urinary tract, hip and feet (48-53).

Some studies also found the association between teenage pregnancies and the risk of congenital anomalies(54-57), but associations found in these studies were not significant and on the other hand the age of the mother was not controlled for other risk factors.

In the last 13 years as a paediatrician I have seen a high incidence of Down syndrome and congenital heart disease (CHD) in advanced age pregnancies (observation). 1.08 million children are born each year in Afghanistan, assuming that the prevalence of Down syndrome is 2-3/1000 live birth in LMICs (18), then an average 2600 children may born per year with Down syndrome alone in Afghanistan.

Study in the UK (RR 1.83) shows relatively high risk of congenital anomalies in advance maternal age (≥35) (34). If we calculate the PAF for Afghanistan, where 30% of women are age 35-49 years (1), and assume a relative risk of congenital anomalies, due to the advanced maternal age is 1.83, then approximately 20% of congenital anomalies could be attributed to advanced maternal age. It is just estimation and could not be generalized to the population and well designed studies are necessary to show the association.

4.1.3. Paternal age: Some studies focused on paternal age and risk of congenital anomalies such as Klinefelter syndrome, Patau syndrome, Edwards' syndrome, Down syndrome, limb anomalies, and congenital heart defects, but the findings in these studies were not conclusive and statistically not significant, though the odds ratio was above one, but the confidence interval was wide, on the other hand the paternal age was not controlled for other factors and therefore more precise and advanced studies are needed before reaching any result (51)(58-61).

4.1.4. Exposure to certain medicines during pregnancy: Certain teratogenic medications are identified by the United States Food and Drug Administration (FDA) as class D and X(61), they should be used with caution during pregnancy, some of these medicines are listed in annex 7.

Use of these medicines is a big concern in most LMICs, due to the lack of regulation, awareness, and easy access to medicines (17). Though some studies proved the teratogenic effects of some drugs, such as anti epileptic drugs, lithium, thalidomide and misoprostal, but studies about the association of anti pyretic and analgesics, such as aspirin, Ibuprofen and prednisone (commonly used in Afghanistan) are not conclusive, statistically not significant and could be biased due to the presence of other factors (62-69).

Studies about, narcotic drugs, chemotherapy agents, benzodiazepine, some antibiotics, marijuana, Angiotensin converting enzyme inhibitor(ACE), fluconazole(anti fungal), zidovudine (antiviral), vitamin-A and many more medicines are showing contradictory results (46).

No study from Afghanistan is available about the irrational use of drugs during pregnancy, but using medicines without prescription is a common practice in this country (observation).

The pharmaceutical sector of Afghanistan is the least developed and unregulated sector. Most of the pharmacies are not registered or run by unprofessional people, almost all medicines are available in vendors and grocery stores to everyone (70). Free availability of medicines, lack of knowledge about medicines, illiteracy, and poverty interlinked to each other may increase the use of irrational drug use during pregnancy and potentially increase the risk of congenital anomalies.

4.1.5. Congenital infections

Congenital infections means that the foetus acquired it during pregnancy, these infections are usually asymptomatic in the mother but it causes severe foetal diseases, the most common infections are called TORCH(toxoplasmosis, rubella virus, cytomegalovirus, herpes simplex, syphilis and others) (17).

4.1.5.1. Congenital Rubella Syndrome (CRS): If a mother contracts the rubella virus in the first trimester of pregnancy, the risk of congenital anomalies is 90% and the risk decreases if rubella is contracted after the first trimester (17)(71)(72). Congenital rubella leads to severe congenital defects of heart, eyes, brain, hearing loss and other systems called CRS (73). A congenital anomaly, due to the rubella virus, was first reported in 1941(74). Although the incidence of congenital rubella syndrome has markedly declined in the developed world, after introduction of vaccines, it is still high in LMICs (17). Afghanistan is among the countries where the rubella vaccine is not introduced till now.

From January 2010 through June 2016, 405 cases of lab-confirmed rubella were reported by the ministry of health to the WHO in Afghanistan, these cases were diagnosed during measles outbreaks(private contact).

Assuming that the incidence of congenital rubella syndrome (CRS) in Afghanistan is similar to the Eastern Mediterranean region (77.4/100,000 live birth) as a whole(75), given the annual birth cohort is approximately 1.08 million in Afghanistan (3), 835 CRS cases/year are estimated to be born in Afghanistan.

4.1.5.2. Syphilis: Syphilis is another common infection and annually 11 million new cases are reported (17). If untreated, syphilis causes stillbirth, congenital anomalies and low birth weight in 52% of pregnant women (76)(77). Increasing coverage of syphilis screening and treatment is a cost effective intervention that could prevent 50% of neonatal deaths due to congenital syphilis (17)(76)(77). According to the WHO, 0.6% of pregnant women attending ANC clinics, were positive for syphilis (78), but no data is available about the outcome of these pregnancies and congenital syphilis. As access to ANC clinics is low, due to multiple factors in Afghanistan, the prevalence may change, if all pregnant women who attend ANC clinics and are tested for syphilis. This also shows the importance of ANC visits in the prevention of congenital anomalies.

4.1.5.3. Cytomegalo virus(CMV): Up to 0.15-2% of all pregnant women has a primary CMV worldwide (72). Risk of foetal infection in these women is 30-40%. The estimated prevalence of a new born infected with CMV, is 4/10,000 birth in LMICs (17). Assuming this prevalence and birth cohort of 1.08 million in Afghanistan, 432 newborns are infected with CMV. Currently there is no intervention to prevent CMV.

4.1.5.4. HIV & ZIKA Virus: In recent years Zika and HIV viruses emerged as a new threat to the developing foetus, in Brazil from 270 confirmed cases of microcephaly, 6 cases showed the evidence of the Zika virus (16). Although transmission of HIV-1 infection to children does not cause any structural congenital anomaly, it increases the risk of dilated cardiomyopathy (79)(80).

In Afghanistan, no case of Zika is reported and the prevalence of HIV is very low (3), therefore its contribution to congenital anomalies is negligible.

4.1.6. Febrile illness during pregnancy: Maternal febrile illness, during the first trimester, may increase the risk of congenital anomalies. A recent systematic review, meta-analysis and several other studies, show the risk of NTDs, congenital heart anomalies, and oral clefts are 1.5-3 fold higher in offspring, of mothers suffering from fever, during the first trimester of pregnancy (34) (61)(81-83). Most studies have been unable to distinguish between independent and joint effects associated with maternal fever, maternal infection and the use of certain medications for febrile illness and increase risk of congenital anomalies (61). More studies are necessary to see the independent risk of fever and its association with congenital anomalies.

4.1.7. Maternal obesity and insulin dependent diabetes: Studies have shown a clear link between glycemic control during pregnancy in diabetic mothers and congenital anomalies (58)(61)(84)(85). A prospective study of obese and diabetic women, showed pregnant women with gestational diabetes without obesity had increased risk for musculoskeletal anomalies, but women with both obesity and diabetes were 3 times more likely to have congenital anomalies compared to normal women (86). A meta-analysis of 14 cohort studies showed mothers who has a preconception diabetic treatment and glycemic control has 2.5% of their offspring with congenital anomalies compared to 6.5% in women without preconception diabetic control (84). According to the WHO 8.8% of women in Afghanistan are diabetic while 8.3% of women of reproductive age are obese and 29.0% are overweight (13).

No data is available about the type and prevalence of diabetes in women of a reproductive age and its association with congenital anomalies in Afghanistan.

Regular treatment and the controlling of diabetic patients is a challenge in LMICs, including Afghanistan, due to the cost and insufficient health services, this constitutes potentially increased risk of congenital anomalies and other complications in the offspring of a diabetic mothers (17).

4.1.8. Nutritional status of mother: Maternal malnutrition and lack of certain micronutrients, increases the risks of congenital anomalies, particularly neural tube defects, due to the insufficient folic acid supplementation during pregnancy and mental retardation due to iodine deficiency. Congenital anomalies, such as oral cleft, congenital heart diseases, urinary tract anomalies and limb defects are also sensitive to folic acid deficiency(17)(49)(87-90).

4.1.8.1. Folic acid: Studies show that supplementation of 0.2 mg folic acid/day to pregnant women before and during the early stage of pregnancy, reduces NTDs by 20%, while supplementation of 0.4mg/day and 5mg/day will reduce NTDs by 57% and 85% respectively (88). A reduction of 80% in NTDs was seen in a cohort study in China, after supplementation of folic acid (91). The protective effect of folic acid, ideally starting before pregnancy and continue during pregnancy, is proved in several randomized control trials against NTDs (92)(93).

Malnutrition and micronutrient deficiency is common in Afghanistan, 9.2% of women of reproductive age are malnourished, 40% have anaemia, 24% iron deficiency, 95.5% vitamin-D deficiency and 40.7% have iodine deficiency (14).

This high prevalence of malnutrition and micronutrient deficiency, lack of folic acid supplementation and iodine deficiency could be important maternal determinants for congenital anomalies in Afghanistan. Assuming 21.9 per 10,000 births prevalence of NTDs in Eastern Mediterranean region (94), each year 2292 children will be born with NTDs in Afghanistan, most of these cases could be prevented through folic acid supplementation.

Folic acid is provided through ANC services to all pregnant women in Afghanistan, but ANC services are underused, 59% of pregnant women have an ANC visit during pregnancy but only 18% of women completed 4 ANC visits and 38% did not attend the ANC. 42% of pregnant women received iron and only 13.8 folic acid (3)(14). Educated women, women from urban areas and wealthy families were more seeking the ANC, compared to uneducated and women from rural areas (3). Low attendance of the ANC services by pregnant women deprives them of measures which could be taken during these visits, to prevent congenital anomalies such as folic acid, which is advised to every pregnant women regardless of their folic acid level.

4.1.8.2. Iodine deficiency: Iodine deficiency is a global health problem and one of the preventable causes of brain damage, intellectual, motor and auditory disabilities (Iodine deficiency disorders) in children (17). Severe iodine deficiency during pregnancy, leads to foetal hypothyroidism and mental retardation (89)(90)(95). Iodine deficiency disorders are common in inland, dry and mountainous regions (17). Afghanistan is an example of such regions, where 80% of land is covered by mountains and deserts (2).

Several studies show iodine supplementation, to women in endemic areas, improves the neurological and developmental outcomes of children born to these women(90)(96). A Cochrane review concluded that iodized salt is a cost effective intervention, to prevent iodine deficiency and its disorders, but the effects on mental and physical development of a child is not conclusive (97). A review of 5 studies about iodized cooking oil showed 73% reduction in cretinism and 10-20% increase in the developmental score (98).

40.8% of women of reproductive age and 30% of children have iodine deficiency in Afghanistan (14), but the level of the iodine deficiency (mild, moderate or severe) and consequences related to iodine deficiency are not reported. Although salt iodizing is mandatory in Afghanistan and 78.5% household use iodized salt (14). Still iodine deficiency is common, which may be due to poor quality control of the salt produced in Afghanistan or imported from other countries. Research is required to find out the causes of iodine deficiency in Afghanistan and its impact on child and maternal health.

4.2. Behaviour factors

Maternal behaviour such as alcohol consumption and smoking during pregnancy increases the risk of foetal congenital anomalies (16)(17).

4.2.1. Smoking: Studies show an increased risk for oral clefts and congenital heart anomalies with maternal smoking (34)(99-102). The results of a recent systematic review, which included 173,687 children with different congenital anomalies and 11.7 million control children, show a positive association between maternal smoking and different congenital anomalies such as congenital heart defect, limb reduction, musculoskeletal anomalies, orofacial defect, clubfoot, eye defects, anal atresia and gastroschisis (103). Smoking is prohibited by cultural and religious norms in Afghanistan and prevalence is extremely low among women (3), therefore it's attribution to congenital anomalies is not important in context of Afghanistan.

4.2.2. Alcohol consumption: Worldwide 9.8% of pregnant women use alcohol during pregnancy. One in every 67 of these women give birth to a child with foetal alcohol syndrome(FAS) and 119,000 children are born with FAS each year worldwide(104). FAS includes a wide range of congenital disorders such as hearing, vision, mental and heart problems. Several studies showed an association of alcohol consumption during pregnancy and congenital heart anomalies (101)(105-107).

The contribution of alcohol to congenital anomalies is not an important risk factor in the context of Afghanistan, because the use of alcohol is prohibited by cultural, religious norms and government.

4.3. Environmental Factors

4.3.1.Socio-economical condition(SEC): The **s**ocio economic condition, at household level, is influenced by general socio economic conditions at country level and both influence other determinants of congenital anomalies, see figure 8.

According to the WHO, a low socioeconomic status is an indirect determinant for congenital anomalies. The lack of insufficient foods during pregnancy, the lack of access to health services, infections and exposure to various teratogenic substances can be related to low socioeconomic condition (16). It is likely that the low educational level increased exposure to teratogens, due to the poor level of knowledge about these substances and its risks (108).Several studies across the globe show the effect of the socio-economic condition and the risk of congenital anomalies (109-112).

A meta-analysis, including 31 case-control and 2 cohort studies, concluded that the level of maternal education(pooled RR 1,11 CI 1.03-1.21), family income (pooled RR 1,05 CI 1.01-1.24) and maternal occupation (pooled RR 1.51 CI 1.02 -2.34) were risk factors for congenital heart anomalies(113). These studies did not show the independent effect of SEC and congenital anomalies and could be biased due to the presence of other confounders.

Afghanistan has poor SEC indicators(3), there is a positive relation between the education level, family income and the place of residency and some effective interventions (see chapter 5) that play an important role in the control of congenital anomalies. For example, educated women, women living in urban areas are more likely to attend the ANC, have less children, use nutritious food and iodine compared to uneducated women and women from rural areas(3). The same relation is seen with the level of income (3).

4.3.2. Socio cultural factors: Afghanistan has a traditional and religious society and 99.8% of the population is Muslim (1). As discussed in section 4.1 of this chapter social, economic and cultural preferences are behind high prevalence of consanguinity, which is a risk factor for congenital anomalies in most Muslim countries (33)(44).

Due to cultural and social norms and values 89% of the women have one or more problems in access to the health services in Afghanistan and only 5% take a decision alone about their health care (3). 70% of the women are not allowed to go alone, 51% need to get permission and 67% needs to get money from other members of the family (3). Gender based violence such as wife beating, control on income and decision making power are justified, culturally to men in Afghanistan (3). All these cultural norms and values lead to depriving women from timely seeking health care which, affects their nutrition status and potentially increases risks of congenital anomalies, as discussed in previous sections.

4.3.3. Physical environment:

Maternal exposure to certain pesticides, insecticides, solvents, chemicals and radiation during pregnancy either due to the working environment (certain occupations) or living near to waste and industrial sites, may increase the risk of congenital anomalies, the risk is much higher when the mother has other risk factors simultaneously (16).

4.3.3.1. Occupational Exposure: In many countries 50% of the workforce are women and the majority of them in the reproductive age, women occupation may expose them to various substances and potential risks for congenital anomalies (114).

Several studies, published from 1992 to 2009, have shown an association between congenital anomalies and different maternal occupations(115). A recent analysis of data from a multicenter population-based case control study also show this association (OR range 1.72-3.99) (116).

Studies on a laboratory technicians, hairdressers, textile dye workers and cleaners, show a potential risk of congenital anomalies in women working in these fields (117). But most of these studies were not adjusted for other confounders and do not show the duration of exposure to these substances and the dose relation of different chemicals during pregnancy and could be biased. Occupational exposure may increase the risk of congenital anomalies in the presence of other risk factors. But its role as an independent risk factor needs further research.

Women participation in the labour market is very low in Afghanistan, only 13% of current married women are employed and the majority of them in managerial positions (3), which indicates that the risk of occupational exposure, in married women, to teratogens is unlikely in Afghanistan.

Few studies are available on paternal exposure and risk of congenital anomalies of the heart but still results do not show a significant association and are not conclusive (61).

4.3.3.2. Exposure to ionizing radiation: Teratogenic effects of ionizing radiation depends on dose and gestational age of the foetus, see annex 8. Health workers, working as radiographer, have an increased risk of exposure to radiation, but diagnostic or occupational radiation exposure, including those of the lower abdomen, will not expose the foetus to levels that cause health effects (118)(1119).

The possible harmful effects of X-rays are at doses above 0.05 Gray (Gy) equals to 5rads, but the real teratogenic effects, which may lead to congenital malformation, are seen at the dose of 0.10-0.20 Gy or 10-20 rads (119).

Studies reported by Shi L (2001) show contradictory results and most of these studies are not conclusive and there was even no association found between radiation and congenital anomalies in a study (114). But the benefits of any procedure with radiation should be justified and informed decision should be taken before advising X-rays to pregnant women.

As mentioned before, the majority of women in Afghanistan are jobless and their exposure to radiation is unlikely, in my personnel experience, I have never seen women working as a radiographer and generally X-rays are not advised during pregnancy by physicians.

4.3.3.3. Agriculture occupation and exposure to pesticides and insecticides: An increased risk of congenital anomalies was reported in women working in agriculture sectors in several studies and consistency is seen in the results from most developed countries (120-125). Most of these studies are not adjusted for other confounders such as maternal age, behaviour factors, congenital infections, duration of exposure and dose of substances, and the chance of a recall bias about exposure is also high in these studies, therefore an absolute contribution of these substances to congenital anomalies is not clear. More precise, research is necessary to study the effects of substances used in the agriculture sector and congenital anomalies.

Since Afghanistan's economy mostly depends on agriculture (40% of GDP belong to this sector) and 70% of the rural population are engaged in agricultural fields, where 50% of the agricultural workforce are women (2)(126).

The possibility of pregnant women to be exposed to such chemicals is high in rural areas, which may be interlinked to other factors discussed before, will increase the chance of congenital anomalies.

4.3.3.4. Living near to hazardous and waste sites: Air pollution , contamination of water and soil due to chemicals released from industrial and other waste disposals, may affect the human health and may lead to negative pregnancy outcomes of low birth weight and congenital anomalies (16)(127). Though some studies, in European and other countries, found a positive association between living near to these places (128-130). Other studies did not find any evidence and association between living near to hazardous industrial sites and an increasing risk of congenital anomalies (131). A recent systematic review, analyzing the evidence found in several studies, shows positive association between, living near to these sites and congenital anomalies, but the study also found a certain limitation in current knowledge to reach a final conclusion and well designed studies were recommended about this association (132).

Afghanistan is not an industrialized country, there are a few factories which are located far from residential places, on the other hand, 75% of the population is living in rural areas and busy with agriculture (3), therefore a chance of living in such places is rare and the risk of congenital anomalies is extremely low and negligible in Afghanistan from chemical release from these sites.

4.4. National level of health care

The health system of the country and the available health services have a direct effect on the overall prevalence and burden of congenital anomalies (17). Availability of health services, for congenital anomalies, extends the life expectancy of patients and the years of productivity, and decreases the prevalence through basic reproductive health care and preventive measures (17). For example women who attends more ANC have less chance to have children with congenital anomalies (133).

The health system in Afghanistan is still lagging behind in many aspects, lack of human resource, poor infrastructure, lack of equipment and dependency on foreign donors are main challenges faced by the MoPH in Afghanistan (8)(9). No explicit service is available for diagnosis and treatment of congenital anomalies and there are insufficient interventions in current reproductive and child care programs to address congenital anomalies (10), For current policies, see section 2&2.1.

Although access to primary health centres improved in the last 15 years (9), these centres do not offer services for diagnosis and treatment of congenital anomalies. Few public and private hospitals in the capital city, Kabul provide surgery for some congenital anomalies, but access to these services are time consuming and indirect cost is too high for patients coming from remote areas (observation). ANC services and family planning, which play important role in prevention of congenital anomalies, are underused due to multiple factors (3).

Services for prenatal diagnosis, screening and genetic counselling are not available, no education program, to increase awareness about congenital anomalies and it's risk factors, is in place. The rubella vaccine are not introduced until now and there is insufficient trained professionals in the field of congenital anomalies.

4.5. Genetic factors

Abnormalities of genes and chromosomes exist before conception and include single gene defects, chromosomal disorders and multifactorial disorders(interaction between genetic and environmental disorders), these anomalies can be inherited from parents or may be due to mutations in single pregnancy(17).

Chromosomal anomalies account for 6% and single gene defects account for 7.5% of all congenital anomalies in industrialized countries and each year 7.9 million children (6% of total births worldwide) are born with genetic or partially genetic congenital anomalies (17).

Evidence shows that environmental factors, such as radiation, ethnicity, race, parents' age, consanguinity, exposure to certain substances and some medicines increase the risk of genetic mutation and genetic anomalies. For example sickle cell disease is common in African-Americans and thalassemia is common in Mediterranean region (16).

No specific data is available to show the prevalence of genetic disorders in Afghanistan, but a high prevalence of consanguinity, high fertility rate, advance maternal age, poor socioeconomic conditions and lack of genetic screening are factors that increase the risk of genetic anomalies in Afghanistan. Assuming a high fertility rate in Afghanistan and 1.08 million births per year 64,000 children may be born with genetic or partially genetic anomalies, but due to lack of diagnostic centres, professional staff and lack of an explicit policy for congenital anomalies, most of these children remain undiagnosed.

4.6. General Socio-economic and political situation

Afghanistan is a low income country with an unstable economy and political situation and mostly depending on foreign aid (8)(12). On the other hand due to the ongoing conflict, much focus is given to other sectors compared to the health sector, 7.1% of general government expenditure is allocated to the health and the rest either by donors (20.8%) or in the form out of pocket money by people (73.3%) (134).

The political and economical situation, at country level, directly affects family income, access to education, health services, nutritional status of the mother and other socio cultural and socio economic conditions, and as discussed before, all these factors, either individually or together, increase the risk of congenital anomalies.

Other determinants influenced by the political and economic situation are discussed before, this section will discuss adverse effects of the migration and armed conflict and different types of weapons used for 38 years in Afghanistan.

4.6.1. Weapons use during war: According to reports, depleted uranium and chemical weapons, were used during the war in Afghanistan by the United States and the Russian army(135)(136). Substances used in these weapons have proven to have negative effects on the development of the foetus(137-139).

A case-control study in 2005 from Iran shows an increased risk of congenital anomalies in offspring of parents exposed to mustard and sulphur during the 1987 war (OR 3.54 CI 1.58-7.93) (140).

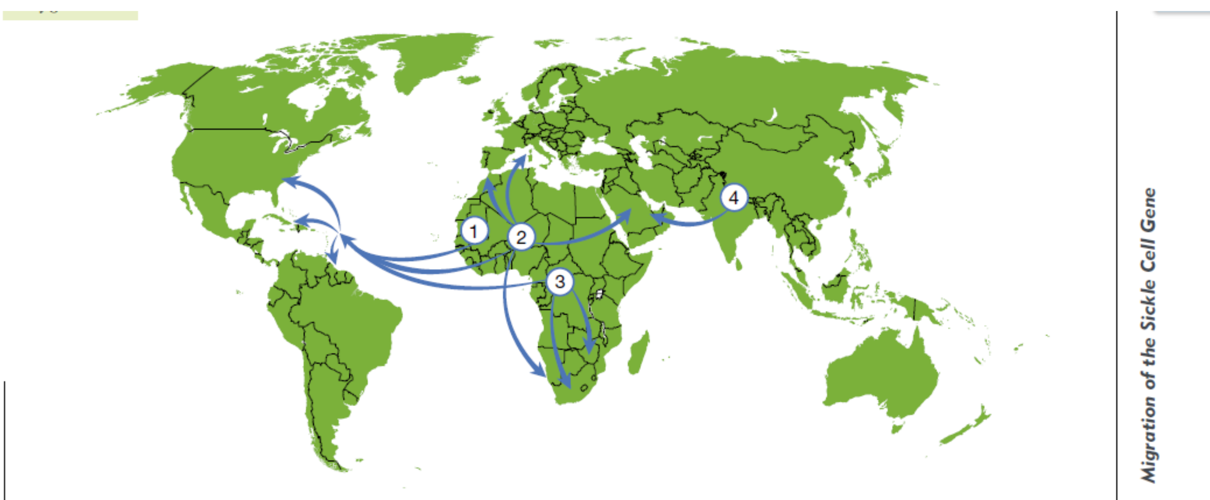
In Iraq an increasing risk of congenital anomalies was seen in Basrah and the Fallujah region after the 1991 gulf war and it was thought that this could be due to the depleted uranium used during the war (135)(141).

Meta analysis of studies from Vietnam, where Agent Orange was used by the US, shows the relative risk of congenital anomalies is 1.95 times higher in infants of parents exposed to this substance (142)(143).

Till this date, no study is conducted on the effects of the different weapons used in Afghanistan, but evidence from other countries show long-term health consequences of weapons used in conflicts areas, which could also be considered in Afghanistan where the offspring of the fourth generation are growing up in war.

4.6.2. Migration: Immigrants with carrier state of genetic disorders can introduce the affected genes to the new context or they may get certain genes from hosting people through marriages. Genetic migration of haemoglobinopathies to Europe and America, Huntington disease to Venezuela, spinocerebellar atrophy in Cuba, sickle anaemia in South Africa by immigration, are examples of such diseases (17).

Figure(9): shows transfer of sickle cell gene through migration



The mutations that cause sickle cell anemia had four independent origins. Three mutations arose in west and central Africa. The African mutations traveled with the slave trade to the Americas. The second mutation spread by trans-Saharan caravans to North Africa and the Mediterranean region and countries in southern Europe. The third mutation, originating in equatorial central Africa, spread east and south with inter-African population migration as far as the northern borders of South Africa. The fourth mutation, originating in the Indian sub-continent, spread through the Middle East by traders. Mutations two and three have been introduced into South Africa in the last decade by people from west and central Africa migrating for political and economic reasons. SOURCE: Stuart and Nagel, 2004; Krause A, University of the Witwatersrand, personal communication, 2004.

Source: March of Dimes global report on birth defects (2006)

There have been huge immigration flows in the last 38 years from Afghanistan to Pakistan, Iran and other countries and two million Afghans are still living as immigrants, the majority of them in Iran and Pakistan (144). Marriages are taken place between Afghan immigrants and the local population in these countries that potentially increases the transfer of affected genes to each other and if reproduction continues, the affected genes will be transferred to the next generation.

On the other hand these marriages are not consanguine and the chance of other congenital anomalies is low in these couples if they are not carriers of such affected genes.

Besides the transferring of genetic disorders, migration affects socio economic conditions of families, access to health service, nutritional condition and exposing people to various environmental hazards and risky behaviours which may increase the risk of congenital anomalies.

4.7. Summery

To summarize, congenital anomalies are among the main causes of infant and neonatal mortality in Afghanistan, but precise data about the burden of congenital anomalies and its determinants are not available and most of the data are based on modeling and estimation. Based on available data and a rough estimation from other countries, consanguinity has a strong social and cultural roots in Afghanistan and is one of the main determinants for congenital anomalies and potentially contributes to 32.9% congenital anomalies.

Advanced maternal age, micronutrient deficiency, and congenital infections (rubella, syphilis) are other main risk factors for congenital anomalies after consanguinity. While low socio economic condition and insufficient health services indirectly influence other determinants.

These results are based on studies from other countries and cannot be generalized, and context based research is necessary to find determinants of congenital anomalies in Afghanistan.

Most of the studies about fever during pregnancy, medicines, paternal age, occupation, living conditions are not conclusive , statistically not significant and further investigations is necessary.

Chapter 5

Strategies and policies to address congenital anomalies

This chapter will discuss the current available best practices for the prevention of congenital anomalies. The types of interventions will be discussed according to the WHO recommendations for care of congenital anomalies and suggested interventions by March of Dimes(16)(17). Three types of preventions are suggested for the control of congenital anomalies, primary prevention (preconception and during pregnancy), secondary prevention(before, during and shortly after delivery) and tertiary prevention (postnatal neonate and child care) (17). The contribution of some interventions in saving lives of children born with congenital anomalies is shown in annex 8 (17).

5.1. Primary prevention:

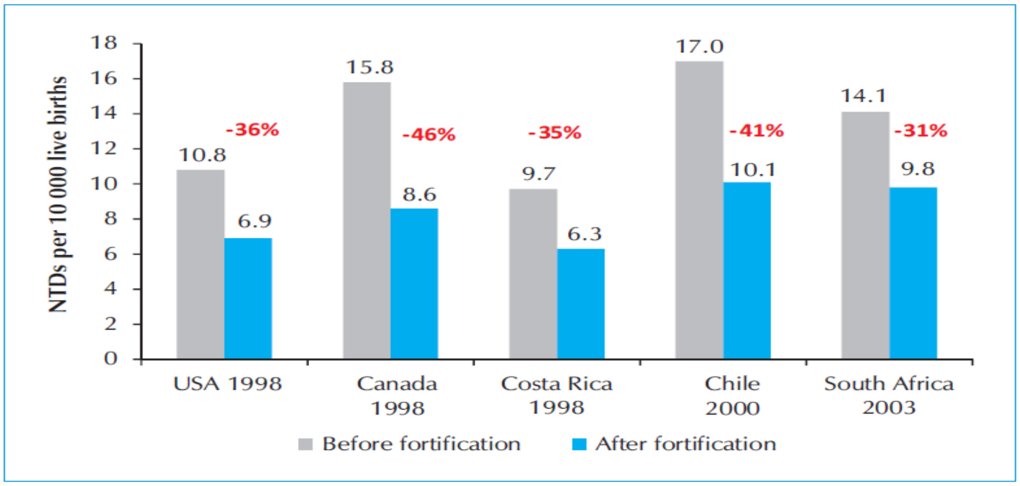
It is the main level of prevention, because it ensures a normal conception and an infant free of congenital anomalies, the main focus of these interventions is on the preconception period to conceive normal and the first 8 weeks of pregnancy (16)(17). Vaccines against rubella, iodine and folic acid supplementation, family planning, control and treatment of diabetes are examples of primary interventions.

5.1.1.Folic acid supplementation: Folate is an essential nutrient, required for the normal cellular function and synthesis, it plays an important role in the normal foetal development. Current literature shows that folic acid is provided either through tablets supplementation or food fortification to pregnant women**.**

A protective effect of folate against the development of neural tube defects (NTDs) and other congenital anomalies such as CHD and oral clefts has been well established by multiple clinical research studies and was discussed in section 4.1.8 of chapter 4.

Chile experience is a good example of wheat flour fortification by folic acid (2.2 mg folic acid/ kg of wheat) starting in 2000. After the introduction of fortified wheat with folic acid, a study comparing the birth prevalence of NTDs, between years before folic acid fortification (1999-2000) and after that (2001-20002), found 40% reduction in the incidence of neural tube defects (145). Several other countries also showed a reduction in NTDs in this region after food fortification(146) figure 10. The food fortification program of the US, Canada, Costa Rica, Argentine, Brazil and South Africa are other success stories(147). A Cochran systematic review, including all RCTs and quasi-RCTs, conclude that folic acid supplementation prevents the first (mother who had no child with NTDs) and second occurrences (mothers who had history of NTDs in previous child) of NTDs, but still there is not enough evidence for its role in reducing risk for other congenital anomalies (148).

Figure (10): effects of food fortification with folic acid on reducing neural tube defects



Source : south east asia regional dtratgeic framework for control of birth defects (2013)

Supplementation of folic acid in the U.S saves US$607 million/year by averting 767 cases of spina bifida each year 149. While in four provinces of South Africa, folic acid supplementation saved South African Rand(ZAR)40.6 million/year which is equal to US$ 580,000 with cost effective ratio of ZAR 30 to 1 and declining NTDs by 30.6% (150). Studies from China, and south American countries also showed positive cost effective ratio of folic acid supplementation (146)(151).

Table (1): Annual averted direct costs and cost saving of folic acid in control of NTDs in the USA(153)

Scenario	Number of live births averted	Total direct cost per birth with spina bifida averted (nearest $100)	Total direct cost averted (nearest $100,000)	Cost savings (reduction in direct costs, nearest $100,000)
Base-case	767	791,900	607.3 million	603.3 million
	767	577,000[a]	442.4 million[a]	438.4 million[a]
Worst case	614	712,700	437.5 million	417.5 million
	614	519,300[a]	318.8 million[a]	298.8 million[a]

[a]Excluding caregiver time costs

Source: Grosse et al / Am J Prev Med 2016;50(5S1):S74–S80

5.1.1.1. Folic acid supplementation in Afghanistan: The MoPH provides folic acid to all pregnant women during antenatal care visits but due to several factors the majority of women does not have access to these services (18% of pregnant women completed 4 and 38% had no ANC visit). Data show that only 13.8% of pregnant women received folic acid supplementation (3)(14). 38.7% women have knowledge about folic acid (14). On the other hand, most of these ANC visits take place after pregnancy is confirmed (3), which is too late to optimize the effects of folic acid and other micronutrients on the developing foetus. This shows that folic acid supplementation through ANC services is not effective enough and it is important to reconsider the current strategies and policies to improve the coverage and time of folic acid supplementation.

5.1.1.2. Food fortification in Afghanistan with folic acid and other micronutrients: The MoPH has developed the first draft of the food fortification regulation and is waiting for its approval from the government, flour and oil fortification is mandatory in this regulation (152). The MoPH and the world food program (WFP) begun wheat flour fortification with folic acid and other micronutrients in 2006 by fortifying flour in local mills, to provide micronutrients to families, Recently, the fortification of edible oil with vitamin A and D has started in local factories in Afghanistan (152).

In the current situation, it is not possible to fortify all wheat flour in the local market and to control the quality of imported wheat flour, on the other hand, most of the population are living in rural areas and depend on their own cultivations (3), therefore wheat fortification strategies will not be feasible to increase folic acid and other micronutrients supplementation in the current situation.

Improving the current ANC services and supplying enough folic acid to the primary health clinic with health promotion is a good option for the MoPH in short and midterm for folic acid supplementation but because not all women will have access to health services, a food fortification program will be considered as a long term strategy to cover all women at household level.

5.1.2. Iodine supplementation: Several studies show that iodine supplementation to women in endemic areas improved the neurological and developmental outcomes of children born to these women (90)(96).

A Cochrane review concludes that iodized salt is a cost effective intervention, to prevent iodine deficiency and its disorders, but the effects on the children mental and physical development is not conclusive (71).

Iodizing of salt is mandatory in Afghanistan and all salt, either produced in local market or imported, should be iodized (3)(152). 78.5% of households used iodized salt, but still 40.8% of women and 30% children under five have iodine deficiency (14), That could be due to a low quality of iodized salt produced in or imported to Afghanistan. Strict quality control and increased awareness, through improving the current health promotion program, is necessary to cover the remaining 22% of households.

5.1.3. Rubella vaccine and prevention of congenital rubella syndrome

Congenital rubella is almost eliminated in high-income countries after the introduction of rubella vaccines and till 2003 more than 193 countries and counties add rubella vaccines in the routine immunization schedule, efficacy of vaccines after a single dose is 95% and provide long-lasting immunity (17)(73).

Two approaches are recommended for an implementation based on health situation analysis of country

1. Vaccination of women of childbearing age to prevent CRS
2. Vaccination of children as well as women of childbearing age for elimination and prevention

Rubella vaccines are not indicated for pregnant women and pregnancy should be avoided till one month after vaccination (73). The rubella vaccine is available either in monovalent form, or combined with measles (MR) or measles and mumps (MMR), the first dose is administered in 9 or 12-15 months and second 15-18 months or 4-6 years based on the country level immunization policy (73).

Until this date, all evidence shows a positive cost–effective ratio of rubella vaccine (73), studies from Denmark, Finland, Norway, USA and the developing countries, such as Guyana, Suriname, Barbados and the Caribbean, show that rubella vaccines are cost effective and have economic benefits (153).

In the Caribbean and Suriname, treatment of 1,500 cases of CRS would cost US$60 million, but the cost of the immunization program will be US$4.5 million to prevent these cases, it means US$37,000 saved per case for the health system through rubella vaccines (153).

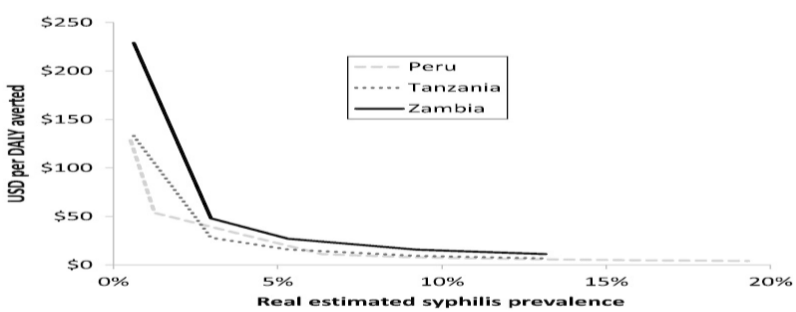
Countries in the path of eliminating measles, should use this opportunity to eliminate rubella by adding this vaccine with measles (MR). But all countries should ensure that routine vaccination coverage is over 80% before introducing the rubella vaccine (73)(153).

5.1.3.1. National immunization program of Afghanistan: According the MoPH policy, all children in Afghanistan should receive routine vaccines before their first birth day, the vaccines included are OPV, DPT, Hepatitis B, Hib, pneumococcal, and measles. All pregnant women are vaccinated against tetanus. Over all the coverage of vaccination is 46% and measles coverage is 60% (3). Rubella is not a reportable disease in Afghanistan and rubella vaccines are not introduced till now. An estimated 835 children are born with CRS in the country, which could be averted through rubella vaccines.

Afghanistan is on the way to eliminate measles and it is good opportunity for the MoPH to advocate for the introduction of rubella vaccines in the national immunization program. A surveillance study of rubella and the congenital rubella syndrome is currently in progress in several provinces with the cooperation of the centre for disease control (CDC) and the MoPH to collect evidence for international donor agencies to introduce rubella vaccines in the national immunization schedule (private contact).

5.1.4. Syphilis screening and treatment: Antenatal syphilis screening and treatment can reduce 50% of neonatal death and stillbirths due to congenital syphilis (17)(76). ANT syphilis screening is the cost effective way to find true cases of syphilis in pregnant women and treat it while in the absence of syphilis screening these cases will be missed (77). A detail cost effectiveness analysis (CEA) of different antenatal syphilis screening approach in Peru, Tanzania and Zambia show cost per 1000 women screened for syphilis by rapid plasma reagen (RPR) test was US$335 in Tanzania and US$2180 in Zambia, while US$2535 in Peru with rapid syphilis test(RST). The analysis shows that the cost of per DALYs averted is related to true prevalence of syphilis (high prevalence low cost and vice versa), figure 11 (77).

Figure(11):The relationship between cost-effectiveness (US $/DALY averted) and syphilis prevalence



Source : Terris et all Int J Gynaecol Obstet. 2015 Jun; 130(1): S73–S80.

Although syphilis screening is part of ANC in Afghanistan, no official data is available about congenital syphilis from MoPH. Data from WHO shows that 0,6% of women attended ANC clinics were positive for syphilis in Afghanistan(78), although it shows low prevalence but still treatment of these women will helpful in reducing congenital syphilis.

As discussed all pregnant women are not coming for ANC clinics or coming too late where offering treatment will be not as effective as in early stage of pregnancy, therefore there is a need to review the current syphilis screening approach and treatment guidelines in Afghanistan find the gaps and improve syphilis screening and treatment.

5.1.5.Avoiding alcohol consumption and smoking during pregnancy: Using alcohol during pregnancy can cause foetal alcohol syndrome, while smoking also increases the risk of congenital anomalies, which can be prevented by avoiding alcohol and smoking. Public campaign in schools, family planning sessions and media is necessary in countries with a high prevalence of smoking and alcohol consumption to increase awareness about the risk of alcohol and smoking during pregnancy (154).

5.1.6.Avoiding teratogenic medicines during pregnancy: Known teratogenic medicines that potentially increase the risk of congenital anomalies, should be used with caution during pregnancy (61). Providing information about these medicines, to women through education campaigns in health facilities during ANC visits and prescribing medicines are simple ways to increase awareness about these medicines**.** When discontinuation of such medicines is not possible than an alternative medicine or method with a lower risk of congenital anomalies is preferred, for example mono therapy instead of poly therapy in case of epilepsy will decrease the risk of congenital anomalies in women with epilepsy (66)(154).

5.1.7.Family Planning: Family planning will reduce the risk of congenital anomalies by reducing the fertility and birth rate. Studies show a low fertility rate, 2-3children/women reduce the birth prevalence of genetic anomalies by 40-50%, and by encouraging women to stop pregnancy after the age of 35 it will further decline Down syndrome by 50% (155). Health professionals, working for the control of congenital anomalies, should support all activities that increase access and availability of family planning to everyone (155).

Fertility is high in Afghanistan and each year a cohort of 1.08 million new children are born and among them 64,000 may born with severe congenital anomalies due to genetic causes, if we assume the prevalence of genetic congenital anomalies is 6% of total births (17). This prevalence could be reduced by reducing the total fertility rate from 5.8 children/women to 2-3 child/women through family planning. Coverage of family planning is very low in Afghanistan and only 23% of married couples use family planning methods, 25% of married couples have unmet need for family planning (3).

Therefore improving the coverage of family planning is a feasible and cost effective intervention for control of congenital which may lead to decrease total fertility rate and congenital anomalies.

5.1.8.Prevention of the herpes simplex virus(HSV)and toxoplasmosis: Performing caesarean section in women with active genital herpes lesions decreases the risk of neonatal HSV by less than 10%, and hand washing after handling raw meat, avoiding contact with cat faeces and avoiding raw milk decreases the chance of neonatal toxoplasmosis(154).

5.2. Secondary prevention

Main goal of these interventions is to decrease the number of children to be born with congenital anomalies (17). The main focus is on the pregnancy period. Antenatal screening for syphilis, Down syndrome, NTDs, carrier status screening for thalassemia and sickle cell disease, prenatal diagnosis by ultrasound, amniocentesis or villus biopsy are examples of secondary preventions(16)(17). After diagnosis, couples are offered counselling and a treatment option about the current pregnancy and how to reduce or prevent the risk in future (17).

For example termination of pregnancy and abortion for some severe congenital anomalies is offered in some countries and decrease the prevalence of some congenital anomalies such as Down syndrome(17). Afghanistan is an Islamic country and abortion is illegal according to article 402-6 of penal code by law (156), as well culturally it is sensitive, and not a feasible option in Afghanistan.

5.2.1. Screening for genetic disorders and prenatal diagnosis: Genetic screening helps to prevent some genetical disorders and decline over all burden of congenital anomalies. screening for genetical anomalies needs a high specialized staff and diagnostic facilities and certain criteria are necessary to be met for an anomaly to be screened or not(154). Screening for thalassemia, sickle cell disorder, glocuose-6-phosphate deficiency(G6PD), cystic fibrosis, phenylketonuria and chromosomal disorders over the age of 35 are examples of such screenings (17)(154).

Premarital genetic counselling and screening is implemented in countries with high consanguineous marriages and inherited blood disorders(33). Success stories of thalassemia control, through premarital genetical screening in Iran, is a good example of the impact of screening on congenital anomalies (157). The best possible information should be provided to parents, after prenatal diagnosis about nature of anomaly, complications, causes, future risks, information about treatment, prognosis and the parents should be sent to genetic counselling (17). No such services are available in Afghanistan until now and due to the lack of financial and human resources, the sustainability of such programs is questionable.

5.3. Tertiary prevention

These interventions are mainly focus on postnatal period once infant born with congenital anomaly. Early diagnosis, medical treatment (thalassemia, sickle cell anaemia, Phenylketonuria), surgical treatment (cleft lip, cleft palate, club foot, congenital heart disease and cataracts) and rehabilitation services are tertiary preventions (16)(17).

5.3.1.Provision of the improved treatment for congenital anomalies:

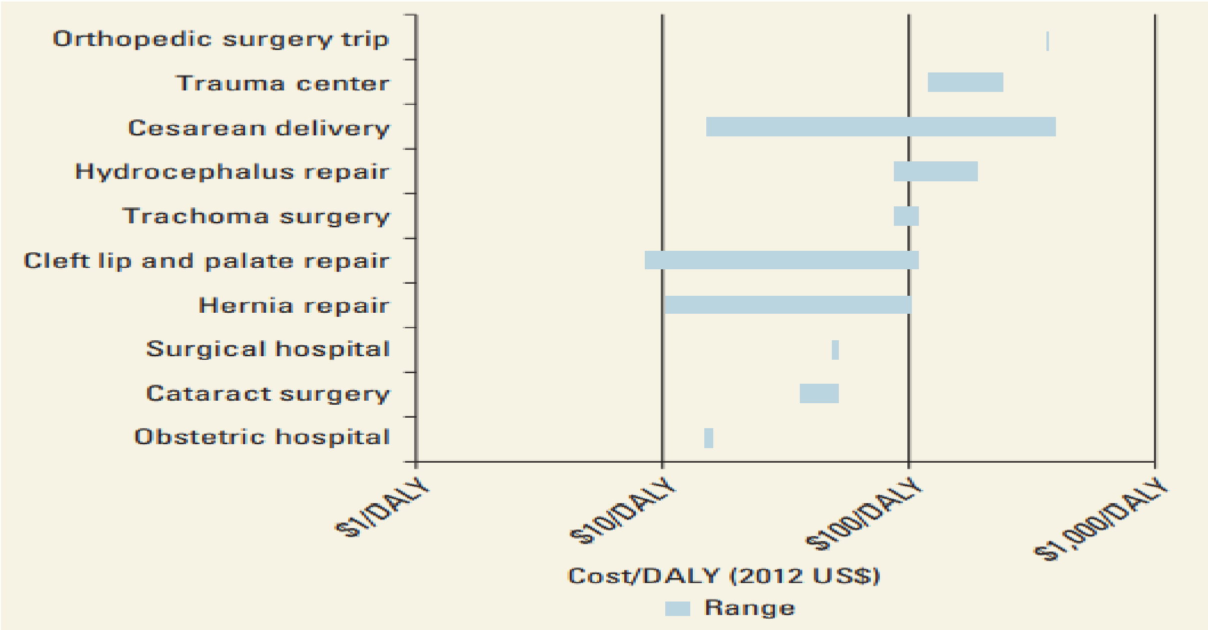
Treatment of congenital anomalies is mostly depended on the level of available health care in the country, and basic medical treatment for some congenital anomalies is possible in each LMICs countries at primary health care regardless of their health budget (17).

Some congenital anomalies can be treated partially or entirely, while for some anomalies there is no treatment (154). Diagnosis of congenital anomalies, in the prenatal period or neonatal period, provides the best possible treatment options(154). Advanced surgery for complex congenital anomalies is limited in most LMICs, but simple cost effective surgical procedures are available for the treatment of cataracts, oral clefts, cleft palate, hypospadias, hernia, NTDs, and club foot(17)(158). Based on context, cleft lips and cleft palate repair costs $10-110/ DALYs averted, cataract $50/DALYs averted and inguinal hernia $10-110/DALY averted (158) figure 12**.**

In my own observation and experience, surgical services for cleft lip, cleft palate, club foot, hypospadias and some other structure defects are available in a few hospitals in Kabul, the capital of Afghanistan, but access is very difficult from other parts of the country. On the other hand, no curative medical or surgical treatment protocol is available at the primary health care level for congenital anomalies (10).

Integrating some medical cost effective interventions in to primary health care, for treatment of congenital anomalies and essential surgical procedures for some congenital anomalies at provincial hospitals, is a feasible option in Afghanistan until the extension of specialized hospitals in whole country.

Figure(12) : Averted burden of disease including some congenital anomalies by surgical procedure in LMICs



Source: Disease Control Priorities, 3rd Edition: Volume 1: Essential Surgery (158)

5.3.2 Rehabilitation: Children and adults with severe congenital anomalies are facing long lasting disability and need social support through rehabilitation programs (17). Several models of rehabilitation are available; community based rehabilitation, school based rehabilitation, institution or hospital based and primary health care models (154)**.** The MoPH should consider one of these models for rehabilitation and the socio psychological support of children and adults with congenital anomalies in Afghanistan.

5.4. Increasing awareness about consanguinity

Although it is not possible to entirely discourage consanguineous marriages at the population level, because it is an integral part of the culture (32)(33)(159). There is need for increasing public awareness about consanguinity at individual, family and community levels through health education, premarital screening and preconception care at the primary health care level (32)(159).

Premarital screening and preconception care, besides decreasing the chance of genetic disorders, also help to increase the awareness about risks of consanguinity and decline consanguineous marriages in long term (32)(160).

A three stranded extended service development approach (family oriented approach) to address the needs of consanguineous families, affected by autosomal recessive disorders, was developed in UK, which was effective and successful, to increase awareness about genetical disorders (159). The number of couples, to see genetic counselling, from the affected south Asian communities in UK, increased after the approach (159).

These approaches need financial resources and its sustainability is questionable in countries with a high prevalence of consanguinity and low resources such as Afghanistan.

Table (2): Three strands of extended service development program in UK (159)

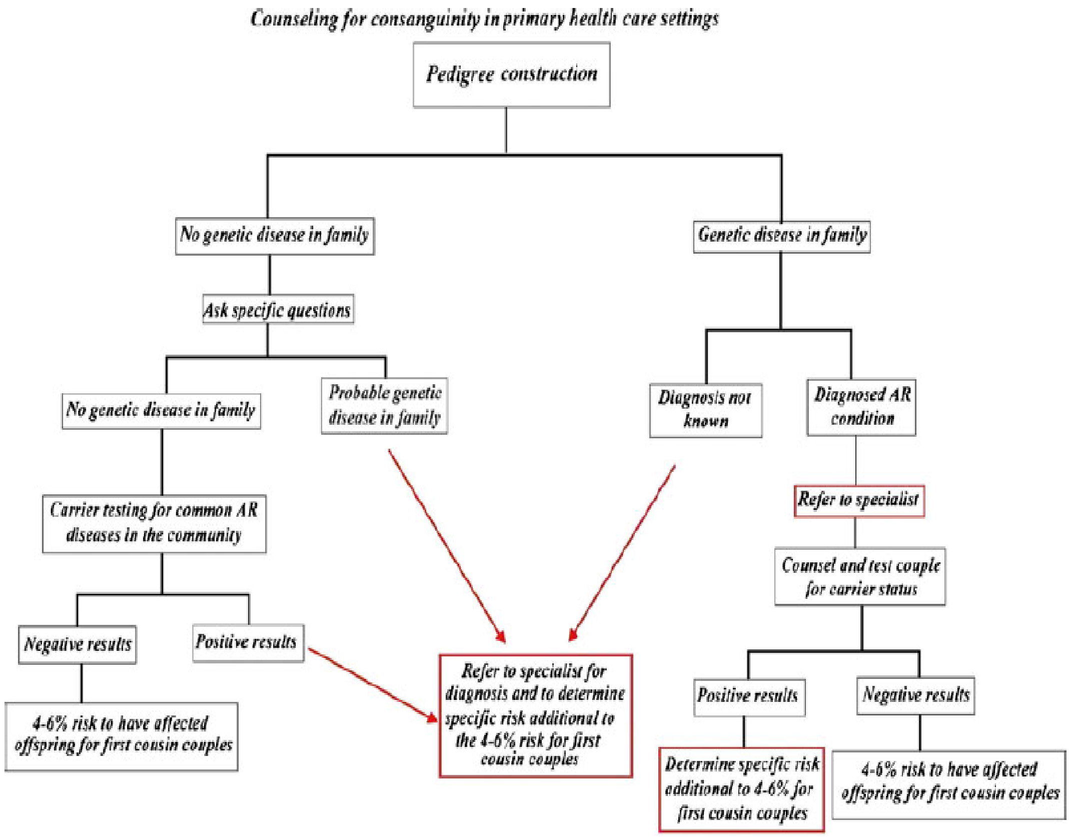
Start date	Development	Purpose
2007 onward	Family center genetic counseling services for consanguineous families	Providing genetic services for high risk families: identifying affected individuals, trace family members, offering genetic counseling and genetic testing
2012 onward	Training for front line professional and community workers	Address poor understanding of genetic counseling; develop skills and confidence for health care workers to provide preliminary genetic information and make appropriate referral to specialist genetic services
2014 onward	Establish community genetic outreach work posts	Develop community engagement activities to raise awareness of genetic issues, increase uptake of services and support affected families

Source: Khan N, Kerr G, Kingston H.(2016)

Preconception consanguinity counselling at primary health care level is another approach to educate people and increase awareness (32). In this approach each consanguineous couple is counselled according to a guideline, shown in figure 14, and then based on the history referred for further genetic investigation

(161). Though this approach also needs trained staff and genetic services, but could be partially adapted to current reproductive services in Afghanistan to educate people about consanguinity and its effect on health.

Figure(13): steps in preconception counselling for consanguineous couples(161)



Source: Hamamy, Hanan, et al. (2012): consanguineous marriages "Preconception consultation in primary health care settings

5.5. Preconception health care

Preventive public health measures, during the preconception period, timely treatment and diagnosis of congenital anomalies decreased the burden of congenital anomalies (155)(162).

Preconception care is a comprehensive approach, including all effective interventions (primary, secondary and tertiary) for prevention and treatment of congenital anomalies, the components of preconception care are (163).

- Assessment of women: Behaviours, family history, obstetric history, physical examination
- Vaccination: Rubella, hepatitis-B and mumps
- Screening: Sexual transmitted disease(STD), HIV, TORCH, genetic screening
- Counselling: Folic acid and micronutrient consumption, avoiding smoking and alcohol, weight management, Avoiding certain medicines and pesticides

Preconception health care is also recommended as one of the main strategies in the south Asian region framework for control of congenital anomalies (20). Most of interventions in this package are evidence based and clinical guidelines are available for some of them. Details on preconception care and its components are in Annex 5a and 5b.

The pre-pregnancy care program in Sri Lanka to control congenital anomalies is an adaptation of preconception health care which addresses many risk factors related to congenital anomalies (20).

Some components of preconception health care exist in the current ANC services and child care programs in Afghanistan (10). In Afghanistan 30% women are coming during first trimester for ANC, 18% in 4-5th months of pregnancy and remaining after 5th month of pregnancy, the percentage of women who are coming for ANC before conception is very low (3).

It shows that the ANC is started after pregnancy is confirmed and the preconception period, which is a critical period for prevention of certain risk factors is ignored by health professional. Therefore it is necessary to change the image of the ANC to preconception health care by integrating the preconception of health care approach in current mother and child health services.

Integrating preconception care in to current BPHS will cover all the current components of the ANC in a comprehensive way that will decline congenital anomalies as well as improve general maternal and child health.

5.6. Summary

To summarize effective interventions and strategies are available for the control of congenital anomalies that could be implemented before, during and after pregnancy.

An useful strategy that integrates most of the these interventions is preconception care packages which could be integrated in reproductive and child health care services.

There is no explicit strategy for control of congenital anomalies in Afghanistan, although there are a few interventions in current reproductive and child care services, that potentially help to, but are insufficient to address the burden of congenital anomalies.

Rubella vaccines, integrating preconception health care, improving folic acid supplementation, effective family planning and awareness about congenital anomalies and its risk factors particularly consanguinity is a feasible option for the MoPH and relevant stakeholders in Afghanistan.

Chapter 6

Conclusions and recommendations

6.1. Conclusions

This literature review shows that congenital anomalies make an important contribution to under five, infant and neonatal mortality in Afghanistan, but there is lack of data about the absolute spectrum and burden of congenital anomalies and like many developing countries, available data in Afghanistan is also based on modelled estimations (estimated prevalence of congenital is 74.9/1,000 live births in Afghanistan). This lack of data and studies has led to the lack of awareness among health professionals, policy makers and communities about congenital anomalies, which further underestimates this important public health problem.

To fill the gap, the MoPH with relevant stakeholders can establish a surveillance system for congenital anomalies, to develop more precise data on the prevalence and types of congenital anomalies. Establishing data and a reporting system will help the MoPH to prioritize specific congenital anomalies and develop a strategic plan for the control of congenital anomalies. Beside surveillance of congenital anomalies, the MoPH should encourage research institutes to design and conduct studies about the type ad risk factors of congenital anomalies in Afghanistan.

Like other LMICs, multiple factors exist in Afghanistan, which increase the potential risk of congenital anomalies, a high prevalence of consanguinity marriages, due to social and cultural norms and values, is the main factor contributing probably to a third of congenital anomalies in Afghanistan.

High fertility, pregnancy in an advanced maternal age, micronutrient deficiency, and congenital infections are other determinants, which contribute to congenital anomalies in Afghanistan. Low socio economic conditions, political and economic instability, the lack of health services are indirect determinants that influence congenital anomalies.

Currently there is no explicit strategy or policy for the control of congenital anomalies in Afghanistan. Although a few interventions, such as folic acid supplementation, family planning, STD screening, already exist in current reproductive and child care programs in Afghanistan, but interventions such as vaccine against rubella, prenatal screening, an education program to increase awareness about congenital anomalies and its risk factors do not exist, and treatment facilities for congenital anomalies are limited.

There is a need for initiating a comprehensive control program that focuses on control of congenital anomalies including preventive and curative options that could be integrated in the current packages of reproductive and child care programs at different levels of health system in Afghanistan.

The MoPH does not have unlimited resources to tackle all challenges related to congenital anomalies, but the existent policies on maternal and child health, can be modified to address the issue of congenital anomalies.

Integration of preconception health care approach, which is an integrated package of primary, secondary and tertiary interventions for prevention of congenital anomalies could be feasible in Afghanistan.

Besides its role for congenital anomalies, preconception health care also influences the overall maternal and child health.

6.2. Recommendations

These recommendations are for MoPH and relevant stakeholders including research institutes in Afghanistan

6.2.1. Short term and midterm

- Advocacy for Increasing awareness about congenital anomalies among health professionals, policy makers and the general public through mass media and other health promotion activities
- Develop a congenital anomalies surveillance system by integrating congenital anomalies in current health information system and considering congenital anomalies as a reportable disease. That will help to recognize common congenital anomalies and relevant interventions
- Establish or strengthen national policies and programs for congenital anomalies prevention and control by integrating congenital anomalies prevention and control strategies into public health, maternal and child health, nutrition and other relevant programs
- Ministries of public health, in collaboration with other government departments should establish regulations to reduce occupational exposure to teratogens and create programs to raise public awareness of the risks, including congenital anomalies, associated with these substances

6.2.2. Long term

- Expand and strengthen the national capacity by training physicians, nurses and allied health staff in the field of congenital anomalies
- Integrating preconception care strategy in reproductive and child care services and replacing the current conception of antenatal care to preconception care
- Provision of various screening processes and facilities including genetic screening of patients should be made more affordable and accessible to the general population
- Further research to investigate, prevalence, types and risk factors of congenital anomalies in Afghanistan

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Annexes

Annex 1 : Key words: These key words were used either individually or in combination

Congenital anomalies, Afghanistan, LMICs, birth defects, congenital malformation, risk factors, genetic disorders, cost effective interventions consanguinity, maternal age , smoking , alcohol consumption, maternal nutrition status , waste site and birth defects, occupational and congenital anomalies, genetic birth defects, prevalence of congenital anomalies, prevention of birth defects ,down syndrome following terms: ionizing radiation, pregnancy, teratology, X-ray, fetal exposure, malformations, carcinogenetic effects, Systematic review, Residential proximity, Polluted sites, Reproductive outcome, congenital heart disease, toxic waste sites, environmental pollution, air pollution. Folic acid, neural tube defect, prevention, myelomeningocele, anencephaly, spina bifida, risk reduction Rubella Syndrome, Congenital/prevention and control; Rubella vaccine/economics; Measles-mumps-rubella vaccine/ economics; Immunization programs; Developed countries; Cost-benefit analysis, toxoplasmosis, syphilis, chemical weapon effects, anti-natal care, insecticide and pesticides, WHO, policies and strategies, deafness and cataract , food fortification, social determinant, immigration, , preconception care, surgical procedure, cleft lip, cleft palate, syphilis, WHO, preterm birth, iodine deficiency, mental retardation, iodized salt

Annex(2):

WHO recommended interventions to prevent or treat birth defects

Preconception care	**Pregnancy care**	**Newborn infant and child care**
Family planning • Introducing women to the concept of reproductive choice • Reducing the total number of children born with a birth defect • Reducing the proportion of mothers of advanced maternal age, which reduces the birth prevalence of autosomal trisomies, particularly Down syndrome • Allowing women with affected children the option of not having further children Preconception screening and counseling • Using family history taken in primary health care facilities to identify individuals at risk of having affected children • Undertaking carrier screening for common recessive disorders (e.g. thalasemia and sickle cell disorders) Optimizing women's diet before and throughout pregnancy • Promoting the use of salt fortified with iodine to prevent iodine deficiency disorder • 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 • Promoting avoidance of alcohol, tobacco and cocaine • Promoting an adequate general diet (e.g. with sufficient protein, calories, iron) • Ensure adequate general diet (protein, calories, iron) Preventing and treating teratogens induced infections before and throughout pregnancy Such infections include: • syphilis • rubella (67 countries do not have national rubella immunization programmes) Optimizing preconception maternal health and treatment for • Insulin-dependent diabetics • Women on treatment for epilepsy • Women on treatment with warfarin	Antenatal screening for: • Rhesus status • Syphilis • Individuals at risk of having children with birth defects using a family history • Down syndrome (advanced maternal age; maternal serum screening; early ultrasound scanning) • Neural tube defects (maternal serum screening) • Major malformations (ultrasound fetal anomaly scanning (18+ weeks gestation) • Carriers of common recessive disorders (e.g. thalasemia and sickle cell disorders) Prenatal diagnosis • Ultrasound • Amniocentesis • Chorionic villus biopsy Fetal treatment for • Syphilis • Fetal anemia with intrauterine transfusion	Newborn infant examination • Trained examiner clinically examining all newborn infants for birth defects Newborn infant screening • Congenital hypothyroidism • Phenylketonuria • Cystic fibrosis • Others, as dictated by each country's needs and circumstances Medical treatment Examples: • Neonatal jaundice in glucose-6-phosphate dehydrogenase deficiency and Rhesus incompatibility • Treatment and care for children with blood disorders such as sickle-cell disorder, thalasemia, etc. • Treatment of some inborn errors of metabolism • Care of children with cystic fibrosis Surgery Examples include the correction of: • Simple congenital heart defects • Cleft lip and palate • Club foot • Congenital cataracts Rehabilitation and palliative

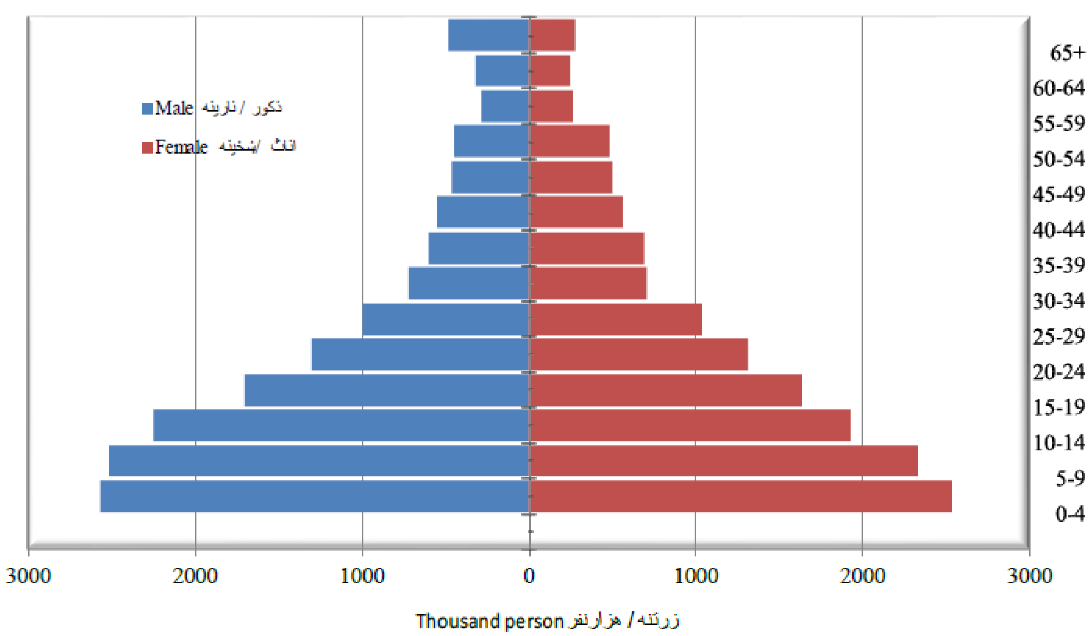
Source: WHO secretariat report 2010 page 7 (sixty-third world health assembly) http://apps.who.int/iris/bitstream/10665/2378/1/A63_10-en.p

Annex 3 : Afghanistan population statistics

Population by Sex and Age Groups-2017-18

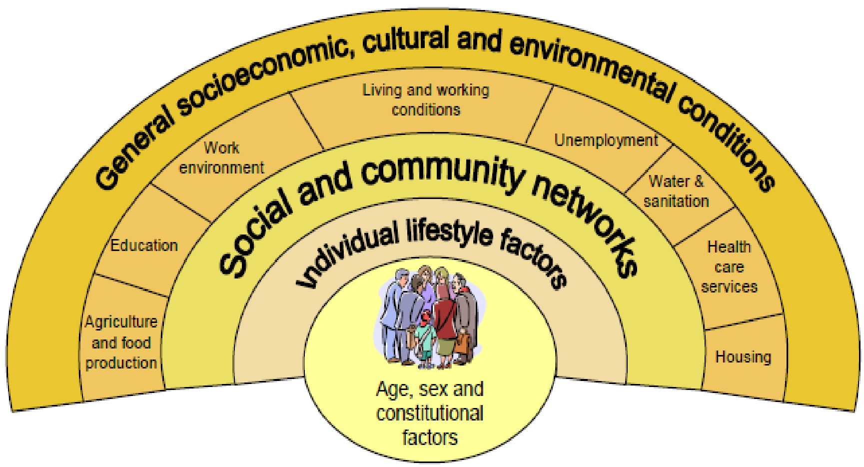
دهاتی کليوالي Rural			شهری ښاري Urban			کوچی Nomidic			مجموع نفوس تول وګړي Total population			گروپ سن دعمرګروپ Age group
ذکور نارينه Male	اناث ښځينه Female	مجموع ټول Total	ذکور نارينه Male	اناث ښځينه Female	مجموع ټول Total	ذکور نارينه Male	اناث ښځينه Female	مجموع ټول Total	ذکور نارينه Male	اناث ښځينه Female	مجموع ټول Total	
10,807,104	10,268,995	21,076,099	3,631,353	3,516,871	7,148,224	769,149	730,851	1,500,000	15,207,605	14,516,718	29,724,323	Total
1,908,007	1,884,533	3,792,540	520,969	494,928	1,015,897	140,502	155,133	295,635	2,569,478	2,534,594	5,104,072	00-04
1,854,052	1,699,963	3,554,015	506,032	479,725	985,757	158,351	146,586	304,937	2,518,436	2,326,273	4,844,709	05-09
1,574,605	1,356,617	2,931,221	551,669	487,947	1,039,616	120,633	84,663	205,297	2,246,907	1,929,227	4,176,135	10-14
1,158,774	1,097,506	2,256,281	469,972	482,574	952,546	75,887	60,639	136,526	1,704,633	1,640,719	3,345,352	15-19
874,682	896,684	1,771,366	377,352	361,046	738,398	50,490	52,944	103,434	1,302,524	1,310,673	2,613,198	20-24
712,791	738,079	1,450,870	240,181	251,605	491,787	41,734	52,211	93,945	994,707	1,041,896	2,036,602	25-29
518,019	499,053	1,017,072	164,557	167,516	332,073	36,383	39,402	75,784	718,958	705,971	1,424,929	30-34
414,968	474,022	888,990	151,690	176,360	328,050	31,386	41,068	72,454	598,044	691,450	1,289,494	35-39
388,084	396,571	784,655	132,425	142,291	274,716	28,563	25,470	54,033	549,072	564,333	1,113,404	40-44
320,240	364,504	684,745	125,988	118,190	244,178	19,703	20,894	40,597	465,931	503,588	969,519	45-49
331,807	327,059	658,866	99,341	132,099	231,440	18,191	20,780	38,972	449,339	479,939	929,278	50-54
198,457	178,290	376,747	76,050	68,621	144,671	13,103	13,555	26,658	287,610	260,466	548,076	55-59
221,862	176,478	398,340	81,143	63,499	144,642	15,607	6,962	22,570	318,612	246,939	565,551	60-64
330,755	179,636	510,391	133,985	90,469	224,454	18,614	10,544	29,158	483,354	280,649	764,003	65+

Population by Sex and Age Groups-2017-18



Source: Central statistics organization of Afghanistan 2017

Annex 4 : Dahlgren and Whitehead model of social determinants of health



Social Model of Health – Dahlgren & Whitehead

Dahlgren and Whitehead (1991) talk of the layers of influence on health. They describe a social ecological theory to health. They attempt to map **the relationship between the individual, their environment and disease. Individuals are at the centre with a set of fixed genes. Surrounding them are influences on health that can be modified. The first layer is personal behaviour and ways of living that can promote or damage health. –eg choice to smoke or not-Individuals are affected by friendship patterns and the norms of their community. The next layer is social and community influences, which provide mutual support for members of the community in unfavourable conditions. But they can also provide no support or have a negative effect. The third layer includes structural factors: housing, working conditions, access to services and provision of essential facilities.**

Source: Dahlgren G, and Whitehead 1991: policies and strategies to promote social equity in health. Stockholm, Sweden: Institute for future studies

Annex (5 a) :

Components of preconception care

Chronic diseases: Diabetes; heart disease; high blood pressure; thyroid disease; asthma; anemia; kidney disease; metabolic and haematological disorders; depression and other mental disorders; autoimmune disease; and physical disability (access) 2 **Infectious diseases:** Vaccine-preventable diseases (rubella, hepatitis B, varicella, influenza, and tetanus); HIV/AIDS; syphilis, Chlamydia, and other sexually transmitted diseases; periodontal disease; toxoplasmosis, and cytomegalic inclusion virus 3 **Reproductive concerns:** Unplanned pregnancies; contraception; infertility; adverse past pregnancy outcomes (preterm delivery, birth defects, fetal/infant death, maternal complications) 4 **Genetic/inherited conditions:** Sickle cell anaemia; thalassemia; Tay-Sachs disease; fragile X syndrome; Down syndrome; cystic fibrosis; muscular dystrophy; hearing and vision loss associated with genetic Predisposition 5 **Medications and medical treatment:** Prescription medications contraindicated in pregnant women (FDA's Category X Drugs, 117 products in 2001 PDR, antiepileptic drugs, oral anticoagulants for maternal clotting disorders, and Accurate); diagnostic radiation exposures 6 **Personal behaviours and exposures:** Smoking; alcohol consumption; illicit drug use; overweight/underweight; folic acid supplement use; domestic violence; eating disorders; exposure to infections; exposures to chemicals and other environmental toxins; consumption of over-the-counter medications; hyperthermia (e.g., from sauna use)

Annex (5b):

Preconception risk factors for adverse pregnancy outcomes for which clinical practice guidelines have been developed

Folic acid. Daily use of vitamin supplements containing folic acid has been demonstrated to reduce the occurrence of neural tube defects by two thirds

- **Rubella seronegativity.** Rubella vaccination provides protective seropositivity and prevents the occurrence of congenital rubella syndrome
- **Diabetes (preconception).** The three-fold increase in the prevalence of birth defects among infants of women with type 1 and type 2 diabetes is substantially reduced through proper management of diabetes
- **Hypothyroidism.** The dosages of LevothyroxineTM required for treatment of hypothyroidism increases in early pregnancy. LevothyroxineTM dosage needs to be adjusted for proper neurologic development
- **HIV/AIDS.** If HIV infection is identified before conception, timely treatment can be administered and women (or couples) can be given additional information that can influence the timing of the onset of pregnancy
- **Maternal phenylketonuria (PKU).** Women diagnosed with PKU as infants have infants with mental retardation. However, this adverse outcome can be prevented when mothers adhere to a low phenylalanine diet before conception and continue it throughout their pregnancy
- **Oral anticoagulant.** Warfarin, which is used for the control of blood clotting, has been demonstrated to be a teratogens. To avoid exposure to warfarin during early pregnancy, medications can be changed to a non teratogenic anticoagulant before the onset of pregnancy
- **Anti-epileptic drugs.** Certain anti-epileptic drugs are known as teratogens. Before conception, women who are on a regimen of these drugs and who are contemplating pregnancy should be prescribed a lower dosage of these drugs
- **Isotretinoins (Accutan**e **):** Use of isotretinoins in pregnancy to treat acne results in miscarriage and birth defects. Effective pregnancy prevention should be implemented to avoid unintended pregnancies among women with childbearing potential who use this medication
- **Smoking.** Preterm birth, low birth weight, and other adverse perinatal outcomes associated with maternal smoking in pregnancy can be prevented if women stop smoking during early pregnancy. Because only 20% of women successfully control tobacco dependence during pregnancy, cessation of smoking is recommended before pregnancy [
- **Alcohol misuse.** No time during pregnancy is safe to drink alcohol, and harm can occur early, before a woman has realized that she is or might be pregnant. Fetal alcohol syndrome and other alcohol-related birth defects can be prevented if women cease intake of alcohol before conception
- **Obesity.** Adverse perinatal outcomes associated with maternal obesity include neural tube defects, preterm delivery, diabetes, cesarean section, and hypertensive and thromboembolic disease.Weight loss before pregnancy reduces these risks
- **STD.** Chlamydia trachomatis and Neisseria gonorrhea have been strongly associated with ectopic pregnancy, infertility, and chronic pelvic pain. STDs during pregnancy might result in fetal death or substantial physical and developmental disabilities, including mental retardation and blindness
- **Hepatitis B.** Vaccination is recommended for men and women who are at risk for acquiring hepatitis B virus (HBV) infection. Preventing HBV infection in women of childbearing age prevents vertical transmission of infection to infants and eliminates risk for infection and sequelae, including hepatic failure, liver carcinoma, cirrhosis, and death

Source: Hani K preconception care for improving perinatal outcome (Matern Child Health J (2006) 10:S3–S11 DOI 10.1007/s10995-006-0100-4)

Annex 6 :

Prevalence of Down Syndroem and other chromosomal abonormalities in different maternal age

Maternal Age	Risk for Down Syndrome	Total Risk for Chromosomal Abnormalities
20	1/1,667	1/526
21	1/1,667	1/526
22	1/1,429	1/500
23	1/1,429	1/500
24	1/1,250	1/476
25	1/1,250	1/476
26	1/1,176	1/476
27	1/1,111	1/455
28	1/1,053	1/435
29	1/1,000	1/417
30	1/952	1/417
31	1/909	1/385
32	1/769	1/322
33	1/602	1/286
34	1/485	1/238
35	1/378	1/192
36	1/289	1/156
37	1/224	1/127
38	1/173	1/102
39	1/136	1/83
40	1/106	1/66
41	1/82	1/53
42	1/63	1/42
43	1/49	1/33
44	1/38	1/26
45	1/30	1/21
46	1/23	1/16
47	1/18	1/13
48	1/14	1/10
49	1/11	1/8

Sourece: Lucas, Adetokunbo O., Barbara J. Stoll, and Judith R. Bale, eds. Reducing birth defects: meeting the challenge in the developing world. National Academies Press, 2003

Annex 7 :

Table of some common drugs with Proven Teratogenic Effects in Human

Drug	Teratogenic Effect
Aminopterin,[b] methotrexate	Central nervous system (CNS) and limb malformation
Angiotensin-converting enzyme inhibitors	Prolonged renal failure in neonates, decreased skull ossification, renal tubular dysgenesis
Anticholinergic drugs	Neonatal meconium ileus
Antithyroid drugs (propylthiouracil and methimazole)	Fetal and neonatal goiter and hypothyroidism, aplasia cutis (with methimazole)
Carbamazepine	Neural tube defects (NTDs)
Cyclophosphamide	CNS malformations, secondary cancer
Danazol and other androgenic drugs	Masculinization of female fetuses
Diethylstilbestrol[b]	Vaginal carcinoma and other genitourinary defects in female and male offspring
Hypoglycemic drugs	Neonatal hypoglycemia
Lithium	Ebstein's anomaly
Misoprostol	Moebius sequence
Nonsteroidal anti-inflammatory drugs	Constriction of the ductus arteriosus,[c] necrotizing enterocolitis
Paramethadione[b]	Facial and CNS defects
Phenytoin	Growth retardation, CNS defects
Psychoactive drugs (e.g., barbiturates, opioids, benzodiazepines)	Neonatal withdrawal syndrome when drug is taken in late pregnancy
Systemic retinoids (isoretinoin and etretinate)	CNS, craniofacial, cardiovascular, and other defects
Tetracycline	Anomalies of teeth and bone
Thalidomide	Limb-shortening defects, internal organ defects
Trimethadione[b]	Facial and CNS defects
Valproic acid	NTDs
Warfarin	Skeletal and CNS defects, Dandy-Walker syndrome

Source: Lucas, Adetokunbo O., Barbara J. Stoll, and Judith R. Bale, eds. *Reducing birth defects: meeting the challenge in the developing world*. National Academies Press, 2003

Annex 8

Relative contribution of different interventions in maximum post natal saves of congenital anomalies(17)

Group of Disorders	Birth Prevalence (per 1,000 live births)	Intervention (Primary, Secondary, Tertiary)	Maximum Postnatal Lives Saved (per 1,000 live births)	Maximum Reduction %	Estimated Average Increase in Longevity Per Head of Population (Years)
Congenital Malformations	36.5	Pediatric Surgery (3°)**	17.70	48.5	1.24
		Folic Acid Supplement (1°)**	11.50	31.5	0.81
		Prenatal Diagnosis (2°)**	3.50	9.6	0.25
		Total Congenital Malformations:	**32.70**	**89.6**	**2.30**
Chromosomal Disorders	3.8	Family Planning (1°)**	0.75	19.7	0.05
		Prenatal Diagnosis (2°)**	0.50	13.2	0.04
		Total Chromosomal Disorders:	**1.25**	**32.9**	**0.09**
Genetic Risk Factors*	2.4	Routine Antenatal and Neonatal Care (3°)**	2.40	100.0	0.17
Inherited Disorders (severe, early onset)	11.5	Genetic Counseling (1°)**	1.73	15.0	0.12
		Neonatal Screening (3°)**	0.70	6.1	0.05
		Prenatal Diagnosis (2°)**	1.15	10.0	0.08
		Total Inherited:	**3.60**	**31.1**	**0.25**
TOTAL:	**54.2**		**39.9**	**73.7**	**2.80**

G6PD deficiency and Rhesus hemolytic disease of the newborn* * 1° = Primary prevention 2° = Secondary prevention 3° = Tertiary prevention*

Source: March of Dimes (2006): global report of birth defects

Annex(9): potential health effects of prenatal radiation exposure according radiation dose and gestational age

Table 1: Potential Health Effects (Other Than Cancer) of Prenatal Radiation Exposure

	Time Post Conception				
			Fetogenesis		
Acute Radiation Dose* to the Embryo/Fetus	**Blastogenesis (up to 2 wks)**	**Organogenesis (2 –7 wks)**	**(8–15 wks)**	**(16 –25 wks)**	**(26 –38 wks)**
< 0.05 Gy (5 rads)†	Noncancer health effects NOT detectable				
0.05–0.50 Gy (5–50 rads)	Incidence of failure to implant may increase slightly, but surviving embryos will probably have no significant (noncancer) health effects	• Incidence of major malformations may increase slightly • Growth retardation possible	• Growth retardation possible • Reduction in IQ possible (up to 15 points, depending on dose) • Incidence of severe mental retardation up to 20%, depending on dose	Noncancer health effects unlikely	
> 0.50 Gy (50 rads) *The expectant mother may be experiencing acute radiation syndrome in this range, depending on her whole-body dose.*	Incidence of failure to implant will likely be large,‡ depending on dose, but surviving embryos will probably have no significant (noncancer) health effects	• Incidence of miscarriage may increase, depending on dose • Substantial risk of major malformations such as neurological and motor deficiencies • Growth retardation likely	• Incidence of miscarriage probably will increase, depending on dose • Growth retardation likely • Reduction in IQ possible (> 15 points, depending on dose) • Incidence of severe mental retardation > 20%, depending on dose • Incidence of major malformations will probably increase	• Incidence of miscarriage may increase, depending on dose • Growth retardation possible, depending on dose • Reduction in IQ possible, depending on dose • Severe mental retardation possible, depending on dose • Incidence of major malformations may increase	Incidence of miscarriage and neonatal death will probably increase depending on dose§

Note: This table is intended only as a guide. The indicated doses and times post conception are approximations.

*	Acute dose: dose delivered in a short time (usually minutes). Fractionated or chronic doses: doses delivered over time. For fractionated or chronic doses the health effects to the fetus may differ from what is depicted here.
†	Both the gray (Gy) and the rad are units of absorbed dose and reflect the amount of energy deposited into a mass of tissue (1 Gy = 100 rads). In this document, the absorbed dose is that dose received by the entire fetus (whole-body fetal dose). The referenced absorbed dose levels in this document are assumed to be from beta, gamma, or x-radiation. Neutron or proton radiation produces many of the health effects described herein at lower absorbed dose levels.
‡	A fetal dose of 1 Gy (100 rads) will likely kill 50% of the embryos. The dose necessary to kill 100% of human embryos or fetuses before 18 weeks' gestation is about 5 Gy (500 rads).
§	For adults, the LD50/60 (the dose necessary to kill 50% of the exposed population in 60 days) is about 3-5 Gy (300-500 rads) and the LD100 (the dose necessary to kill 100% of the exposed population) is around 10 Gy (1000 rads)

Source: Radiation and Pregnancy : A Fact Sheet for the Public [Internet]. CDC. 2011 [cited 2017 Jul 21]. p. 1–2. Available from: https://emergency.cdc.gov/radiation/prenatalphysician.asp