

# CLINICAL PRACTICE GUIDELINES FOR THE DETECTION, DIAGNOSIS OF FETUS AND NEONATAL CONGENITAL ANOMALY

## Purpose and Goal Description

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To outline the protocol for detection, diagnosis, treatment of fetus or newborn with congenital anomaly who meet pathway criteria.  
To monitor infants for potential mortality or morbidity effects related to congenital anomaly.

## Abbreviations

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|               |  |
|---------------|--|
| Amniocentesis | Antenatal procedure involving the removal of a sample of amniotic fluid for the purposes of chromosomal or genetic testing |
| CA            | Congenital Anomaly   |
| CCHD          | Critical Congenital Heart Disease  |
| CPAP          | Continuous Positive Airway Pressure  |
| CPG           | Clinical Practice Guideline  |
| EBM           | Evidence-Based Medicine  |
| FNB           | Fetal Nasal Bone   |
| FNT           | Fetal Nasal Translucency   |
| NICU          | Neonatal Intensive Care Unit   |
| NTD           | Neural Tube Defect   |

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## Source CPG Developer

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## Introduction

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Congenital anomalies (also called birth defects) include a wide range of structural and functional abnormalities that are present at birth, or that occur later but originate in the prenatal period. Diagnosis may occur before birth, at birth, or months or years after birth. Major anomalies can result in death and/or disability and require substantial medical care throughout life, causing significant economic and social burden (for example, spinal cord and heart anomalies). In Saudi, major congenital anomalies occur in about 4.1% of newborns and 8% to 10% of stillbirths.<sup>1</sup>

Many countries offer to all pregnant women at least one routine mid-trimester fetal ultrasound scan (anomaly scan), with the goal of detecting congenital anomalies<sup>2-3</sup>. Additionally, pregnant women at high risk for congenital anomalies are normally offered a detailed fetal anatomical examination<sup>1</sup>, usually called 'referral scan'. In some countries, there are networks that allow sonographers and physicians who perform screening scans to refer pregnancies with suspected or detected fetal anomalies to specialized centers which not available in our settings. A referral scan consists of a detailed ultrasound examination that requires specific expertise and its aim is to confirm and define the anomaly<sup>3,4</sup>. At the referral center, cases with confirmed fetal anomalies are managed by a multidisciplinary team<sup>2</sup> and may undergo other imaging investigations, such as magnetic resonance imaging<sup>5</sup>, fetal invasive procedures<sup>6</sup> and individualized counseling<sup>7</sup>.

Fetal risk factors for structural anomalies have been well-described, including suspected fetal anomaly at the anomaly scan<sup>7</sup>, increased nuchal translucency (NT) thickness in the first trimester<sup>2</sup>, early-onset fetal growth restriction (FGR)<sup>9</sup> and known fetal genetic anomaly<sup>9</sup>.

In Saudi Arabia, prevalence of major congenital anomalies in Saudi Arabia is a largely understudied area. Knowing the prevalence of birth defects and their trends is important in identifying potential factors that are either causative or preventative. Kurdi et al estimated that the birth prevalence of CA is 4.12% in Saudi Arabia. The common types of CA are congenital heart disease (148 per 10 000), renal malformations (113), neural tube defects (19) and chromosomal anomalies (27)<sup>1</sup>.

In Saudi Arabia, birth defects remain the leading cause of death among children, with high rates of consanguineous marriage and genetic diseases<sup>19-10</sup>.

The aim of this clinical protocol guideline (CPG) is to provide evidence-based recommendations for management of fetus or neonates with CA including detection, diagnosis Early antenatal of major congenital anomalies for possible termination of pregnancy, fetal or neonatal care.

**Knowing the prevalence of birth defects and their trend is important in identifying potential novel factors that are either causative or preventative.**

## Scope and Purpose

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### **Disease/Condition:**

Congenital anomalies or birth defects are defined as structural abnormalities diagnosed antenatally, at the time of birth or in the first few years of life<sup>11</sup>.

### **Guideline Objective(s)**

This CPG aims to provide evidence-based recommendations for the early detection, diagnosis and treatment of neonates with CA in order to decrease the perinatal mortality, if not long-term disability in the diagnosed infant and are a burden to families, society and the healthcare system.

### **Health / Clinical Question (PIPOH)**

#### **P: Patient (Target Population):**

Fetus or Newborn infants at risk of or diagnosed with CA

#### **I: Interventions and Practices Considered / CPG Category:**

Early detection and diagnosis and treatment

#### **P: Professionals (Intended / Target Users or Stakeholders):**

Healthcare professionals in primary, secondary, and tertiary care of neonatal and maternity services including physicians, nurses, pharmacists, laboratory technicians

### **Clinical Specialties**

Physicians (pediatricians, neonatologists, geneticist, obstetricians, and radiologists), clinical pharmacists, nurses, radiology & laboratory technicians, and midwives. These identified target users will use this CPG to inform their clinical decision- making and standards of care.

### **O: Major Outcomes Considered:**

1. Decrease death (Mortality)

2. Decrease major neurodevelopmental disability in surviving babies (Morbidity)
3. Prevention of common CA.

#### H: Healthcare Settings:

Primary, secondary, and tertiary neonatal healthcare services are mainly nurseries, NICUs, and outpatient clinics in Saudi Arabia.

#### Recommendations

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Definitions of Quality of Evidence (QoE) and Strength of Recommendations (SoR)

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#### ■ Preconception:

##### Key Recommendations

Detection:

Some **congenital anomaly** are common in some families and to be detectable during planned pregnancy and others are not. Screening is offered by MOH maternity services to maximise antenatal detection of specified conditions where pregnant people choose, and present in time.

| Investigations                             | History, clinical exam and Tests  |
|--|---|
| <b>Routine visit preconception</b>         | <ul style="list-style-type: none"> <li>• History of the following:</li> <li>• If previous documented birth defect or genetic disease by genetic test (from the list) in the family either partner</li> <li>• If High Risks Cases:</li> <li>• Chronic disease e.g. epilepsy, diabetes, lupus</li> <li>• Recurrent unexplained abortion more than two</li> <li>• History of IUFD not related to OBGYN causes</li> </ul>         |
| <b>Specific investigations (if needed)</b> | <ul style="list-style-type: none"> <li>• Referral to specialized center center ( MFM) in the cluster</li> <li>• If MFM not available , referral made to Virtual Genetic or combined Services by calling # 0502440062</li> <li>• Email: <a href="mailto:svh_operation@moh.gov.sa">svh_operation@moh.gov.sa</a></li> <li>• Blood to be done accordingly</li> <li>• Report should go back to committee (Excel sheet )</li> </ul> |

▪ **During pregnancy:**

| Investigations                             | History, clinical exam and Tests  |
|--|---|
| <b>Routine visits during pregnancy</b>     | <ul style="list-style-type: none"> <li>• History of previous documented genetic disease in the family or previous preconception</li> <li>• History of suspicious or confirmed congenital anomaly in this pregnancy</li> </ul>   |
| <b>Specific investigations (if needed)</b> | <ul style="list-style-type: none"> <li>• <b>1<sup>st</sup> Trimester:</b></li> <li>• NIPT at gestational age 9-10 weeks</li> <li>• Fetus US at 11-13 (FNB and FNT)</li> <li>• Cordocentesis Or Amniocentesis at gestational age 13-15weeks</li> <li>• <b>2<sup>nd</sup> Trimester:</b></li> <li>• AFP screening 16-18 weeks</li> <li>• Anatomical FUS 18-20 weeks</li> <li>➤ If results Negative and normal to be back to primary physician</li> <li>➤ If result suspect or confirmed disease from the list to be refer to genetic center according to pathway and document result to committee (Excel sheet )</li> </ul> |

▪ **Neonatal period:**

| Investigations  | History, clinical exam and Tests  |
|---|---|
| <b>Routine examination post delivery by pediatrician or neonatologist</b> | <ul style="list-style-type: none"> <li>• History of previous suspected or documented anomaly disease in the pregnancy</li> <li>• If alive follow pathway</li> <li>• If IUFD or died post-delivery Skeletal survey (to be saved in the PACS and blood in the filter paper (NBS) should be done (under mother medical record number)</li> </ul>   |
| <b>Specific investigations (if needed)</b>                                | <ul style="list-style-type: none"> <li>• Neonatal workup (if it's not available in the same center referral should made to Virtual Genetic or combined Services by calling # 0502440062</li> <li>• Email: <a href="mailto:svh_operation@moh.gov.sa">svh_operation@moh.gov.sa</a></li> <li>• If results Negative and normal case to be closed</li> <li>• If confirm CA diagnosis, to be register in Report should go back to committee (Excel sheet )</li> </ul> |

## ▪ Pediatric period:

| Investigations                       | History, clinical exam and Tests   |
|--------------------------------------|--|
| child workup according to geneticist | <ul style="list-style-type: none"> <li>History of previous documented congenital anomaly disease in antenatal or neonatal period</li> <li>Blood test (to be determined) by MRP or Geneticist</li> <li>Confirm diagnosis pathway in Genetic Registry</li> <li>Counselling for future pregnancy</li> </ul> |
| Specific investigations (if needed)  | <ul style="list-style-type: none"> <li>Requiring Test to be decided by MRP or Geneticist</li> </ul>  |

### Management:

Clinical Management of infants who suffer from CA is essentially supportive. Or according to the disease.

### Implementation Strategies and Tools

Several implementation frameworks and manuals have recommended the following strategies or interventions:

1. Leadership commitment, engagement, and support.
2. Local clinical and quality champions.
3. Dissemination (printed and electronic).
4. Regular training and education.
5. Regular audit and feedback (along with regular review and update promotes the concept of the 'living CPGs'.
6. Networking with relevant existing projects
7. Parents

### Implementation Tools

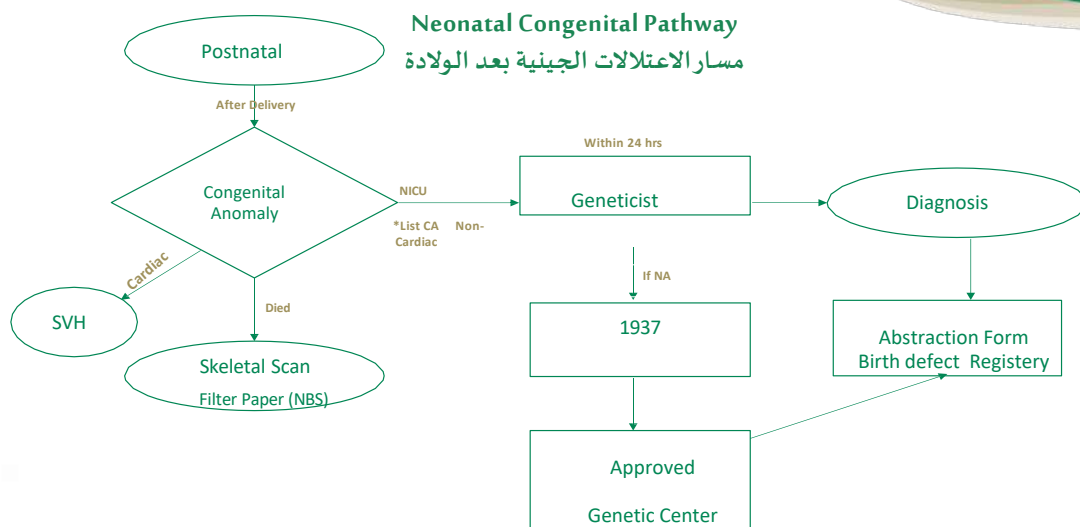
The CPG adaptation group decided to adopt all of the CPG implementation tools proposed by the QMN CPG.

#### 1. Checklist for CA



## 2. Flowchart/ Algorithm: Management

### Perinatal Congenital Pathway مسار الاعتلالات الجينية للولادة وما قبلها



### 3. Flowchart: CA investigations and definition

| Term                                     | Definition  |
|--|---|
| Antenatal                                | The period from conception to birth.  |
| Antenatal diagnosis                      | A diagnosis in a pregnancy at any gestation prior to delivery.  |
| Birth prevalence of congenital anomalies | The total number of babies diagnosed with a congenital anomaly (live births, stillbirths, late miscarriages, and terminations of pregnancy for fetal anomaly) compared to the total number of births (live births and stillbirths). |
| Births/total births                      | Live births and stillbirths as recorded by the MOH  |
| Infant mortality                         | The number of infant deaths per 1000 live births.   |
| Late miscarriage                         | Late fetal deaths from 20 to 23 completed weeks of gestation.   |
| Live birth                               | A baby showing signs of life at birth as recorded by the MOH  |
| Live birth prevalence                    | The total number of babies diagnosed with a congenital anomaly that are live born compared to the total number of live births.  |
| Total births                             | Total number of live births and stillbirths.  |
| Perinatal deaths                         | Feta deaths >28weeks GA and deaths under 7 days of age as recorded by the MOH.  |
| Perinatal mortality                      | The number of perinatal deaths per 1000 total births.   |
| Neonatal mortality                       | The number of neonatal deaths per 1000 live total births.   |
| Post-neonatal period                     | From 28 days of life to 1 year of age.  |

| Term                            | Definition  |
|---------------------------------|---|
| Congenital anomaly              | Condition present at delivery, probably originating before birth, and includes structural, chromosomal, genetic, and biochemical anomalies.                 |
| Genetic anomalies               | Includes genetic syndromes, hereditary skin disorders, skeletal dysplasias and chromosomal anomalies  |
| Non-genetic anomalies           | Includes anomalies with no known genetic cause. Not all babies undergo genetic testing, so it is likely that some of these anomalies are of genetic origin. |
| Amniocentesis                   | Antenatal procedure involving the removal of a sample of amniotic fluid for the purposes of chromosomal or genetic testing.                                 |
| Chorionic villus sampling (CVS) | Antenatal procedure involving the removal of a sample of placental tissue for the purposes of chromosomal or genetic testing.                               |
| Fetal Nasal Bone                | Fetal nasal bone determination. The nasal bone may not be visualized in some babies with certain chromosome abnormalities, such as Trisomy 21               |
| Fetal Nuchal Translucency       | Nuchal translucency screening uses an ultrasound to examine the area at the back of the fetal neck for increased fluid or thickening.                       |
| Full karyotype                  | Visual inspection of all chromosomes down the microscope, enabling assessment of chromosome number and integrity.   |
| Stillbirths                     | A baby born after 24 or more completed weeks of gestation and which did not, at any time, breathe or show signs of life as recorded by the MOH              |
| Teratogen                       | Substance or other factor that can cause congenital anomaly by affecting fetal development.   |

| Term                                 | Definition  |
|--------------------------------------|---|
| Invasive testing                     | Antenatal tests including amniocentesis and chorionic villus sampling used to diagnose chromosomal and genetic anomalies. In these tests, a needle is inserted directly into the uterus to take a sample.   |
| Non-invasive prenatal testing (NIPT) | Screening test for specific chromosomal disorders by testing fragments of fetal DNA found in the maternal blood stream.   |
| Rapid aneuploidy testing             | A genetic test with a short turnaround time; it counts the copy number of specific regions on chromosomes 13, 18, 21, X and Y.  |
| FNSP conditions<br>Checklists:       | <p>The auditable conditions screened under the Fetal or neonatal Anomaly Screening Programme (FASP).</p> <p>All NTD</p> <p>All CCHD</p> <p>Cleft lip +/- palate</p> <p>Bilateral renal agenesis</p> <p>Lethal skeletal dysplasia</p> <p>Congenital diaphragmatic hernia</p> <p>Omphalocele</p> <p>Gastroschisis</p> <p>Trisomy 21</p> <p>Trisomy 18</p> <p>Trisomy 13</p> |

APPENDIX

- Clinical Pathway for Intrauterine Fetal Demise (IUFD) with a Focus on Genetic Disorders
- Data Abstraction Form (Attached)
- ICD 10 DIAGNOSIS Attached



Data Abstraction Form

| سجل المتابعة للأمراض الوراثية والجينية |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               | 1     |         |     |    |
|--|--------------------|---|----------------------|-------------------------------|-----------------|---|---|---|----------------|-----------------------|---|---------|----------------------------|------------|-----------|---------------|-------|---------|-----|----|
| رقم التواصل<br>الأسري                  | الطبيب المعالج     | في حال<br>الوفاة، اذكر<br>تاريخ الوفاة    | الوزن عند<br>الولادة | العمر<br>الحمل<br>عند الولادة | في حال نعم ذكره | هل يوجد<br>تاريخ عائلي<br>أو عوامل<br>خطورة   | هل تاريخ مرضي<br>لعدوى خلال<br>الحمل (الإيجابية<br>نعم/لا ) | هل الزواج<br>زواج قرابة<br>(الإيجابية<br>نعم/لا ) | نتيجة<br>الفحص | الفحص الذي تم<br>عمله | تشخيص<br>الاعتلال<br>الجيني<br>والوراثي                       | المنطقة | المنشأة المحال<br>منه      | رقم الهوية | رقم الملف | الميلاد       | الاسم | التاريخ | م   |    |
| Family Contact<br>Number               | Treating Physician | If Baby died,<br>Mention<br>date of death | Baby Wt at Birth     | Genital Age at<br>Birth       | If Yes, Mention | Family History or<br>Risk factors(<br>Yes/No) | maternal infections<br>History (Yes/No)                     | Cousanguinity<br>Marriage<br>(Yes/No)             | Test Result    | Test Inadequate       | Congenital and<br>Chromosomal<br>diagnosis based<br>on ICD 10 | Region  | Name of health institution | Id No.     | MRN       | Date of Birth | Name  | Date    | Sl. |    |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 2  |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 3  |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 4  |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 5  |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 6  |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 7  |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 8  |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 9  |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 10 |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 11 |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 12 |
|  |                    |   |                      |                               |                 |   |   |   |                |                       |   |         |                            |            |           |               |       |         |     | 13 |

## ICD 10 DIAGNOSIS

|     | <b>Birth defects</b>                        | <b>ICD-10 CODE</b>            |
|-----|---|-------------------------------|
| 1.  | Nervous system                              | Q00-07                        |
| 2.  | Anencephaly                                 | Q00.0                         |
| 3.  | Encephalocele                               | Q01.0                         |
| 4.  | Microcephaly                                | Q02                           |
| 5.  | Congenital Hydrocephalus                    | Q03.0                         |
| 6.  | Holoprosencephaly                           | Q04.0                         |
| 7.  | spina bifida                                | Q05.0                         |
| 8.  | Eye, ear, face and neck                     | Q10-18 ( can ask the doctor)  |
| 9.  | Anophthalmos                                | Q11.0                         |
| 10. | Microphthalmos                              | Q11.2                         |
| 11. | congenital cataract                         | Q12.0                         |
| 12. | Aniridia                                    | Q13.1                         |
| 13. | Congenital glaucoma                         | Q15.0                         |
| 14. | Anotia                                      | Q16.0                         |
| 15. | Microtia                                    | Q17.2                         |
| 16. | circulatory system                          | Q20-28 ( can ask the doctor)  |
| 17. | Transposition of great arteries             | Q20.3                         |
| 18. | Single ventricle                            | Q20.4                         |
| 19. | Ventricular Septal defect                   | Q21.0                         |
| 20. | Tetralogy of fallot                         | Q21.3                         |
| 21. | pulmonary valve atresia/ stenosis           | Q22.0                         |
| 22. | Patent ductus arteriosus                    | Q25.0                         |
| 23. | Coarctation of aorta                        | Q25.1                         |
| 24. | Respiratory system                          | Q30-34 ( will ask the doctor) |
| 25. | Choanal atresia                             | Q30.0                         |
| 26. | Cleft palate                                | Q35                           |
| 27. | Cleft lip                                   | Q36                           |
| 28. | Cleft lip with palate                       | Q37                           |
| 29. | Cleft hard palate with unilateral cleft lip | Q37.1                         |
| 30. | Cleft soft palate with bilateral cleft lip  | Q37.2                         |
| 31. | Digestive system                            | Q38 ( can ask the doctor)     |



|     |  |                              |
|-----|--|------------------------------|
| 32. | Esophageal atresia/ stenosis             | Q39.0                        |
| 33. | Congenital Hypertrophic pyloric stenosis | Q40.0                        |
| 34. | Duodenal atresia/ stenosis               | Q41.0                        |
| 35. | Small intestine atresia/ stenosis        | Q41.0                        |
| 36. | Anorectal atresia/ stenosis              | Q42.0                        |
| 37. | Congenital megacolon                     | Q43.1                        |
| 38. | Atresia of bile duct                     | Q44.2                        |
| 39. | Genital organs                           | Q50-56                       |
| 40. | Undescended testicle                     | Q53.0                        |
| 41. | Hypospadias                              | Q54.0                        |
| 42. | Indeterminate sex                        | Q56.0                        |
| 43. | Urinary system                           | Q60-64 ( can ask the doctor) |
| 44. | Renal agenesis                           | Q60.0                        |
| 45. | Renal Dysplasia                          | Q61.4                        |
| 46. | Cystic kidney                            | Q61.0                        |
| 47. | Congenital Hydronephrosis                | Q62.0                        |
| 48. | Obstructive genitourinary defect         | Q62.0                        |
| 49. | Musculoskeletal system                   | Q65-79                       |
| 50. | Congenital hip dislocation               | Q65.0-65.9                   |
| 51. | Club foot-talipes equinovarus            | Q66.0                        |
| 52. | Polydactyly                              | Q69.0                        |
| 53. | Syndactyly                               | Q70.0                        |
| 54. | Total limb reduction defects             | Q71.0                        |
| 55. | Arthrogryposis multiplex congenital      | Q74.3                        |
| 56. | Craniosynostosis                         | Q75.0                        |
| 57. | Achondroplasia/ hypochondroplasia        | Q77.4                        |
| 58. | Diaphragmatic hernia                     | Q79.0                        |
| 59. | Omphalocele                              | Q79.2                        |
| 60. | Gastroschisis                            | Q79.3                        |
| 61. | Other and unspecified                    | Q80                          |
| 62. | Chromosomal abnormalities                | Q90-99 ( can ask the doctor) |



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