NHS
Greater Glasgow and Clyde

Final

CONGENITAL ANOMALY SURVEILLANCE

2015-2016

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Review of data relating to Congenital Anomalies detected in NHS Greater Glasgow &Clyde between 1st April 2015 and 31st March 2016.

Source data provided by Hilary Jordan of Information Services.

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Congenital Anomaly Surveillance

CONGENITAL ABNORMALITY

Congenital anomalies comprise a wide range of abnormalities of body structure or function that are present at birth and are of prenatal origin. The focus of this report is on major structural anomalies. These are the structural changes that have significant medical, social or cosmetic consequences for the affected individual and will typically require medical intervention.

A congenital disorder, or congenital disease, is a condition existing at birth. The disorder may be the result of genetic abnormality, errors of morphogenesis, the intrauterine environment, infection or chromosomal abnormality.

Congenital anomalies are of four clinically significant types.

- **Malformations**: the development of a structure is arrested delayed or misdirected early in embryonic life and the effect is permanent
- **Deformations**: distinct from malformations in both timing and impact. They are conditions that arise from the application of mechanical stress to normally formed tissues. They may occur later in pregnancy and can be temporary
- **Disruptions**: complete breakdown of normal tissues
- **Dysplasias**: Cellular abnormality of the originating tissue e.g. expansion of immature cells with a corresponding decrease in the number and location of mature cells.

Congenital disorders may consist of more than one abnormality. When multiple effects occur in a specified order the disorder is known as a **sequence.** When the order is not known, it is called a **syndrome**.

Congenital anomalies may be classified in a variety of ways e.g. regarding onset, morphogenesis or aetiology during organogenesis. The cause of congenital anomaly can be reliably determined in only a small percentage of cases.

POPULATION-BASED CONGENITAL ANOMALIES SURVEILLANCE

A population-based congenital abnormality surveillance programme has a defined source population, (typically defined by maternal residence), and all identified congenital anomalies occurring within that source population are ascertained and included regardless of delivery site.

This review includes all fetuses and neonates with a congenital anomaly born to mothers living within the catchment area of Greater Glasgow & Clyde Health Board during 2015 - 2016.

The denominator used to calculate prevalence consists of all births to resident mothers. The corresponding numerator consists of fetuses or neonates with congenital anomalies born to resident mothers, (see below for explanation of prevalence calculations).

Data sources include all health facilities within the catchment area where the births occur, birth and stillbirth registries, referral treatment centres for individuals with congenital anomalies, administrative databases and any identifiable fetus or neonate with a congenital anomaly. Using multiple sources improves the completeness of the case ascertainment.

Experienced information analysts and health board staff conduct core data abstraction. They have electronic access to participating institutions and actively review multiple data sources to identify cases. This type of case ascertainment requires considerable resources and personnel. Active case ascertainment seeks to enhance case detection and case reporting and improves data quality because more extensive clinical details are collected.

PURPOSE

In general terms, Public Health Surveillance is the ongoing systematic collection, analysis and interpretation of health data for planning, implementation and evaluation of health strategies. The primary users of surveillance information are usually public health professionals and healthcare providers.

The objectives of this surveillance programme are to: -

- Measure the prevalence of congenital anomalies within the community
- Monitor trends in the prevalence of different types of anomaly within the defined population
- Improve management to minimize complications and adverse outcomes amongst those who are affected by congenital abnormality
- Allow evaluation of screening and prevention programmes
- Assess the effect of prenatal screening and diagnosis on birth prevalence
- Disseminate findings and interpretations to health care partners and appropriate organizations
- Provide a basis for epidemiologic research and prevention programmes

WHY PREVALENCE?

All congenital anomaly registers report the number of babies with anomalies born during a calendar year. Perhaps this should mean that they would all report incidence rates. However, in practice many congenital anomaly registers report prevalence estimates. In birth defects epidemiology, the terms live birth prevalence, birth prevalence and total prevalence are commonly used. It is worth considering why this is the case.

The incidence is the rate of occurrence of new cases of a disease or condition over a specified period expressed as a ratio or percentage.

Incidence = number of new cases over specified period/size of population under consideration

The appropriate denominator for calculation of the incidence, (the size of the population under consideration who are initially disease free), is debatable. In the circumstances of this review it would be the number of maternities booked through antenatal services over the year 1st April 2015 and 31st March 2016, (Appendix 1).

The reason given for the use of prevalence rates is that it is not possible to ascertain all 'new' cases of any anomaly as a proportion of pregnancies affected with an anomaly will miscarry spontaneously before being diagnosed. Indeed, although 16,147 women booked with NHS GG&C between 1st April 2015 and 31st March 2016, a total of 17,477 appointed referrals were made during the same period. This means that at least 1,330 pregnancies were 'lost' from time of referral to booking, (Appendix 1).

Consequently, congenital anomaly registers, such as EUROCAT and BINOCAR, report prevalence estimates per 1,000 or 10,000 total births, (live and stillbirths). These are referred to as **birth prevalence** estimates even though the pregnancy may not result in a 'birth' because of late miscarriage or termination of pregnancy for fetal anomaly, (fetal loss less than 20 weeks' gestation is excluded from prevalence data).

For completeness, it is worth mentioning live birth prevalence and total prevalence. **Live birth prevalence** measures the number of cases with congenital anomalies among live births. Simply all live births with any congenital anomaly divided by all live births during the defined period.

Total prevalence figures measure the number of cases with congenital anomalies in live births, fetal deaths (stillbirths), and elective terminations for fetal anomaly. Total prevalence is hence defined as the number of cases of live birth, fetal death and termination for fetal anomaly (numerator) among a defined cohort of live births, stillbirths and elective terminations, (denominator).

27th October 2016

Jim Robins, with grateful thanks due to Hilary Jordan & Paul Burton.

Links to previous reports

Previous reports are available on-line for download through the GG&C Public Health Screening website.

GG&C CONGENITAL ANOMALY REPORT FOR 2014-2015

http://www.nhsggc.org.uk/media/234839/final-report-2014-2015-jbr-v2.pdf

GG&C CONGENITAL ANOMALY REPORT FOR 2013-2014

http://library.nhsggc.org.uk/mediaAssets/Public%20Health%20Screening/CongenitalAnomaly2013-2014_Final.pdf

GG&C CONGENITAL ANOMALY REPORT FOR 2012-2013

http://library.nhsggc.org.uk/mediaAssets/Public%20Health%20Screening/CongenitalAnomaly2012-2013_FinalDraft.pdf

The reports for 2010-2011 & 2011-2012 are no longer available on-line.

Core Data

This report considers all live-births, stillbirths, fetal losses and terminations of pregnancy between 1st April 2015 and 31st March 2016 that were associated with one or more congenital abnormalities.

The congenital anomaly data used to compile this report are collected from several different sources. The contents of this report are merely a 'snapshot' taken from the database held within Public Health Screening department on 15th August 2016.[1] The data set is evolving and constantly updated as further abnormalities are recognized within this birth cohort.

An essential aspect of the congenital anomalies surveillance programme is the precise and accurate coding of the recorded malformation. The ICD 10 system is the international standard diagnostic classification system for all general epidemiological purposes. However, ICD 10 lacks specificity for coding some congenital abnormalities and most genetic syndromes. The Royal College of Paediatrics & Child Health (RCPCH - formerly the British Paediatric Association), developed an adaptation of the ICD 10 system by adding an extra digit to the code to allow more detailed coding. These extensions are used where they exist to improve data quality.

CASE BASED REVIEW

A total of 345 cases were identified from 344 pregnancies.[2] The case rate is calculated at 276.6/10,000 live and stillbirths.[3] The numbers are dependent on the date of data extraction and the degree of case ascertainment, (proportion of notifications reported out of all cases of congenital abnormality in the population), rather than any real change in congenital anomaly.

Most cases were live births, (n= 256, 74%). There was 1 stillbirth and 2 fetal losses. Termination of pregnancy following prenatal diagnosis of abnormality accounted for 86 cases, (25%), (Figure 1.1).

Overall a total of 579 abnormalities were classified in these 345 cases using the ICD 10 system, the primary abnormality and a variable number of associated abnormalities, (Figure 1.2).

In 218 cases, only one abnormality is listed, (63%). However, in the remaining 127 cases, (37%), two or more abnormalities are classified. Generally accepted figures form WHO and other organizations suggest that approximately 75% of fetuses will have just one anomaly. It is uncertain as to why the collected figures in this report suggest a higher incidence of associated abnormality. It could represent a 'thorough' diagnostic

[1] Multiple sources are aggregated, including Child Health Surveillance (Health Visitor data), SMR01 (Hospital Discharge data), Scottish Birth Record, PNBS, Clinical Genetics (prenatal and postnatal data), QEUH's obstetric ultrasound system (Excelicare™), NRS Deaths and Stillbirths data.
[2] One set of twins, each co-twin exhibiting an abnormality.
[3] This is calculated from the number of live and stillbirths for residents of NHS GG&C from 1st April 2015 to 31st March 2016, (Appendix 1).

assessment but may simply be due to the process of active data collection from multiple sources as well as the inclusion of what may be considered by some as more 'minor' abnormalities.

Figure 1.1: Pregnancy outcome, (n=345)

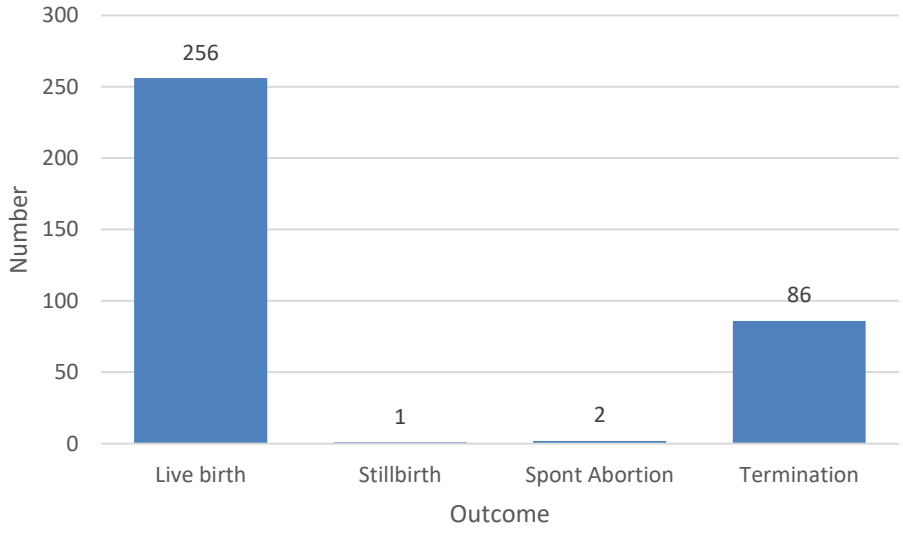
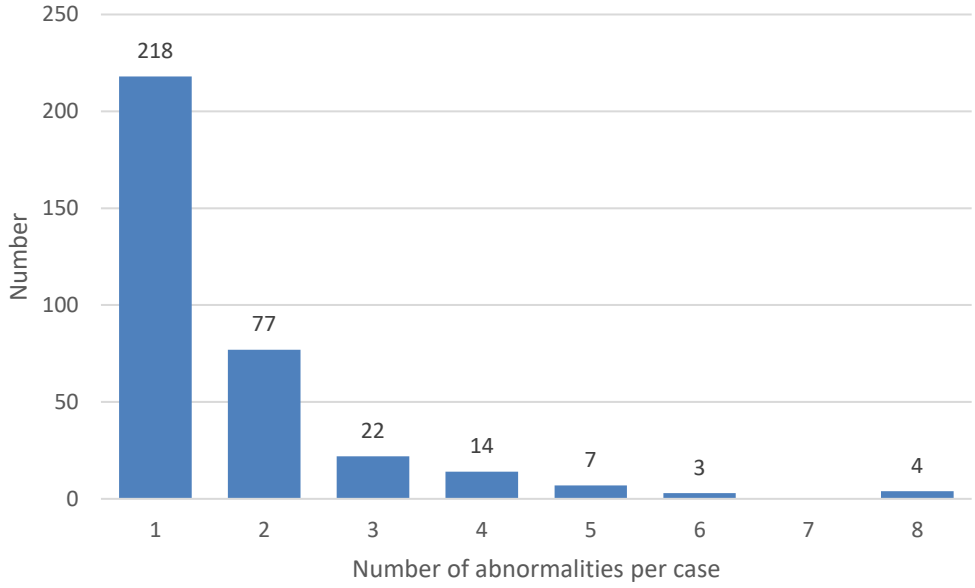


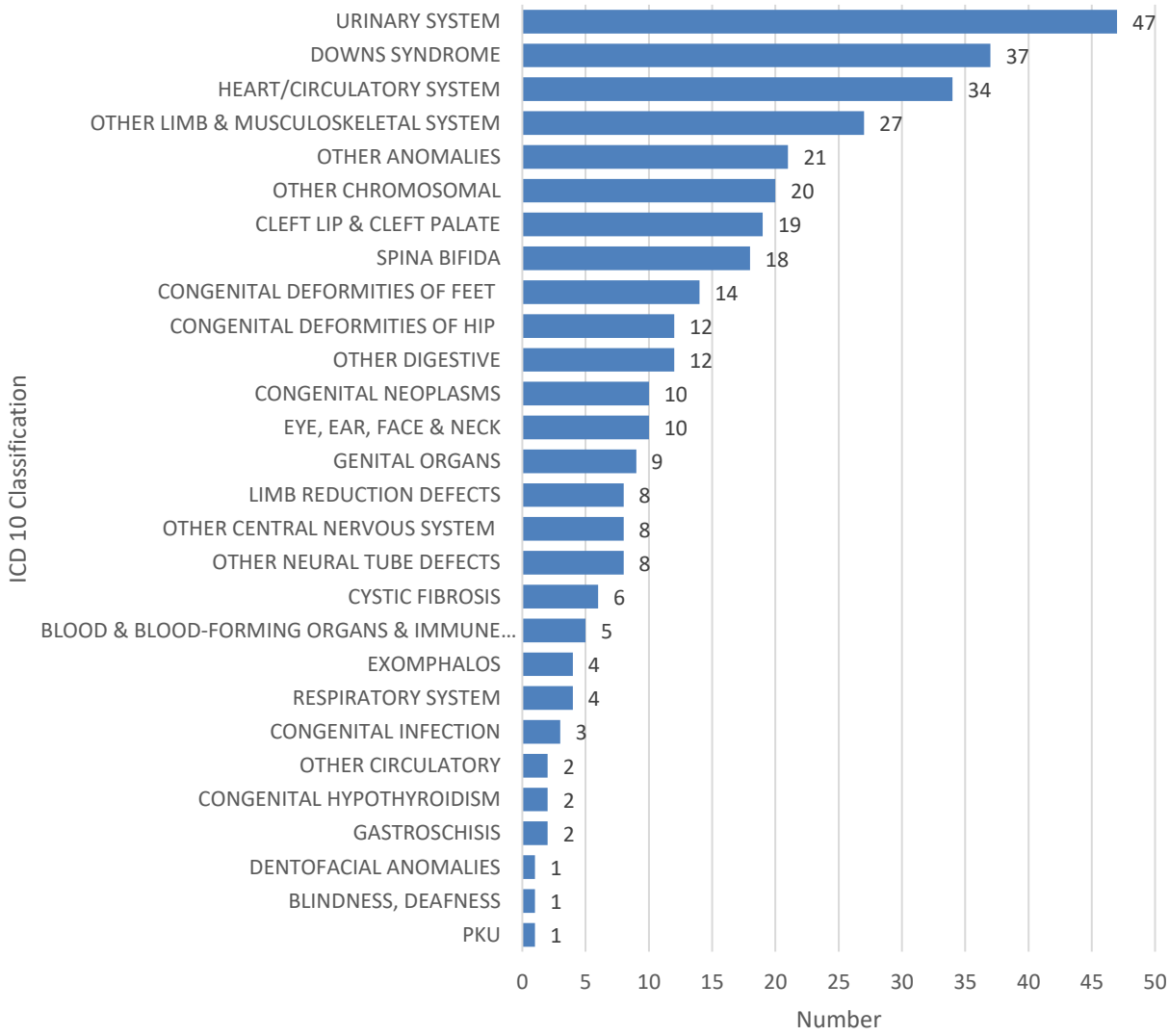
Figure 1.2: Abnormalities per case, (n=345)



The principle data set on the 345 cases, including associated abnormalities, is provided as a list ordered based on the primary abnormality as defined under ICD 10. It includes pregnancy outcome and 'point of diagnosis' data. Additional information has also been collected on gestational age at time of birth or termination, gestational age at 'point of diagnosis' if prenatal, maternal age, birth order for multiple pregnancy and gender. Further supporting data has been made available from the GG&C Pregnancy & Newborn Screening (PNBS) data base.

The basic data set can be summarized as a table listed by Congenital Malformation Category as coded under ICD 10, (Figure 1.3).

Figure 1.3: Classification by primary abnormality, (ICD 10), (n=345)



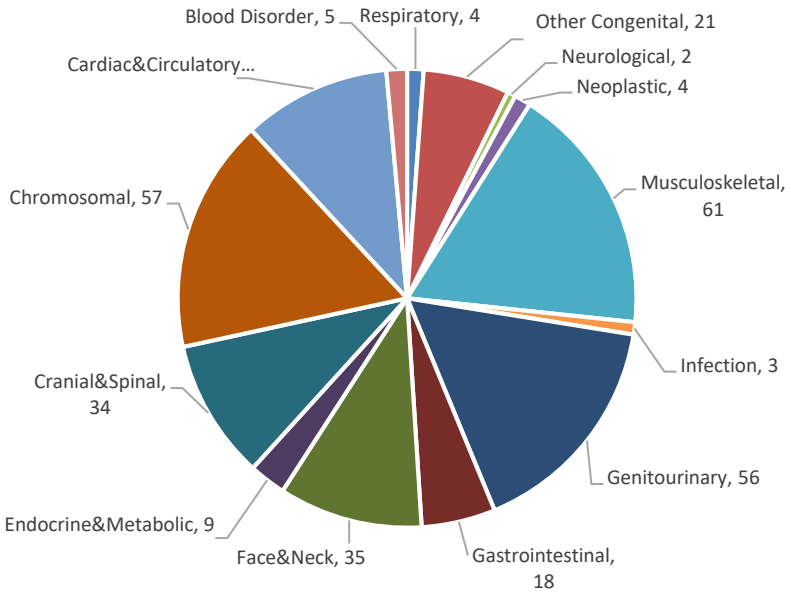
However, it is easier to consider this data if some of these categories are grouped together. Therefore, abnormalities of the musculoskeletal system, comprising 'Congenital Deformities of Hip', 'Congenital Deformities of Feet', 'Limb Reduction Defects' and 'Other Limb & Musculoskeletal System', are the commonest primary classification, (n=61, 17.7%).

Chromosomal abnormality, ('Down Syndrome' and 'Other Chromosomal Disorders'), is the next largest grouping, (n=57, 16.5%), with primary abnormalities of the genitourinary system, ('Genital Organs' and 'Urinary System'), listed for fifty-six of the cases.

Cardiac and circulatory disorders, 'Heart/Circulatory System' and 'Other Circulatory', account for thirty-six of the primary abnormalities, (10.4%). Cranial & spinal abnormalities, ('Spina Bifida', 'Other Neural Tube Defects' and 'Other Central Nervous System), is the preferred primary classification in thirty-four cases, (9.9%).

Clearly even with this regrouping of primary malformation category some disorders, as classified and ordered under ICD 10, are more typically reviewed under other 'systems' and hence an aggregated and simplified classification has been used in these reports to aid case presentation. Thus, exomphalos and gastroschisis are included as abnormalities of the gastrointestinal tract rather than musculoskeletal system, (although the latter is technically correct). This simplification also attempts to correct some errors inherent in ICD 10, (e.g. 'Congenital Lobar Emphysema' (P250) is listed as a 'Congenital Infection' under ICD 10 rather than as a primary disruption of broncho-pulmonary development). However, Di George syndrome has been left as a primary disorder of 'Blood & Blood-Forming Organs' although it is probably best considered as a chromosomal deletion syndrome. An aggregated and simplified chart based on primary abnormality is presented in Figure 1.4.

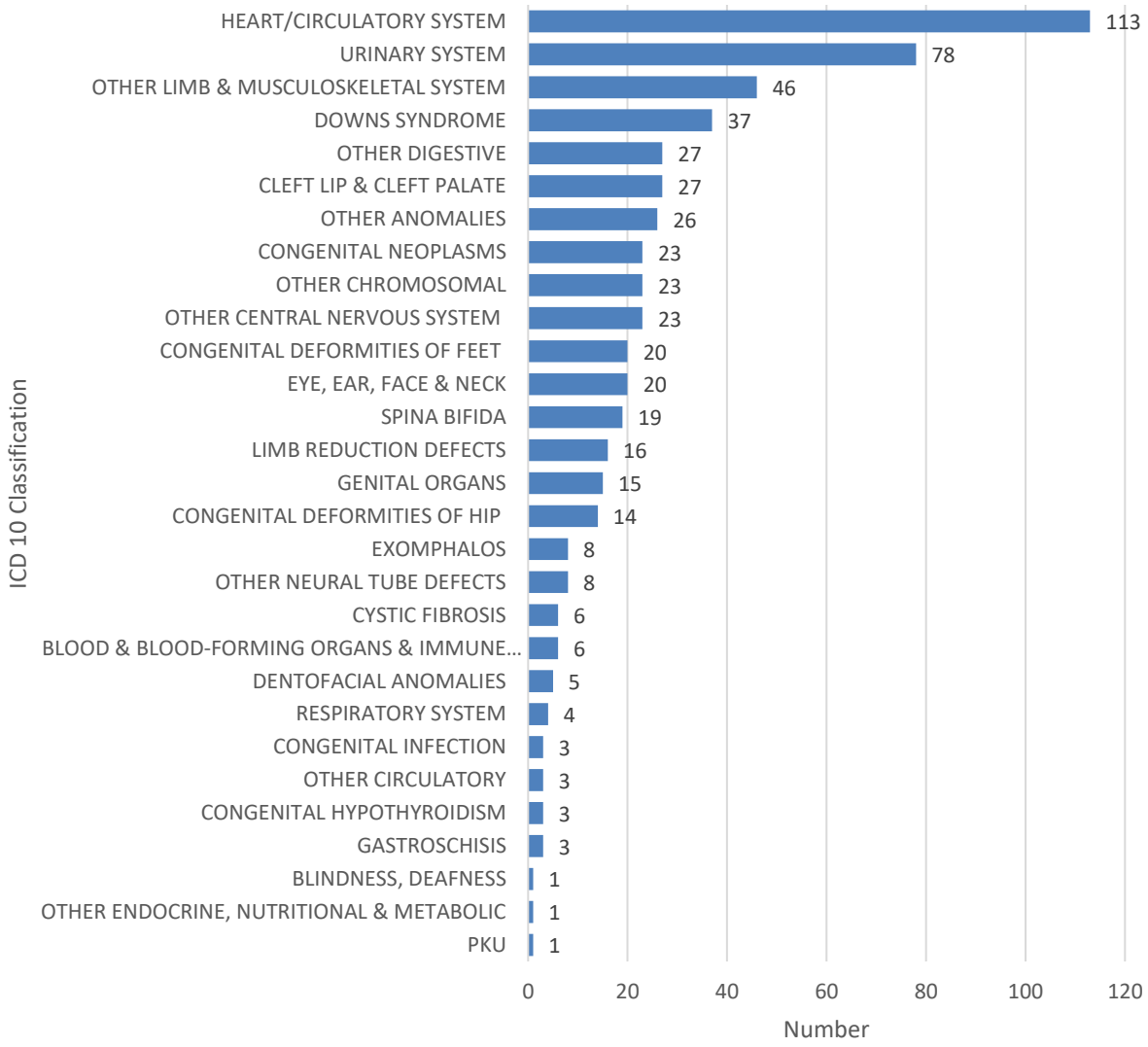
Figure 1.4: Simplified Classification by Primary Abnormality, (n=345)



ABNORMALITY BASED REVIEW

The data are a little more complex when all 579 abnormalities, as defined under ICD 10, are considered, (Figure 1.5). Clearly an infant with an encephalocele, hepatic fibrosis and renal dysplasia will be considered in multiple categories.

Figure 1.5: Anomalies in any diagnostic position by ICD 10 grouping, (non-exclusive), (n=579)

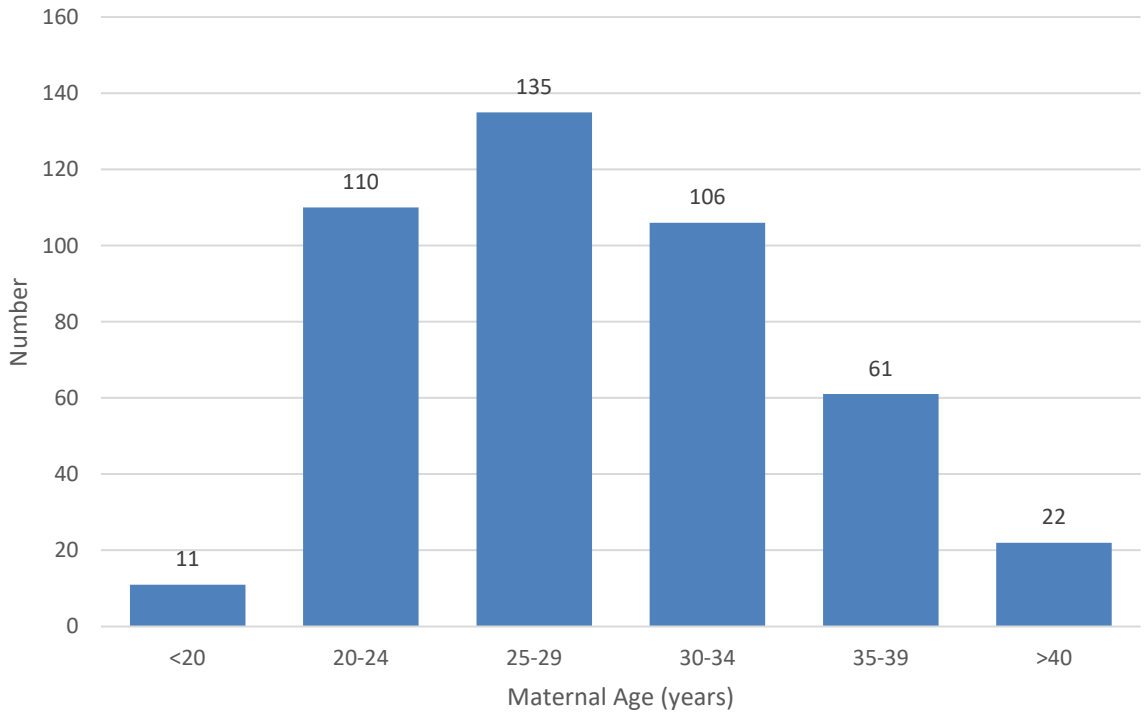


However, Cardiac and circulatory disorders, 'Heart/Circulatory System' and 'Other Circulatory', are now the most prominent grouping accounting for 20% of all listed abnormalities, (n=116). Abnormalities of the musculoskeletal system, comprising 'Congenital Deformities of Hip', 'Congenital Deformities of Feet', 'Limb Reduction Defects' and 'Other Limb & Musculoskeletal System' account for 16.5%, (n=96).

MATERNAL AGE

Overall 344 pregnancies accounted for the 345 classified cases of abnormality.[4] Maternal age at time of delivery, miscarriage or termination ranged from 16 to 45 years, (Figure 1.6). The mean age was 30.2 years. Unfortunately, one mother was to have two pregnancies associated with significant abnormality during the review period and is therefore counted twice, (once for each pregnancy). Although maternal age is recorded in the register no information is held on the father.

Figure 1.6: Maternal age at delivery or loss, (n=344)



Data from WHO, EUROCAT, BINOCAR and other surveillance programmes suggest that mothers under the age of 20 years have the highest prevalence of non-chromosomal anomalies when compared with older mothers, whereas the birth prevalence of chromosomal anomalies increases with age.

A 5-year review of NHS GG&C data has recently been completed relating maternal age to primary malformation, (ICD 10). A data set composed of 1,868 cases with a recognized primary abnormality, (including the data described in this current review), was compared with control data derived from all maternities within the same West of Scotland population, (n=62,366).[5]

[4] One mother delivered twins where each co-twin had a significant abnormality.
[5] Roscoe M & Robins J. *Assessment of Maternal Age and the Prevalence of Primary Congenital Malformation in a West of Scotland Population, (2011-2016).* NHS GG&C Public Health Screening.

GENDER

Gender is recorded for 316 cases. Congenital abnormality was slightly more prevalent in males than females. In 29 cases gender is recorded as 'unknown', (Figure 1.7).

Figure 1.7: Fetal & infant gender, (n=345)

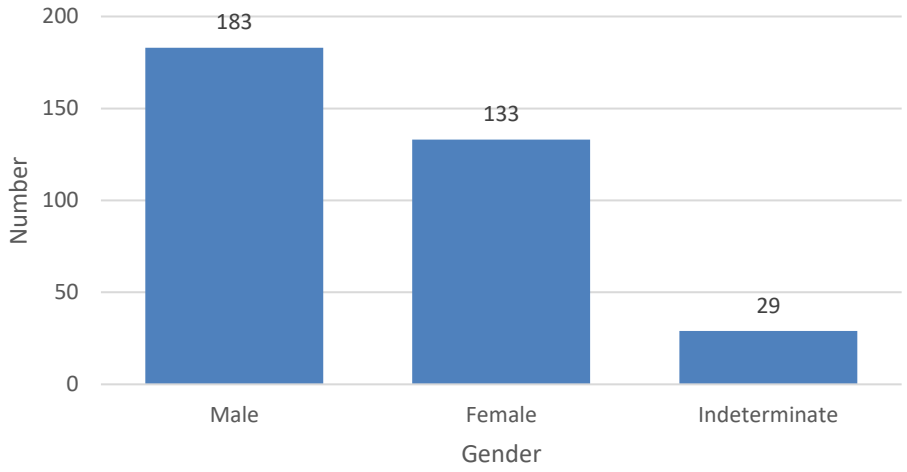
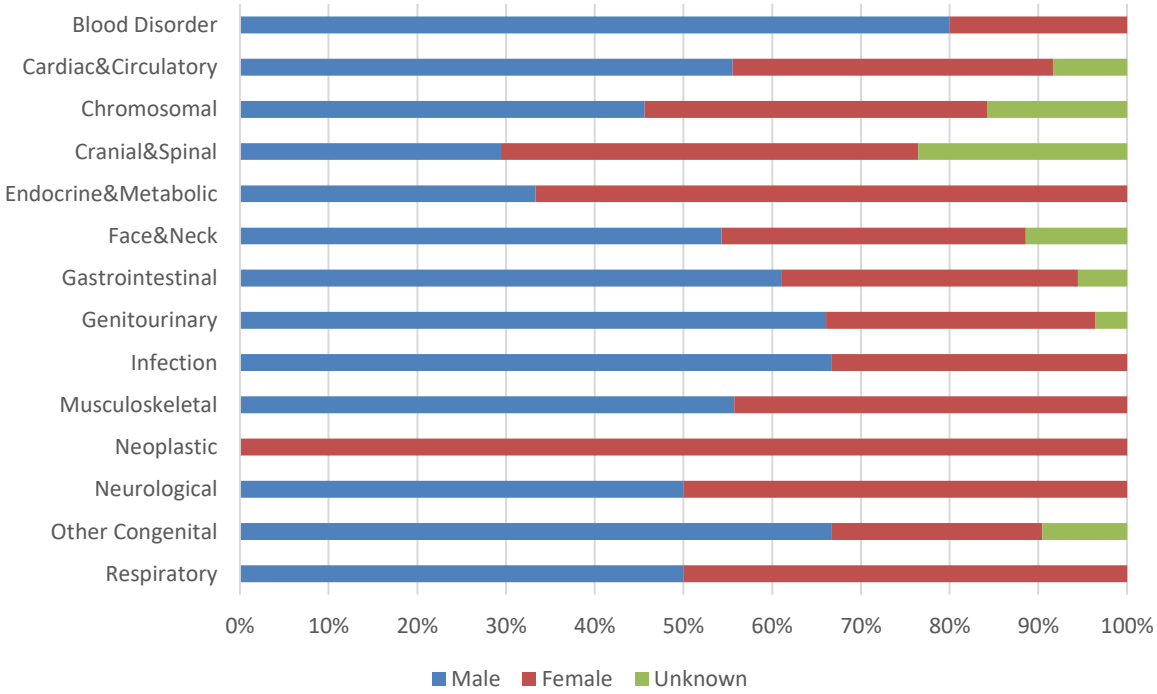


Figure 1.8: Gender by simplified classification



The mean gestation at delivery for the unknown group was 16.17 weeks, (range 12-22 weeks). The majority were terminations of pregnancy, (n=28), with one spontaneous fetal loss. In all cases a prenatal diagnosis of abnormality had been made. Nine were associated with a defined chromosomal abnormality suggesting that genetic sex has been determined but not recorded.

It has been long recognized that overall males are at greater risk than females but gender differences in the prevalence of specific birth defects are common e.g. developmental dysplasia of the hip is much more common in female infants. Apart from neoplastic disorders and cranial and spinal anomalies, most the major categories of birth defect showed a higher prevalence of abnormality amongst males, (Figure 1.8).

MULTIPLE PREGNANCY

There were one-hundred and eighty-seven twin pregnancies resulting in either live-birth or stillbirth in GG&C during 2015-2016.[6] Three hundred and seventy-two babies were live born with two stillbirths: two pregnancies resulted in the birth of both live born and stillborn co-twins.

Fourteen cases of anomaly are recorded from thirteen twin pregnancies.

Q0511	T/L MYELOMENINGOCELE (OPEN) + HYDROCEPHALUS	Live birth; 1st twin; Female
Q213	TETRALOGY OF FALLOT	Live birth; 1st twin; Male
Q213	TETRALOGY OF FALLOT	Live birth; 2nd twin; Female
Q224	TRICUSPID VALVAR STENOSIS	Live birth; 2nd twin; Female
Q3690	CLEFT LIP ® (& GUM)	Live birth; 2nd twin; Male
Q772	ASPHYXIATING SHORT RIB THORACIC DYSPLASIA	Live birth; NND; 2nd twin; Male
Q790	DIAPHRAGMATIC HERNIA (L)	Live birth; 2nd twin; Female
Q874	MARFAN SYNDROME	} Live birth; 1st twin; Male
Q874		} Live birth; 2nd twin; Female
Q900	TRISOMY 21	Live birth; 2nd twin; Male
D1810	CYSTIC HYGROMA (MASSIVE)	MCDA twins; Selective reduction
Q743	ARTHROGRYPOSIS	Selective reduction
Q894	CONJOINED TWINS	Termination at 14 weeks
Q898	ACARDIAC TWIN SEQUENCE (TRAP)	Termination at 16 weeks

Selective reductions were performed in two cases. In both cases, there was no abnormality of the co-twin and the pregnancies progressed to live birth.

Fetal structural defects in twin pregnancies can be grouped into those which also occur in singletons and those specific to the twinning process, the latter being unique to monozygotic twins. For any given defect, the pregnancy may be concordant or discordant in terms of both the presence or type of abnormality and its severity. There is no increased risk of congenital abnormalities in pregnancies from assisted reproduction compared to those achieved spontaneously.

[6] In addition, 24 sets of triplets were delivered during the review period without abnormality.

Discordance within dizygotic pregnancies is the norm; the co-twin is typically unaffected. One example relates to the diagnosis of arthrogryposis. This was a dichorionic/diamniotic twin pregnancy. The second twin was a stillborn male at 37 weeks' gestation, having undergone feticide at 29 weeks' gestation for multiple fetal anomalies. His co-twin, a live born baby girl, was delivered in good condition.

Discordance within monozygotic pregnancy is uncommon.[7] However, in one example listed above a massive cystic hygroma was noted in the first twin of an MCDA pregnancy. The co-twin appeared structurally normal but was appreciably small for dates even in the mid-trimester. Growth parameters improved with the selective reduction of the twin with the hygroma allowing a planned delivery of the survivor at 29 weeks' gestation.

Concordance of defects, (both fetuses being affected), is uncommon, being found in about 10% of dichorionic and 20% of monochorionic pregnancies. Marfan syndrome was formally diagnosed between 1-12 months in dizygotic twins although the diagnosis had been strongly anticipated on basis of family history.

Conjoined twins, (Q894)

Symmetrical conjoined twins are complete same sex twins joined at certain body sites. Conjoined twins occur in 1:50,000 births. The most common type is thoracophagus. Ultrasound diagnosis is based on a lack of separation, synchronicity of movement, and shared body organs. Prognosis depends on the extent of fusion.

Q894	CONJOINED TWINS	Termination at 13 weeks' gestation

In the above case termination of pregnancy was performed following early ultrasound diagnosis at thirteen weeks' gestation. The conjoined twins both had large cystic hygromas and shared a common heart and liver.

Acardiac Twin Sequence/Twin Reverse Arterial Perfusion Sequence, (Q898)[8]

Often considered to be the most severe form of early twin-to-twin transfusion syndrome. Acardius is anatomically misleading term in that most supposedly acardiac foetuses have at least a rudimentary, although non-functioning, heart. Ultrasound diagnosis is based on the detection of a 2nd twin with absent or rudimentary heart, the detection of reversed arterial perfusion and signs of cardiac failure in the pump twin.

Q898	ACARDIAC TWIN SEQUENCE	Termination at 16 weeks' gestation

[7] Discordances in monozygotic twin pregnancies are difficult to explain but various suggestions have been made e.g. the consequence of variation in gene expression (secondary to postzygotic mutation, parenteral imprinting effects or asymmetric X-inactivation); asymmetric splitting of the cell mass, in either volume or cytoplasmic content, resulting in unequal potential for development, (the 'Christmas cracker' hypothesis); splitting after laterality gradients are determined, resulting in malformations of laterality, such as cardiac and mid-line defects; or haemodynamic factors in monochorionic pregnancies resulting in abnormal flow patterns, and thence in cardiac defects or the twin reversed arterial perfusion sequence.

[8] The coding of TRAP sequence should include P023 'TRAP sequence' as the primary malformation with Q249 'Acardia' and Q000 'Anencephaly' as an essential minimum. Other common malformations such as absent upper limbs, rudimentary alimentary tract etc. should also be coded.

GESTATIONAL AGE

The mean gestation at delivery for live born infants with abnormality, (n=256), was 38 weeks, (range 29 to 42 weeks).

Figure 1.9: Gestational age (weeks) at delivery for all live births, (n=256)

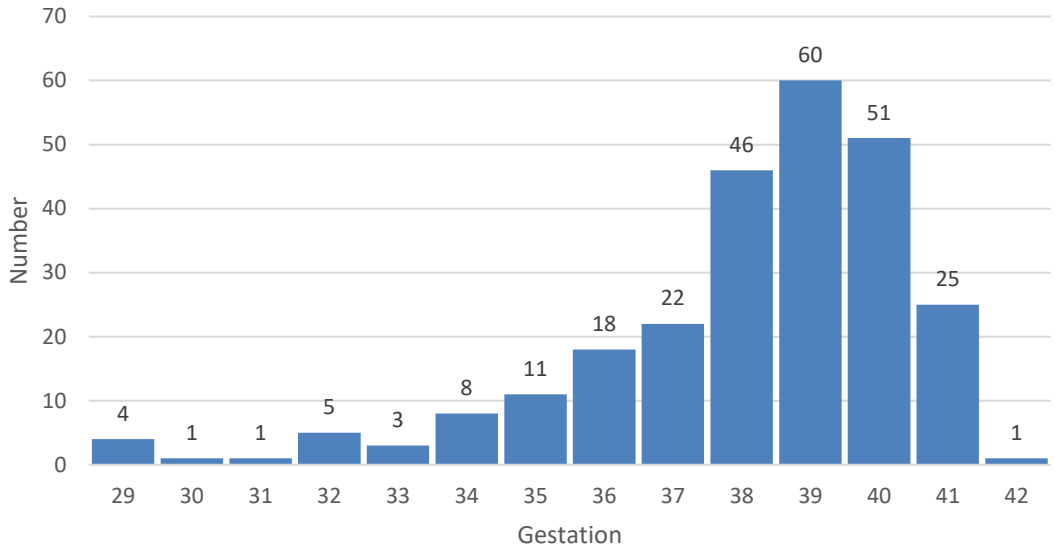
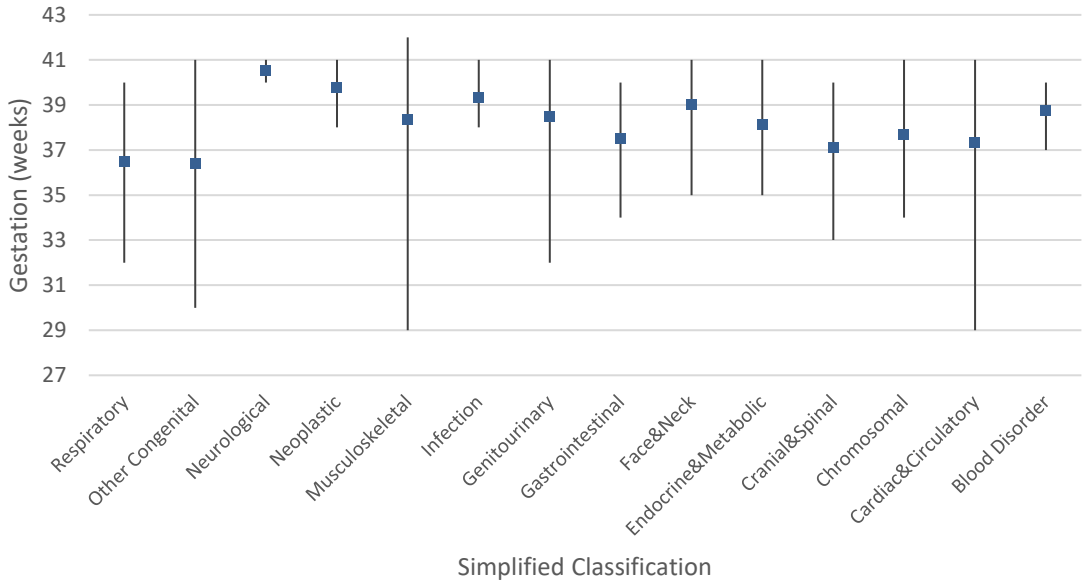
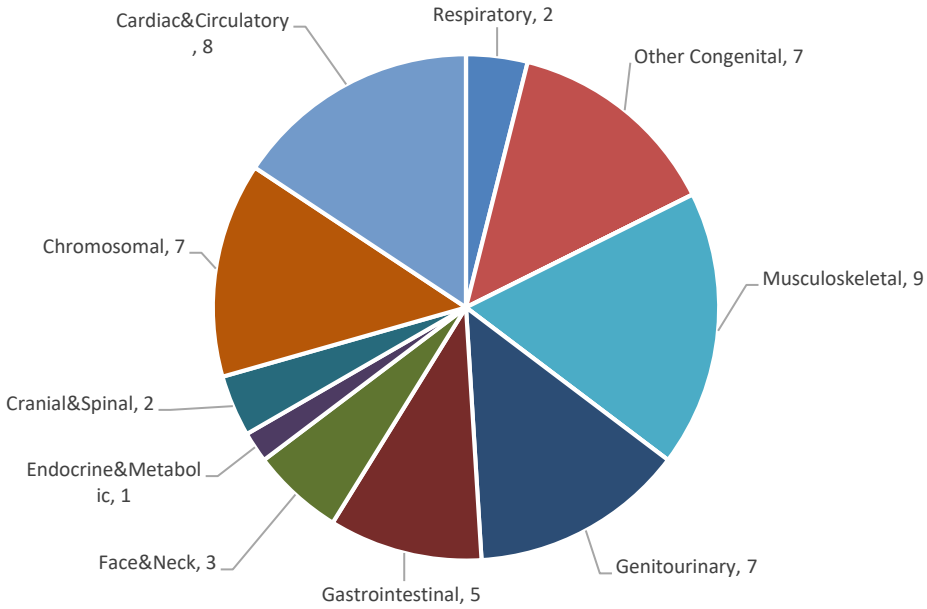


Figure 1.10: Minimum, mean and maximum gestational age at delivery of live born infants by simplified classification



Fifty-one of these infants were delivered prematurely, (< 37 weeks' gestation), (Figure 1.11).

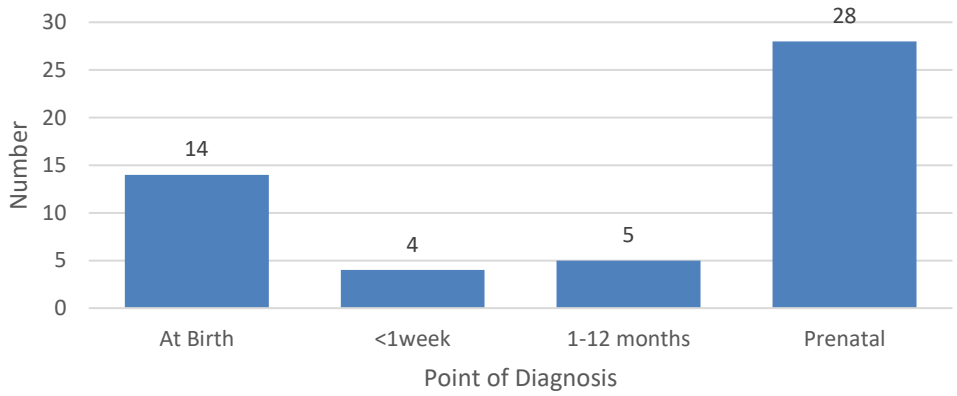
Figure 1.11: Preterm Live births by Primary Abnormality Category, (Simplified), (n=51)



The mean maternal age at time of preterm live birth of an infant with abnormality was 29.2 years, (range 17 – 39 years).

Of those babies delivered prematurely a prenatal diagnosis of abnormality had been made in twenty-eight cases, (54.9%), (Figure 1.12). A diagnosis of primary abnormality was made either at birth or within the first week of life in a further 35%, (n=18).

Figure 1.12: Point of diagnosis of primary abnormality for infants delivered prior to 37 weeks' gestation, (n=51)



Four babies with significant abnormality were delivered prior to 30 weeks' gestation.

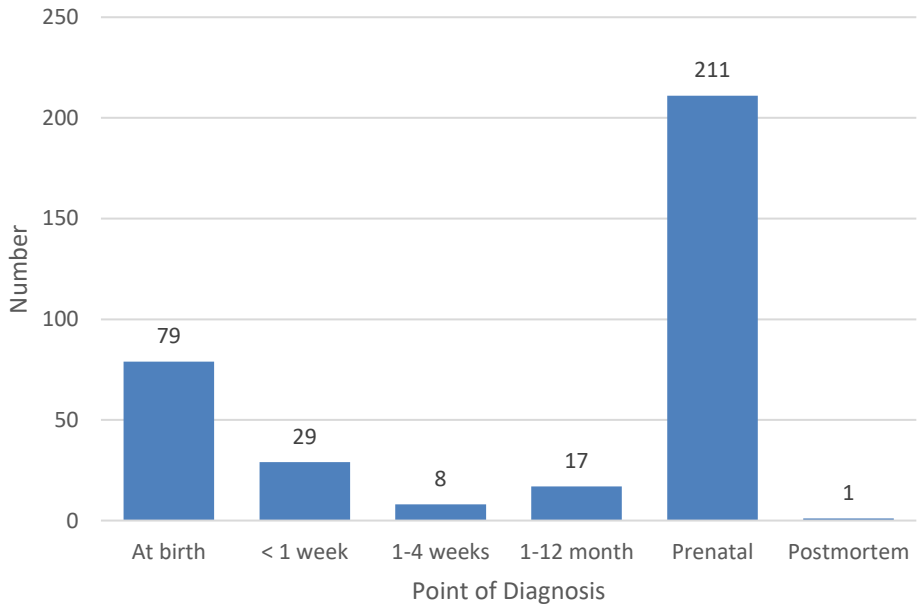
Q2510	COARCTATION AORTA (PRE-DUCTAL)	Female; Diagnosis 1-12 months
Q692	POLYDACTYLY - 6 TOES BILAT	Male; Prenatal Diagnosis
Q772	ASPHYXIATING SHORT RIB THORACIC DYSPLASIA	Male; Prenatal Diagnosis; Twin
Q790	DIAPHRAGMATIC HERNIA (L)	Female; Prenatal Diagnosis; Twin

In each case the mother had presented in preterm labour: these were not iatrogenic preterm births.

Point of diagnosis

Data are available for the 'point of diagnosis' or 'date of discovery' if it is preferred, (Figure 2.1). However, it is important to recognize that this does not necessarily imply the point at which the primary abnormality was first detected or diagnosed and some care must be exercised when considering this data. Under EUROCAT definitions the 'point of diagnosis' is the date on which the fetus or infant is first suspected or recognized as being malformed even if a detailed diagnosis is not available.

Figure 2.1: Point of Diagnosis for Primary Abnormality, (n=345)

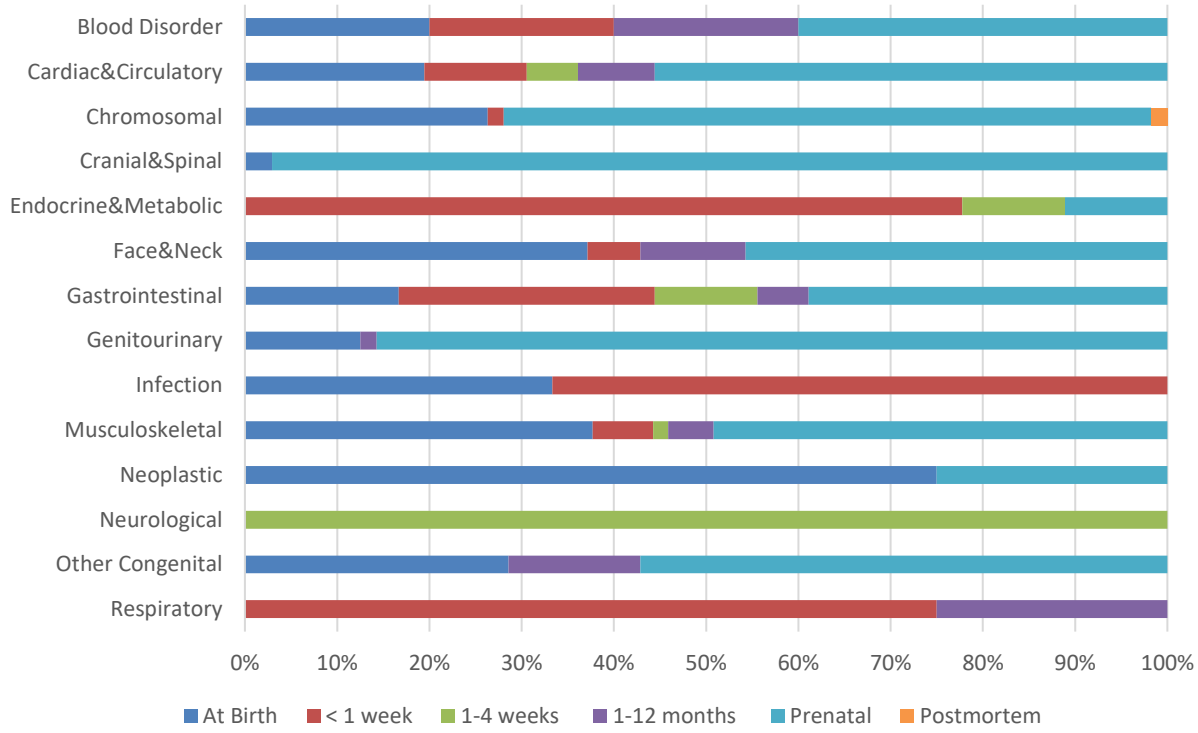


The majority of defined primary abnormalities were diagnosed prenatally, (n=211, 61%). The remaining cases were largely diagnosed either at birth or within the first week of infant life, (n=108, 31%).

A chart demonstrating point of diagnosis of primary abnormality, as defined under the 'simplified' classification described above, is produced, (Figure 2.2).

Ninety-seven percent of 'Cranial & Spinal' abnormalities, 86% of 'Genitourinary' abnormalities and 70% of 'Chromosomal' disorders are diagnosed prenatally. Fifty-six percent of primary 'Cardiac & Circulatory' disorders are also diagnosed on prenatal scan.

Figure 2.2: Point of diagnosis of primary abnormality by category, ('simplified'), (n=345)



AT BIRTH

A total of 79 primary abnormalities were diagnosed at birth.

The majority were abnormalities of the musculoskeletal system, (n=23, 29.1%). Typically, these were cases of talipes equinovarus, developmental dysplasia of the hip and limb defects particularly duplications of the thumb. However, two cases of diaphragmatic hernia and two cases of osteogenesis imperfecta were also diagnosed shortly after delivery.

'Chromosomal' and 'Face & Neck' abnormalities were next most commonly diagnosed at birth. Fourteen cases of Trisomy 21, (Down syndrome)[9], and one case of Trisomy 18, (Edward's syndrome), were diagnosed at birth. Abnormalities of the 'Face & Neck' included 8 cases of oro-facial clefting, 2 cases of congenital cataracts and 2 cases of microtia.

Hypospadias accounted for most 'Genitourinary' abnormalities evident at birth. It was however an incidental finding in a case of Russell-Silver syndrome.

[9] In most cases the mother had declined screening or diagnosis when offered. Of course, a small number of cases will always occur among screened pregnancies deemed to be low risk.

Q8717	RUSSELL-SILVER SYNDROME	Male; Preterm delivery; Hypospadias

Russell-Silver syndrome is associated with significant asymmetry and short stature. Other characteristics can include syndactyly, triangular facial features, short incurved 5th finger and café au lait spots. In a small minority, mild neurological delay can occur. This case had been picked-up antenatally due to significant inta-uterine growth retardation but without formal diagnosis. Labour had been induced at 34 weeks' gestation.

Skin disorders such as portwine stain and haemangioma are first evident at time of birth. A variety of coding opportunities present themselves in these situations and similar lesions may appear under different groupings.

D180	HAEMANGIOMA ® FOREARM	Female; Term delivery
D1800	CAPILLARY HAEMANGIOMA ® EYELID & EYEBROW	Female; Term delivery
Q8250	PORT WINE STANE (L) LEG FROM BUTTOCK TO FOOT	Male; Term delivery
Q8258	CAPILLARY MALF - EXTENSIVE - FOREHEAD/UPPER EYELIDS	Male; Term delivery
Q8581	STURGE-WEBER SYNDROME	Female; Term delivery

Sturge-Weber syndrome is a sporadic congenital disorder involving the brain, skin and eyes. There is a facial port wine stain, a venous angioma of the leptomeninges and choroidal angioma. The angioma usually involves just one side of the brain and varies in extent. Epilepsy is a complication in 75-90% of cases.

WITHIN 1ST WEEK

Congenital abnormality was diagnosed in 29 cases during the first week of life. As might be expected the majority, (n=7, 24.1%), of these diagnoses were related to disorders of the endocrine and metabolic system.

A diagnosis of congenital hypothyroidism was made on routine newborn blood spot testing in two infants. Testing in the first week also identified five cases of cystic fibrosis.

Disorders of the gastrointestinal system where the next most common grouping, (n=5) and included 2 cases of Hirschsprung's disease.

Disorders of the 'Cardiac & Circulatory' system presenting in the first week of life included a peri-membranous VSD, Tetralogy of Fallot, Tricuspid valvular stenosis and coarctation of the aorta.

Developmental dysplasia of the hip was evident within the first week of life in four infants, (all female).

Two further cases of congenital cataract were diagnosed.

The ICD 10 codes P00 to P96 relate to certain conditions that have their origin in the perinatal period even though death or morbidity may not occur until later. This grouping includes infections specific to the perinatal period such congenital rubella, (P350), and CMV, (P351), infections, congenital toxoplasmosis, (P377) and of course congenital pneumonia, (without specified organism).

P239	CONGENITAL PNEUMONIA	Male; Delivered at 38 weeks
P239	CONGENITAL PNEUMONIA	Male; Delivered at 39 weeks

Glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency), is an X-linked recessive inborn error of metabolism that predisposes to haemolysis and resultant jaundice in response to several triggers, such as certain foods, illness, or medication. Neonatal jaundice is a common presentation.

D550	G6PD DEFICIENCY	Male; Delivered at 37 weeks

BETWEEN 1-4 WEEKS

A total of 8 cases were diagnosed between 1 and 4 weeks of infant life. One case of PKU was determined by newborn blood spot screening and routine testing for congenital hearing loss identified two cases.

H919	CONGENITAL DEAFNESS	Male; Delivered at 41 weeks
Q165	HYPOPLASTIC COCHLEAR NERVES	Female; Delivered at 41 weeks

Transposition of the Great Arteries was diagnosed in a female infant. Aortic stenosis with dysplastic valve was diagnosed in a male infant.

There were two cases associated with malrotation of the bowel.

Q433	MALROTATION	Female; Delivered at term
Q4330	MALROTATION DUODENUM	Male; Delivered at 37 weeks

DIAGNOSED AFTER 1 MONTH BUT WITHIN 1 YEAR

A primary congenital abnormality was diagnosed in a total of 17 cases after 1 month but within 1 year of infant life. Abnormalities of the face and neck account for 25% of these cases with two further cases of congenital cataract, one case of congenital glaucoma and a seemingly late diagnosis of cleft soft palate.

Q8708	PIERRE ROBIN SEQUENCE	Male; Live birth at term

Furthermore, a diagnosis of Pierre Robin sequence with cleft soft palate and congenital glaucoma was confirmed.

A female infant, delivered prematurely at 29 weeks' gestation, was diagnosed with a preductal coarctation of the aorta. A male infant born at term had a persisting large PDA which required surgical closure. A diagnosis of dilated cardiomyopathy was also achieved.

I420	DILATED CARDIOMYOPATHY	Male; Live birth at 39 weeks

Dizygotic twins delivered at 35 weeks' gestation had a presumptive diagnosis of MArfan syndrome confirmed by genetic testing.

A male infant was diagnosed with Haemophilia A. Factor VIII levels were very low at just 1 iu/dl. There was no prior history of haemophilia A in the family. Molecular studies subsequently demonstrated a frameshift mutation and confirmed the mother as a carrier.

D66X	HAEMOPHILIA A (FACTOR VIII) - SEVERE	

A male fetus was noted to have a persistently dilated bladder on antenatal ultrasound scan. Despite involvement of fetal medicine and paediatric services a diagnosis of posterior uretheral valves was delayed.

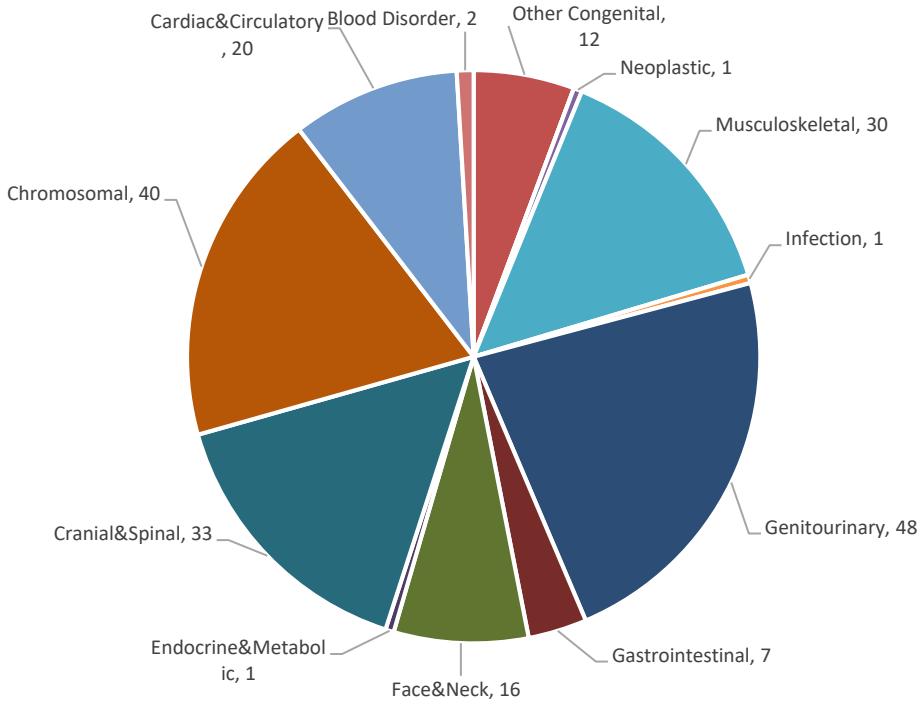
Q6420	POSTERIOR URETHRAL VALVES	Male; Live birth at term

PRENATAL DIAGNOSIS

Most diagnoses of congenital abnormality were made in the prenatal period, (n=211).

Chromosomal disorders and abnormalities of the cranio-spinal system were the predominate diagnostic groupings, closely followed by genitourinary and musculoskeletal disorders, (Figure 2.3).

Figure 2.3: Prenatal diagnosis by primary abnormality (Simplified Classification), (n=211)



POINT OF DIAGNOSIS

Of the 40 cases associated with chromosomal abnormality the majority were Down syndrome, (n=23, 57.5%).

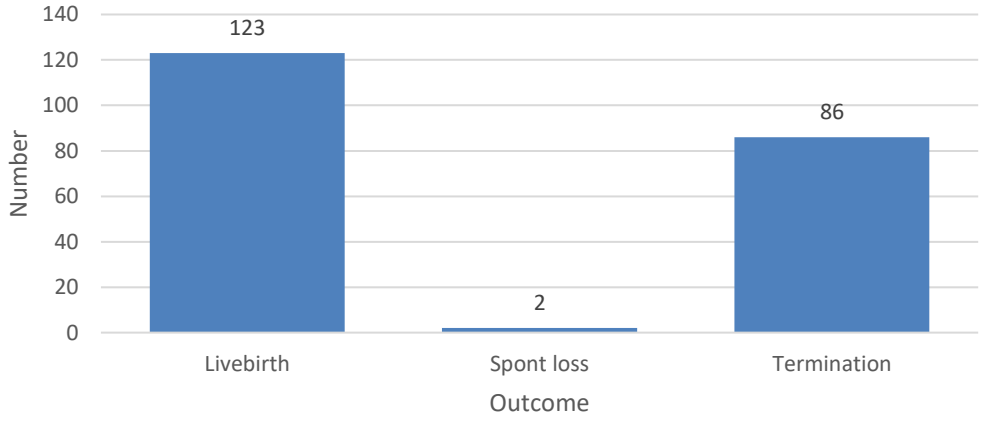
Ninety-seven percent of all cranial and spinal defects were diagnosed on prenatal ultrasound scan.

Cardiac and circulatory disorders diagnosed on antenatal scan included double outlet right ventricle, transposition of the great arteries, isomerism, congenitally corrected transposition, tetralogy of Fallot, total anomalous pulmonary venous drainage and coarctation of the aorta.

Primary disorders of the genitourinary system subject to prenatal diagnosis included ovarian cysts, aphalia, renal agenesis, hydronephrosis, multicystic dysplastic kidney, duplex kidney, ectopic kidney and posterior uretheral valves.

When a prenatal diagnosis of abnormality was made eighty-six cases were terminated, (41%), but in the majority of cases, (n=123, 58%), the pregnancy continued to live birth, (Figure 2.4).

Figure 2.4: Outcome of pregnancy following prenatal diagnosis of abnormality, (n=211)



POSTMORTEM DIAGNOSIS

There was one case where the diagnosis has been recorded as having been made at post-mortem.

Q963	TURNER MOSAIC SYNDROME	Stillborn female infant at 38 weeks' gestation

This was a completely unanticipated stillbirth of a 2.95Kg female infant to a 32-year-old mother. There were no significant external dysmorphic features or internal congenital anomalies. Chromosome analysis demonstrated mosaic Turner syndrome 45X/46XX but a small placenta with evidence of fetal thrombotic vasculopathy was thought to be contributory to intrauterine demise.

Pregnancy Outcome

A pregnancy outcome is recorded for all 345 cases. Most cases, (n=256, 74%), were live-born, (Figures 3.1 and 3.2).

Figure 3.1: Pregnancy outcome, (n=345)

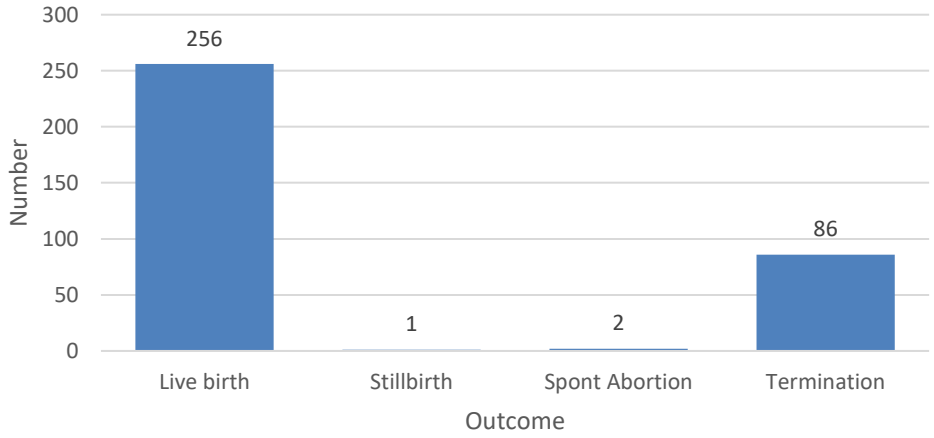
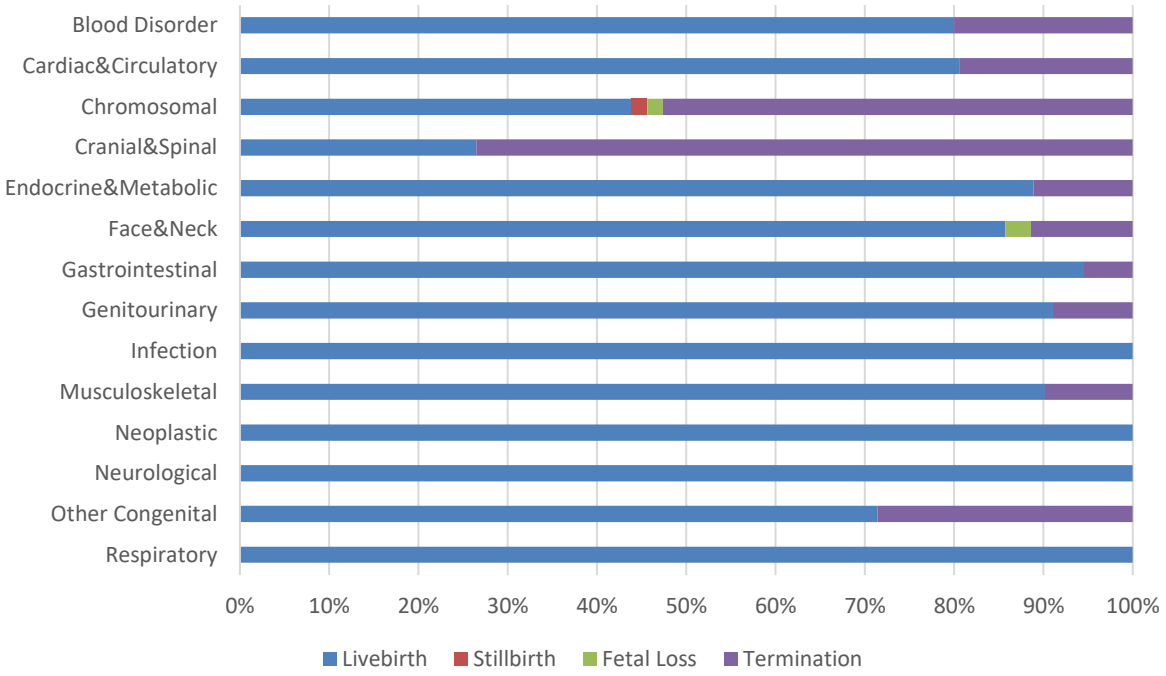


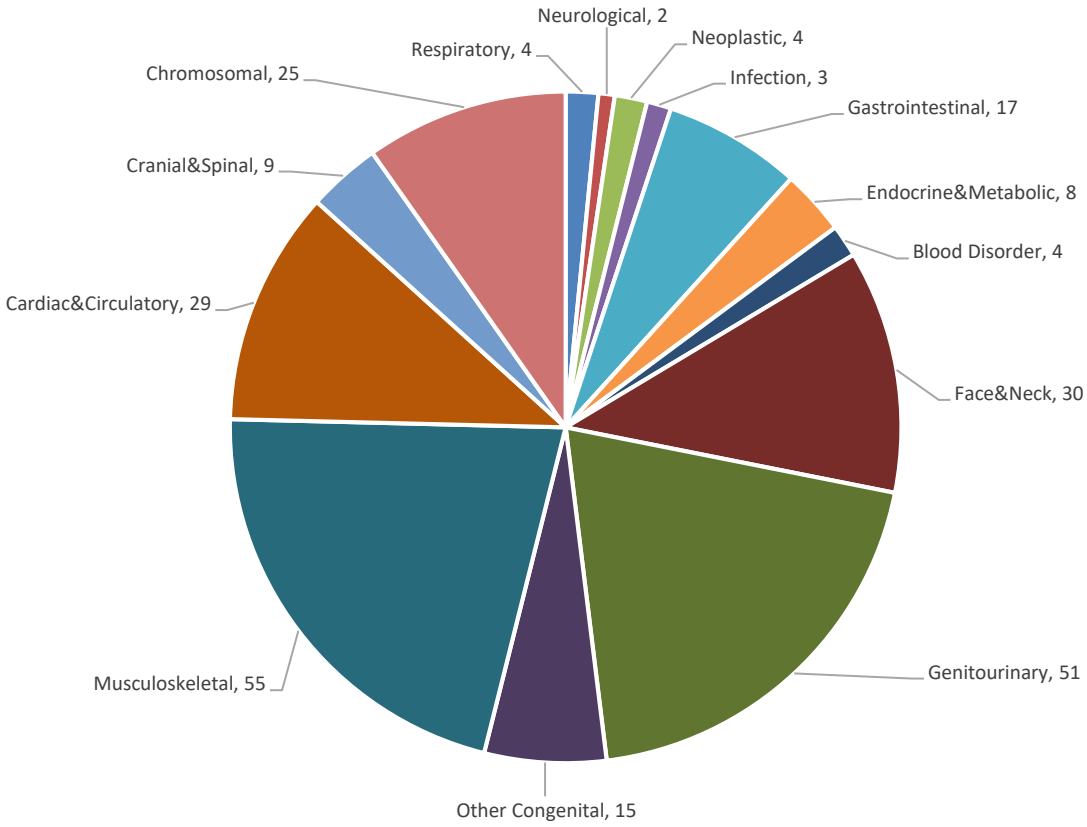
Figure 3.2: Pregnancy outcome by 'simplified' classification, (n=345)



LIVE BIRTHS

Live birth was the documented outcome for 74% of the described cases, (n=256). The mean gestation at delivery was 38 weeks, (range 29 to 42 weeks). All infants with congenital neoplastic lesions, infections or primary abnormalities of the respiratory or neurological systems were live born. Only 26% of diagnoses of cranial & spinal abnormalities resulted in a live birth.

Figure 3.3: Live birth by primary abnormality, (Simplified classification), (n=256)



A total of four 'Neoplastic' abnormalities were coded in the data for 2015-2016. All were associated with live births. Three were classified as hamartomas, (haemangioma and lymphangioma), including a lymphangioma of the left axilla in a female infant. There was one teratoma.

D215	SACROCOCCYGEAL TERATOMA - INTRAPELVIC	Live birth at term; Female infant

Teratomas are germ-cell tumours that contain elements derived from all three germ cell layers. As a result, they contain various epithelial, mesenchymal and neural tissue components. Although rare in absolute

terms, (1:38,500 live births), sacrococcygeal teratoma is the most frequent large tumour of the neonate and most common germ-cell tumour in children. It is more common in female infants.

The above case was diagnosed on ultrasound scan at 32 weeks' gestation. A cystic structure was confirmed within the fetal pelvis and anterior to the sacrum. An MRI scan raised the possibility of Type IV[10] sacrococcygeal teratoma, with a differential including other cystic pelvic tumours such as anterior sacral myelomeningocoele, neurenteric or duplication cyst.

There were two cases of infants with a congenital pneumonia. A single case of congenital CMV had been diagnosed prenatally on 20-week anomaly scan when it was noted that the fetus had slightly bright bowels. An infection screen was performed and primary fetal CMV infection was confirmed by PCR performed on amniotic fluid after an amniocentesis.

P351	CONGENITAL CMV INFECTION	Prenatal diagnosis; Male infant

The neurological lesions diagnosed in live born infants were related to congenital hearing loss.

All cases of coarctation of the aorta, tetralogy of Fallot, tricuspid stenosis and both cases of heterotaxy syndrome were associated with live births.

STILLBIRTH

There were a total of 48 stillbirths in Greater Glasgow & Clyde during 2015-2016. The data records that only one of these stillbirths had a defined congenital abnormality.

Q963	TURNER MOSAIC SYNDROME	Female; Stillborn at 38 weeks

SPONTANEOUS FETAL LOSS

There were two cases classified as spontaneous fetal loss at 20 weeks' gestation. Previous reports have documented a high proportion of chromosomal abnormalities in this group.

D1810	CYSTIC HYGROMA - VERY LARGE	VSD
Q960	TURNER SYNDROME	Cystic Hygroma

A cystic hygroma with generalized fetal hydropic change was noted on 12 week booking scan. A repeat scan confirmed these findings and noted pleural effusion and a small left heart with VSD. The parents declined karyotype and continued with the pregnancy accepting that it would be likely to end with intrauterine fetal demise. Post-mortem examination was declined.

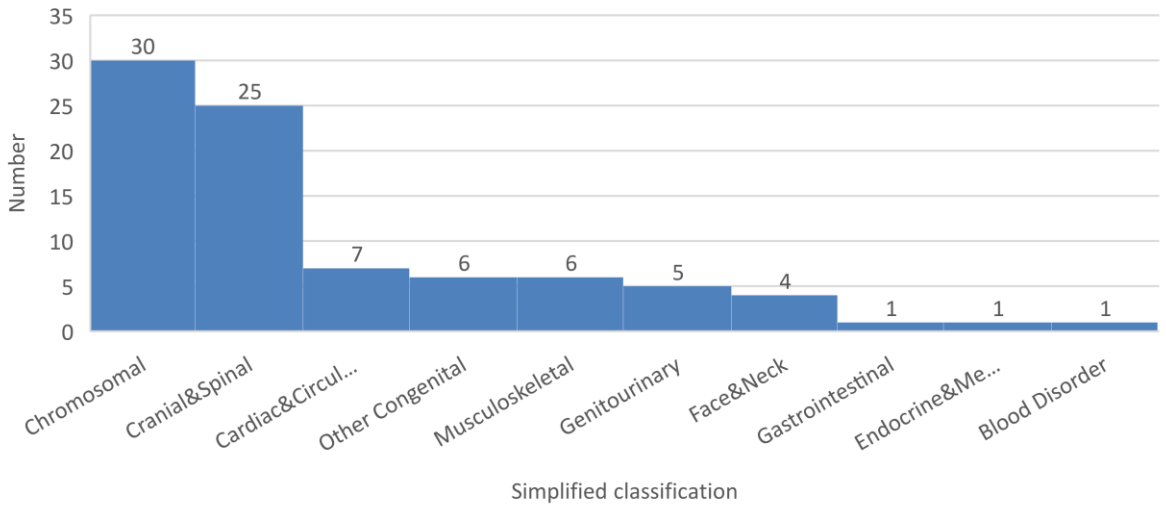
[10] American Academy of Paediatric Surgeons Survey (AAPSS) Classification

TERMINATION OF PREGNANCY[11]

A total of 86 cases were terminated following prenatal diagnosis. The mean gestation for termination was 18.2 weeks, (range 10-31 weeks).

Chromosomal abnormality was the commonest indication for terminations, (n=30), followed by neural tube defects, (Figure 3.4).

Figure 3.4: Diagnostic indication (simplified) for termination of pregnancy, (n=86)



Just what constitutes a serious handicap becomes an issue when termination of pregnancy is likely to take place after 24 weeks' gestation[12].

Live birth is possible after 22 weeks' gestation and when a decision has been made to terminate a pregnancy for abnormality after 22 weeks fetocide should normally be performed. When the abnormality is not compatible with survival termination without fetocide may be undertaken but only after full discussion with parents and health professionals. If the abnormality is not lethal and termination is undertaken after 22 weeks' failure to perform fetocide could result in a live birth contrary to the intention of the process. [13]

Fetocide & termination of pregnancy was performed after 24 weeks' gestation on nine occasions. Cranial and spinal anomalies are the commonest indication for 'late' termination.

[11] With termination of pregnancy a prenatal diagnosis may not be verified for many reasons including the method of termination, the condition of the specimen or a lack of post-mortem examination.

[12] *Termination of Pregnancy for Fetal Abnormality in England, Scotland & Wales.* RCOG. May 2010.

[13] A fetus born alive after termination is deemed to be a child irrespective of gestational age at birth and should be registered as a livebirth.

Q0000	ANENCEPHALY	Termination at 24 weeks
Q234	HYPOPLASTIC (L) HEART	Termination at 24 weeks
Q039	VENTRICULOMEGALY - SEVERE	Termination at 25 weeks
Q870E	PENA-SHOKEIR	Termination at 25 weeks
Q900	TRISOMY 21	Termination at 25 weeks
Q039	VENTRICULOMEGALY - SEVERE	Termination at 30 weeks
Q998	UNBALANCED TRANSLOC CHROMOS 7	Termination at 32 weeks
Q743	ARTHROGRYPOSIS	Termination at 29 weeks; Delivered at 37 weeks
Q0435	HYDRANENCEPHALY	Termination at 38 weeks

A dichorionic diamniotic pregnancy was delivered at 37+3 weeks' gestation. Twin 1 was a live baby girl, born in good condition. However, twin 2 was a stillborn male, having undergone feticide at 29 weeks' gestation for multiple fetal anomalies with a final diagnosis of arthrogryposis.

A woman booked late and had her first scan at about 38 weeks' size. There was considerable concern regarding the baby's head anatomy. Hydranencephaly was diagnosed. Termination of pregnancy was performed with fetocide and then drainage of the fetal head prior to induction of labour.

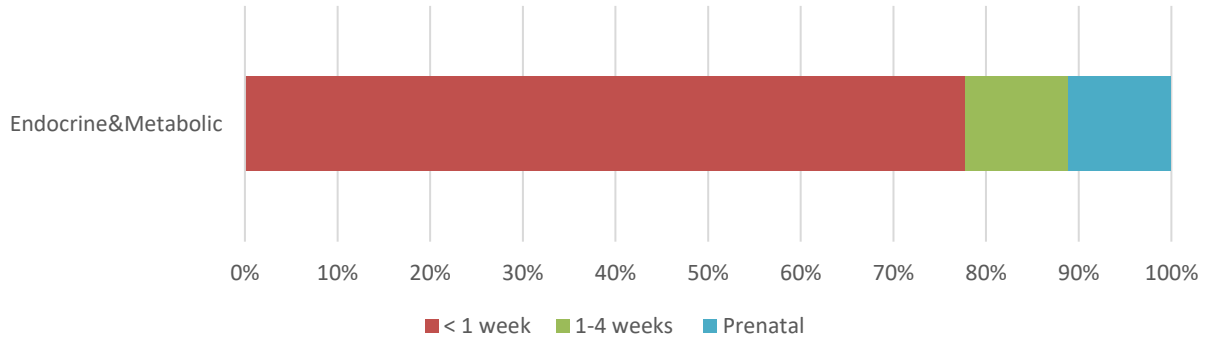
A further 9 cases are listed where fetocide was performed prior to mid-trimester termination.

Q052	L/S SPINA BIFIDA w HYDROCEPH	Termination at 22 weeks
Q052	L/S MYELOMENINGOCELE - MASSIVE + HYDROCEPHALUS	Termination at 22 weeks
Q0521	L/S SPINA BIFIDA (OPEN) + HYDROCEPH	Termination at 22 weeks
Q232	MITRAL ATRESIA	Termination at 22 weeks
D821	DI GEORGE	Termination at 23 weeks
Q234	HYPOPLASTIC LEFT HEART	Termination at 23 weeks
Q641	EXSTROPHY BLADDER	Termination at 23 weeks
Q780	OSTEOGENESIS IMPERFECTA	Termination at 23 weeks
Q938	UNBALANCED DELETION CHROMOSOME 4 - 4p14	Termination at 23 weeks

Endocrine & Metabolic Disorders

A total of 11 cases of endocrine and metabolic disorder are classified in the data. The disorder is classified in the primary position in all but 2 of the instances. These disorders are typically diagnosed as a consequence of new-born bloodspot screening within the first few weeks of life, (Figure 4.1).

Figure 4.1: Point of Diagnosis for Primary Endocrine & Metabolic Disorders, (n=9)



CONGENITAL HYPOTHYROIDISM (E03)

Permanent primary congenital hypothyroidism is the commonest cause of preventable intellectual disability. Congenital hypothyroidism can be the result of a missing or 'misplaced' thyroid gland, hereditary condition, maternal iodine deficiency, maternal thyroid condition and medications. There are many anomalies of development of the thyroid gland including ectopia along the path of descent of the thyro-glossal duct. The thyroid may be completely absent but most typically a sublingual thyroid ectopy without lateral lobes is evident.

Three cases of congenital hypothyroidism are described in the data and all were live born. In each case the diagnosis of hypothyroidism was made on bloodspot screening within the first week of life.

E031	CONGENITAL HYPOTHYROIDISM	Male
E0312	CONGENITAL HYPOTHYROIDISM - SUBLINGUAL ECTOPIA	Female
Q900	TRISOMY 21	Female

IN-BORN ERRORS OF METABOLISM

In-born errors of metabolism, (IEM), are a group of disorders in which a single gene defect causes a clinically significant block in a metabolic pathway leading either to an accumulation of the substrate or a deficiency of the product. They are individually rare but collectively common although some may be present in high

frequency in certain ethnic groups. Many IEM's are associated with significant morbidity and mortality in affected individuals.

DISORDERS OF AROMATIC AMINO ACID METABOLISM (E70)

Phenylketonuria, ('Classical PKU') (E700)

Phenylketonuria (commonly known as PKU) is an inherited disorder that increases the levels of a substance called phenylalanine in the blood. Mutations in the *PAH* gene cause phenylketonuria. The *PAH* gene provides instructions for making an enzyme called phenylalanine hydroxylase. This enzyme converts the amino acid phenylalanine to other important compounds in the body. If gene mutations reduce the activity of phenylalanine hydroxylase, phenylalanine from the diet is not processed effectively. This amino acid can build up to toxic levels in the blood and other tissues. Because nerve cells in the brain are particularly sensitive to phenylalanine levels, excessive amounts of this substance can cause brain damage. Most cases of PKU are detected shortly after birth by new born screening, and treatment is started promptly. Thus, the severe signs and symptoms of classic PKU are rarely seen.

E700 PKU

The case listed above was a male infant delivered at 39 weeks' gestation. The diagnosis was made between 1 – 4 weeks.

Albinism (E703)

Waardenburg syndrome is associated with disorder of skin and hair pigmentation and usually inherited in an autosomal dominant pattern. The four type of Waardenburg syndrome are typically distinguished by their physical characteristics rather their genetic cause which can be confusing, (types I and III Waardenburg syndrome are caused by mutations in the *PAX3* gene, mutations in the *MITF* and *SNAI2* genes are responsible for type II and type IV is associated with mutations in the *SOX10*, *EDN3*, or *EDNRB* genes).

Types I and II have very similar features, although people with type I almost always have eyes that appear widely spaced and people with type II do not. In addition, hearing loss occurs more often in people with type II than in those with type I. Type III is associated with limb defects and hearing loss. Type IV has signs and symptoms of Hirschsprung's disease.

Q660 TEV BILAT Albinism

This was a male infant delivered at term. Prenatal diagnosis is 'claimed' but this in fact relates to the primary malformation diagnosis of Talipes Equino Varus, (TEV) pointing towards, but not confirming, type III disease.

CYSTIC FIBROSIS, (E84)

Cystic fibrosis is inherited as an autosomal recessive condition and affects the lungs, pancreas, liver and intestine. It is caused by any one of many mutations in the gene responsible for the production of the protein cystic fibrosis transmembrane conductance regulator (CFTR). The most common mutation in the West of Scotland population is ΔF508, a deletion of three nucleotides that results in the loss of the amino acid phenylalanine at the 508th position on the protein.

There were six cases of cystic fibrosis diagnosed in the 2015-2016 cohort. The majority were live births with the diagnosis made on blood spot testing in the first week of life. One case was a prenatal diagnosis, (CVS at 12 weeks'), with subsequent termination.

E840[14]	CYSTIC FIBROSIS	Female
E840	CYSTIC FIBROSIS	Male
E840	CYSTIC FIBROSIS	Female
E840	CYSTIC FIBROSIS	Female
E840	CYSTIC FIBROSIS	Female; Ileal atresia
E840	CYSTIC FIBROSIS	Female; Prenatal diagnosis; Termination at 13 weeks' gestation

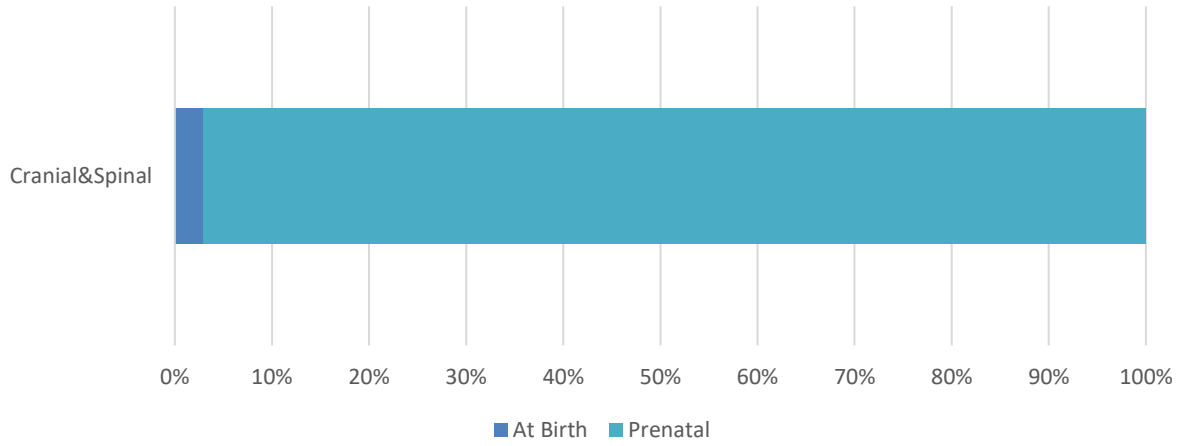
[14] The ICD 10 code E840 implies 'cystic fibrosis with pulmonary manifestations'. A similar coding of E841 would suggest 'cystic fibrosis with intestinal manifestations' such as distal intestinal obstruction or meconium ileus in cystic fibrosis, (but not meconium ileus in cases where cystic fibrosis is not thought to be present). Given the multi-system nature of this disorder it is strange that such a distinction is made.

Cranial & Spinal Abnormalities

CONGENITAL MALFORMATIONS OF THE NERVOUS SYSTEM, (Q00-Q07)

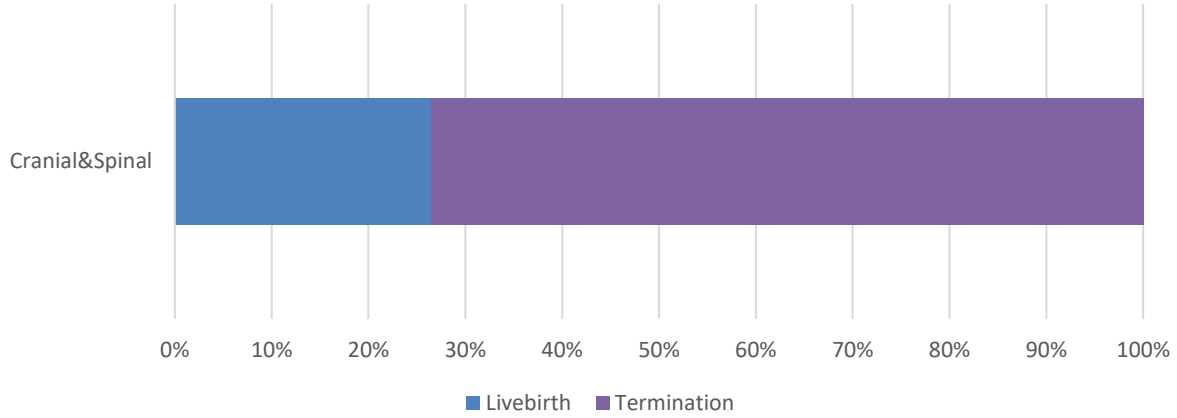
A total of fifty abnormalities of the central nervous system were recorded with thirty-four falling in the primary diagnostic position, (68%). Over ninety percent of diagnoses of primary cranial & spinal abnormality were made on prenatal ultrasound scan, (Figure 4.2).

Figure 4.2: Point of diagnosis bar chart, (n=34)



Most pregnancies in which a primary diagnosis of cranial or spinal abnormality was made ended in termination following prenatal diagnosis, (n=25, 73.5%), (Figure 4.3)

Figure 4.3: Outcome of Primary Cranial & Spinal Abnormalities, (n=34)



CRANIAL & SPINAL ABNORMALITIES

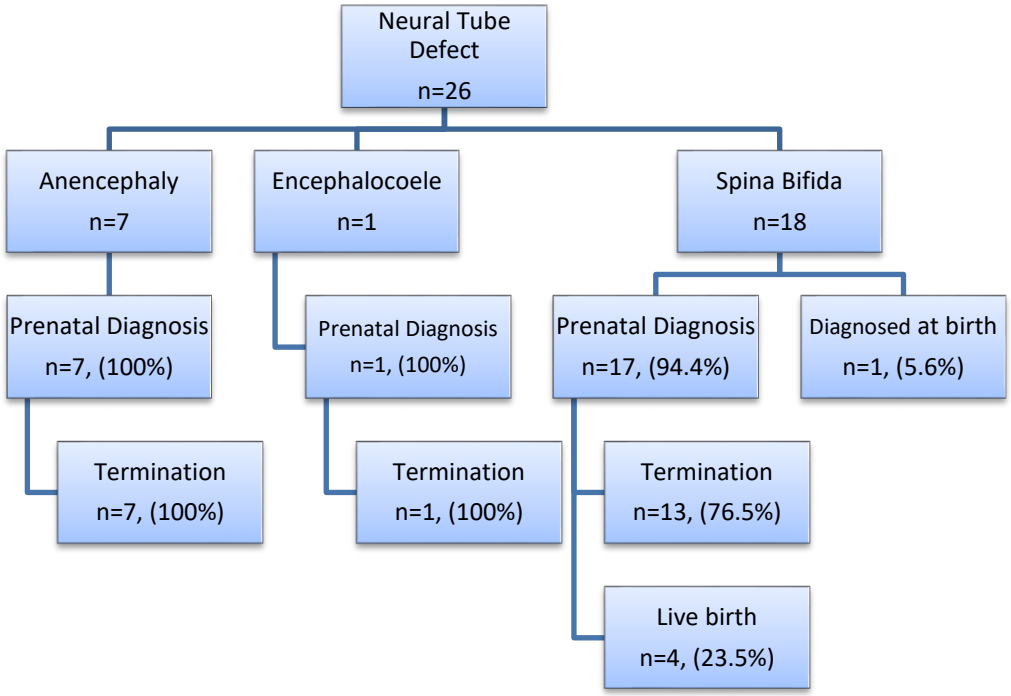
NEURAL TUBE DEFECTS, (Q00, Q01 & Q05)

Neural tube defects, (NTD's) are a heterogenous group of anomalies of the CNS resulting from defective closure of the neural tube during embryogenesis. NTD's can occur in association with chromosomal disorders, genetic syndromes and other patterns of multiple malformations or occasionally as the result of environmental teratogens. A common mechanism that explains all NTD's is yet to be defined. However, most are isolated defects resulting from a presumed interaction between environmental and genetic risk factors. Folate deficiency is the most well established risk factor. Dietary folate supplementation has been shown to reduce the risk of recurrence and even provide some primary prevention

Whereas overall prevalence rates for NTD's are relatively stable, (although some reduction is anticipated through the introduction of folic acid supplementation), the birth prevalence has declined because of early prenatal diagnosis and elective termination of affected pregnancies.

Twenty-six NTD's were defined in the 2015-2016 data, (Figure 4.4). Neural tube defects were always coded in the primary position.

Figure 4.4: Overview of Neural Tube Defects, (n=26)



Anencephaly, (Q000)

Anencephaly is defined as absence of the superior vault and cerebrum. It is the most common and severe anomaly of the central nervous system. The most striking feature at ultrasound is the presence of large

bulging eyes marking the superior boundary of the fetus. Abrupt spasmodic body movements are not uncommon. The prognosis is grave and the severity of the condition justifies termination of the pregnancy.

Seven cases were listed, all as isolated abnormalities. Termination was performed following prenatal diagnosis. One case was a late termination of pregnancy at 24 weeks' gestation.

Encephalocoele, (Q01)

A cephalocoele is a defect in the bony skull through which meninges and brain substance may protrude. It is the result of a defect of neural tube closure during the 6th week of gestation. The location of the defect is mid-occipital in 75% of cases, fronto-ethmoidal in 13% and parietal in 12%. The bony defect is usually small in comparison to the hernia sac. Cephalocoeles may appear in isolation or as a feature of various syndromes, (e.g. Meckel-Gruber syndrome & Roberts syndrome).

Q018	ENCEPHALOCELE - POSTERIOR	Termination at 21 weeks; VSD; Male

One case of encephalocele was diagnosed on prenatal scan and is listed as a posterior defect presumably occipital. On antenatal scan differentiation is required from cystic hygroma and teratoma.

Spina Bifida, (Q05)[15]

Spina bifida is a general term used to describe a neural tube defect of the spine in which part of the meninges or spinal cord or both protrudes through an opening in the vertebral column. Posterior defects of neural tube closure are among the most common fetal abnormalities. Studies have shown that NTD's are ultimately based on the inadequate expression of certain pattern control genes. This may be caused by gene deletion, exogenous teratogenic agents, (e.g. valproic acid), or vitamin deficiency.

In closed spina bifida the bony defect of the posterior vertebral arches, the herniated meninges and neural tissue are covered by a layer of skin.

The commonest associated abnormality was Arnold-Chiari Malformation, (Q070), consisting of downward displacement of the cerebellar tonsils through the foramen magnum.[16]

[15] Coding of spina bifida should be based on one code only. The codes in the Q05 section describe both the site of the defect and if hydrocephalus is present or not. The highest position of the defect is coded e.g. 'thoracic' if both thoracic and lumbar. The BPA 4th digit codes record if the defect was 'open' (1), 'closed' (2) or 'unknown' (9).

[16] There has been some uncertainty regarding the coding of spina bifida with Arnold Chiari malformation. In ICD/BPA9 there was a specified code for spina bifida with Arnold Chiari malformation. This code does not exist in ICD/BPA10. When coding spina bifida with Arnold Chiari malformation it is practice to use the best possible code for spina bifida within Q05 and add the code for Arnold Chiari, (Q070).

Q0511	T/L MYELOMENINGOCELE (OPEN) + HYDROCEPHALUS	Female; Live birth; 1st twin
Q052	L/S SPINA BIFIDA + HYDROCEPHALUS	Termination
Q052	L/S MYELOMENINGOCELE (HUGE) + HYDROCEPH	Termination
Q052	LUMBAR SPINA BIFIDA + HYDROCEPHALUS	Termination
Q052	L/S SPINA BIFIDA w HYDROCEPH	Termination
Q052	L/S MYELOMENINGOCELE + HYDROCEPH	Termination
Q052	L/S MYELOMENINGOCELE - MASSIVE + HYDROCEPH	Termination
Q0521	L/S MYELOMENINGOCELE	Live birth; Arnold-Chiari Malf.
Q0521	L/S SPINA BIFIDA (OPEN) + HYDROCEPH	Termination; Arnold-Chiari Malf.
Q0521	L/S MYELOMENINGOCELE (LARGE OPEN) w HYDROCEPH	Termination; Arnold-Chiari Malf.
Q0521	L/S SPINA BIFIDA - OPEN + HYDROCEPHALUS	Termination; Arnold-Chiari Malf.
Q057	L/S SPINA BIFIDA (LARGE)	Termination
Q0571	LUMBAR MYELOMENINGOCELE – OPEN	Live birth
Q0572	LUMBAR MYELOMENINGOCELE – CLOSED	Live birth
Q0572	L/S MYELOMENINGOCELE - SKIN COVERED	Live birth
Q0579	L/S SPINA BIFIDA	Termination
Q058	SACRAL MYELOMENINGOCELE	Termination
Q059	SPINA BIFIDA - EXTENSIVE (NO HYDROCEPH)	Termination; Arnold-Chiari Malf.

MICROCEPHALY, (Q02)

There were no cases of microcephaly described in the data for 2015-2016. However, current concerns regarding the Zika virus make some comment necessary. It is important to note that the prevalence of microcephaly varies considerably with annual fluctuations a likely consequence of the rarity of this condition. It is therefore difficult to ascertain a baseline prevalence. The shortcomings of many surveillance programmes coupled with the rarity of microcephaly mean that changes in prevalence, potentially due to Zika virus, could be missed.[17]

CONGENITAL HYDROCEPHALUS, (Q03)

Dilatation of ventricular system with impaired circulation and absorption of the cerebrospinal fluid,with or without enlargement of the skull.

Atresia of Foramina of Magendie & Luschka, (Q031)

Dandy Walker malformation is defined by hydrocephalus and partial or complete absence of the cerebellar vermis with a posterior fossa cyst that opens directly into the 4th ventricle. The aetiology is uncertain. The ICD 10 classification reflects the idea that atresia of the foramina of Magendie and Luschka is the underlying cause. However, cases have been described in which atresia has not been present and it is considered that the anomaly is a due to a more complex developmental error. Ultrasound scan reveals a cystic mass in the posterior fossa and an abnormally shaped cerebellum with some dilatation of the lateral ventricles.

[17] Morris JK et al. Prevalence of microcephaly in Europe. BMJ 2016; 354: i4721

One case is recorded with the abnormality as the primary diagnosis.

Q031	DANDY WALKER MALF	Female; Prenatal diagnosis; Live birth

This case was initially diagnosed at 12 weeks' gestation on ultrasound scan. The pregnancy continued with close antenatal monitoring. Delivery was a planned caesarean section at 38 weeks' gestation. The infant, a live born male weighing 3.02Kg, was transferred immediately to the Neonatal Team.

Dandy-Walker malformation is also described in a case of Meckel-Gruber syndrome

Q6190	MECKEL-GRUBER SYNDROME	Prenatal diagnosis; Termination at 20 weeks' gestation

This case is described later under disorders of the genitourinary system.

Ventriculomegaly, (Q038) & Unspecified Congenital Hydrocephalus, (Q039)

Congenital ventriculomegaly may not be due to fluid circulation abnormalities, but should be reported if the size of the ventricles is 15 mm or more. For less severe prenatally detected ventriculomegaly (10-14 mm) it is recommended to follow the case until further imaging and a final diagnosis has been found postnatally. Three cases are coded in the primary position.

Q039	VENTRICULOMEGALY - SEVERE	Prenatal diagnosis; Termination at 30 weeks
Q039	VENTRICULOMEGALY - SEVERE	Prenatal diagnosis; Termination at 25 weeks
Q039	HYDROCEPHALUS	Prenatal diagnosis; Termination at 20 weeks

Hydrocephalus is a secondary abnormality in a further case.

Q900	Trisomy 21	Prenatal diagnosis; Termination at 21 weeks

OTHER CONGENITAL MALFORMATIONS OF THE BRAIN, (Q04)

Agenesis of the Corpus Callosum, (Q0400)

The corpus callosum is a transverse fibre tract that connects the cerebral hemispheres at the base of the longitudinal fissure. It is not fully developed until 20 weeks' gestation. Ultrasound detection of a defect in the corpus callosum is difficult and requires a very detailed examination. The true frequency with which the corpus callosum fails to form is unknown. There may be asymptomatic individuals with partial or complete callosal agenesis.

Q0400	ABSENT CORPUS CALLOSUM	Live birth; Prenatal diagnosis
Q0400	AGENESIS CORPUS CALLOSUM	Live birth; Prenatal diagnosis
Q0400	AGENESIS CORPUS CALLOSUM	Live birth; Prenatal diagnosis; Porencephalic cysts

Agenesis of the corpus callosum is frequently associated with other abnormalities.

Q031	DANDY WALKER MALF	Live birth; Prenatal diagnosis
Q039	VENTRICULOMEGALY - SEVERE	Prenatal diagnosis; Termination at 30 weeks

Other Reduction Deformities of the Brain, (Q043)

Lissencephaly, (Q043)

Lissencephaly, ('smooth brain'), is a disorder consequent on defective neuronal migration between 12-14 weeks' gestation resulting is a failure to develop gyri and sulci.

Q998	MILLER DIEKER SYNDROME (17p13 deletion)	Female; Live birth at 36 weeks

Miller–Dieker syndrome (abbreviated MDS), is a micro deletion syndrome that is characterized by lissencephaly, (see later under 'Chromosomal' disorders).

Reduction Anomaly of the Cerebellum, (Q0432)

Classification systems for malformations of the cerebellum are varied and are constantly being revised as greater understanding of the underlying genetics and embryology of the disorders is uncovered. The prognosis of this developmental disorder is highly dependent on the underlying disorder. Cerebellar hypoplasia may be progressive or static in nature.

Q039	HYDROCEPHALUS	Prenatal diagnosis; Termination at 20 weeks

Hydrancephaly, (Q0435)

Hydranencephaly describes congenital absence of the cerebral hemispheres with preservation of midbrain and cerebellum. Occurrence is sporadic. It is generally considered to be an encepholoclastic lesion originating in the third trimester because of severe ischaemic insult(s) due to widespread vascular occlusion, infections or prolonged severe hydrocephalus.

On ultrasound examination, an intracerebral fluid collection is seen. This differs from hydrocephalus in that the brain mantle is absent. The falx cerebri may be absent or only partially visualized. It can be difficult to differentiate from alobar holoprosencephaly. The prognosis is grave and with prenatal diagnosis pregnancy termination is an option.

Q0435	HYDRANENCEPHALY	Late booker; Late diagnosis

NOTE: Malformations such as congenital spondylolisthesis and hemivertebral syndromes, (but not spina bifida occulta), are classified under 'Congenital disorders of the Musculoskeletal System'.

Cardiac & Circulatory Abnormalities

Congenital heart disease is a leading cause of infant mortality and structural cardiac anomalies are the most lesions most frequently missed by prenatal ultrasonography.

Congenital heart defects are those gross structural abnormalities of the heart or intra-thoracic vessels that are of actual or potential functional significance. They are one of the most important causes of infant morbidity and mortality and continue to constitute an important cause of disability and death in adult life. Birth prevalence is variously quoted between 50 and 150 per 10,000 total births.

There is a large body of evidence emerging on the genetic and non-genetic risk factors for congenital heart disease. The genetic causes include chromosomal syndromes, (e.g. Trisomy 18) and single gene disorders, (e.g. 22q11 Di George syndrome). Other determinants, (some of which are potentially modifiable), include maternal diabetes, therapeutic and non-therapeutic drug exposure and lifestyle characteristics.

The most severe forms of congenital heart disease should be identifiable on prenatal ultrasound by 24 weeks' gestation. The classic 'four-chamber view' will diagnose the majority but not all of these abnormalities. Additional views including visualization of both left and right outflow tracts are recommended to improve diagnostic ascertainment.

EUROCAT DEFINED SERIOUS CARDIAC ABNORMALITY

EUROCAT defines a list of severe congenital heart defects. These are cardiac malformations that require surgical resolution.

Overall thirty-five cases displayed forty abnormalities that would fulfil the EUROCAT criteria for severe congenital heart disease. EUROCAT defined severe congenital heart defects are not always listed as the primary abnormality, (Table 4.1)

Twenty-four of these cases were live births, (68.6%). Eleven cases were terminated following prenatal diagnosis of abnormality, (31.4%).

Twenty-four of these thirty-five EUROCAT defined cases had an abnormality diagnosed on prenatal scan giving an overall case detection rate for severe cardiac abnormality of 68.6%, (Figure 4.5). This detection rate must be viewed with some caution because the cardiac lesions may not have been the defining feature for cases where they are classified in the secondary position. Looking only at the 22 cases where a primary diagnosis of severe cardiac anomaly was made, a prenatal detection rate of 50% is calculated, (n=11), which is disappointing.

CARDIAC & CIRCULATORY ABNORMALITIES

Table 4.1: EUROCAT Severe Congenital Heart Disease

	Primary Coding	Secondary Coding
COMMON ARTERIAL TRUNCUS, Q200	None	1
TRANSPOSITION OF GREAT ARTERIES, Q203	4 ‡	2◊□
SINGLE VENTRICLE, Q204	None	None
AVSD, Q212	None	9◊
TETRALOGY OF FALLOT, Q213	6	None
TRICUSPID ATRESIA & STENOSIS, Q224	2 *	None
EBSTEIN'S ANOMALY, Q225	None	None
PULMONARY VALVE ATRESIA, 220	None	1*
AORTIC VALVE ATRESIA/STENOSIS, Q230	1	None
HYPOPLASTIC LEFT HEART, Q234	4	1
HYPOPLASTIC RIGHT HEART	None	1*
COARCTATION OF AORTA, Q251	4	2‡
TOTAL ANOMALOUS PULMONARY VENOUS RETURN, Q262	1	1□

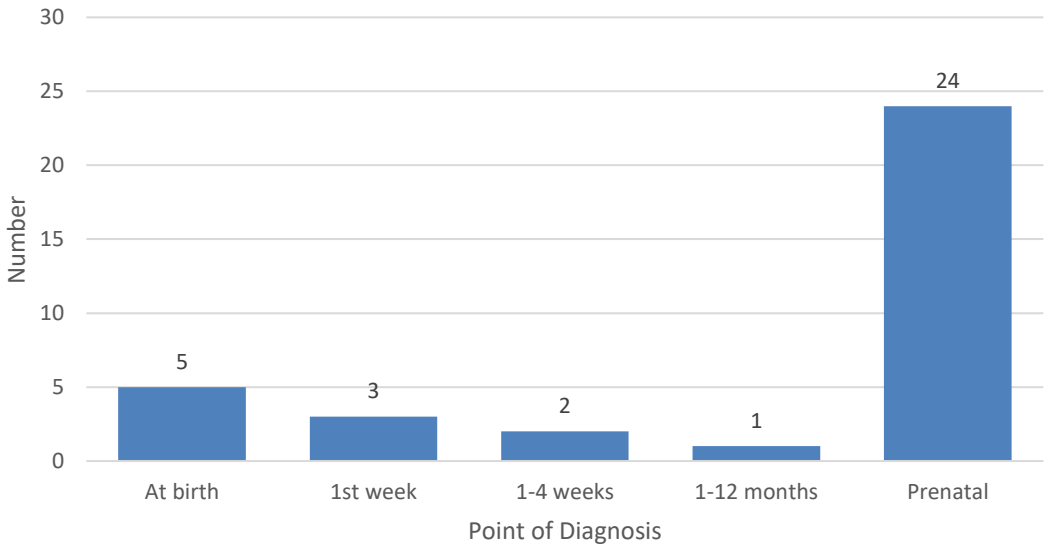
* Single case with Tricuspid valve stenosis, pulmonary valve atresia and hypoplastic right heart

‡ Single case with Transposition of the Great Arteries and Coarctation of the Aorta

◊ Single case with AVSD & Transposition of the Great Arteries

□ Single case with Transposition of Great Arteries and TAPVD

Figure 4.5: Point of Diagnosis for EUROCAT Defined Serious Cardiac Abnormalities, (n=35)



Common Arterial Truncus, (Q200)

In this rare cardiac anomaly, a common arterial trunk arises from the base of the heart and gives rise to the systemic, (aorta), pulmonary and coronary arteries. The only valve, (truncal valve), is usually thickened and dysplastic or stenotic. The four-chamber view can be entirely normal. Genetic disorders and teratogens have been implicated in aetiology, (including maternal diabetes). Other associated cardiac anomalies include mitral atresia, aortic arch anomalies and almost complete absence of the interventricular septum creating a single ventricle. Up to 30% of cases are associated with chromosome 22q11 deletion, (Di George), syndrome.

D821	DI GEORGE	Persistent truncus arteriosus

Transposition of the Great Arteries, (Q2013)

Complete transposition of the great vessels indicates that the aorta arises from the right ventricle and the pulmonary artery from the left ventricle. The four-chamber view and the atrio-ventricular connections will appear normal, (except in cases with an associated VSD). However, the two great vessels will arise in parallel from the base of the heart. The three-vessel view will be abnormal because the pulmonary artery lies below the aortic arch. Transposition is usually isolated but may be associated with a VSD and pulmonary stenosis either alone or in combination. Uncomplicated TGA is not associated with haemodynamic compromise in utero.

There were six cases where transposition of the great arteries is recorded. In four cases, it is the primary abnormality. Prenatal diagnosis was only achieved in 50% of cases.

Q203	TGA	VSD
Q203	TGA	VSD; Coarctation of Aorta
Q203	TGA	No associated anomalies
Q203	TGA	VSD; Pulmonary Artery Atresia
Q206	ISOMERISM - (L) ATRIAL WITH ASPLENIA	TGA; TAPVD
Q263	PARTIAL ANOMALOUS PULMONARY VENOUS DRAINAGE	TGA; AVSD;

Uncomplicated transposition of the great arteries requires surgical treatment in the first few weeks of life and long term outcome is generally good. However, the outcome is less favourable if there is coexisting VSD or pulmonary stenosis.

There was a further related case but one that is not included in the EUROCAT Severe Congenital Heart Disease classification.

Q205	CONGENITALLY CORRECTED TGV	Prenatal Diagnosis; Live birth

In the corrected form of TGA, (levo-transposition or l-TGA), the ventriculoarterial discordance is accompanied by atrioventricular discordance. The right atrium is connected to the morphological left ventricle which gives rise to the pulmonary trunk. The left atrium is connected to the morphological right

ventricle which gives rise to the aorta. Although the vessels are transposed there is no resulting circulatory impairment. This abnormality can be associated with third-degree AV block and heterotaxy syndromes. Extra cardiac abnormalities are rare in 'classic' l-TGA.

Atrioventricular septal defect, (AVSD), (Q212)

In this condition, there is a defect in the lower part of the atrial septum and the inlet part of the ventricular septum. As a result, the two atrioventricular valves do not form normally. Instead a common atrioventricular valve bridges the defect and there is loss of the normal differential insertion seen at the crux on the four-chamber view. Atrioventricular septal defects are one of the most common forms of heart disease seen in prenatal life. The scan appearance is one of a single valve opening into both ventricular chambers. The sizes of both the atrial and ventricular components can be variable. Prognosis depends on the presence of other abnormalities but as an isolated lesion long-term prognosis following correctional surgery is generally good.

This type of defect is often associated with extra cardiac defects and chromosomal disorders, particularly Trisomy 21. An AVSD is listed as a secondary abnormality on nine occasions.

Q790	DIAPHRAGMATIC HERNIA (L)	
Q900	TRISOMY 21	
Q900	TRISOMY 21	
Q900	TRISOMY 21	PDA
Q900	TRISOMY 21	
Q998	UNBALANCED TRANSLOC CHROMOS 7	TEV
Q248	MESOCARDIA	Pulmonary artery atresia
Q263	PARTIAL ANOMALOUS PULMONARY VENOUS DRAINAGE	TGA
Q8714	NOONAN SYNDROME	Hypertrophic cardiomyopathy

Tetralogy of Fallot, (Q213)

Tetralogy of Fallot is characterized by ventricular septal defect, stenosis of the infundibulum of the pulmonary artery, aorta over-riding the intraventricular septum and right ventricular hypertrophy. However prenatally only three features are reliably seen: right ventricular hypertrophy may not be evident until the latter stages of pregnancy or indeed early neonatal life. The four-chamber view alone cannot be relied upon to make the diagnosis. The diagnosis is usually made by demonstrating the aortic root. The aorta arises from the centre of the heart and sits astride the ventricular septum above the peri-membranous VSD. This is done by ensuring that there is continuity between the left ventricle and aortic outflow. The abnormality may also be suspected when there is difficulty identifying the right outflow tract owing to pulmonary stenosis or atresia. Extra-cardiac defects, chromosomal anomalies and genetic conditions, (particularly 22q11.2 deletion), are see in over 30% of cases.

There were six recorded cases of tetralogy of Fallot in the 2015-2016 cohort. All of them resulted in live birth. Unfortunately, prenatal diagnosis was only achieved for one case.

Q213	TETRALOGY OF FALLOT	Diagnosed at birth
Q213	TETRALOGY OF FALLOT	Diagnosed at birth
Q213	TETRALOGY OF FALLOT	Diagnosed at birth
Q213	TETRALOGY OF FALLOT - TRUNCUS VARIANT	Diagnosed at birth
Q213	TETRALOGY OF FALLOT	Diagnosed in 1st week
Q213	TETRALOGY OF FALLOT	Prenatal diagnosis

Corrective surgery can usually be performed as a single procedure in the first year of life with good long-term outcome.

Aortic Valve Atresia or Stenosis, (Q224)

This is a narrowing at the level of the aortic valve. It is rarely associated with extracardiac or genetic causes and is an evolving lesion, progressive during pregnancy.

Q230	AORTIC STENOSIS - WITH A DYSPLASTIC VALVE	Live birth; Diagnosed 1-4 weeks

Hypoplastic Left Heart, (Q234)

This is a group of defects in which the left ventricle may be absent or extremely hypoplastic because of a combination of aortic atresia and mitral valve atresia or stenosis. Approximately 10% of cases are associated with a chromosomal abnormality, usually Trisomy 13, Trisomy 18 or Turner syndrome. Hypoplastic Left Heart syndrome is readily diagnosed on prenatal scan. In severe cases the four-chamber view is already abnormal in the second trimester. The lumen of the left ventricle may be extremely small or simply not visualized. The aorta is extremely hypoplastic and its origin and course are difficult to define. There may be reversed flow in the aortic arch. The mitral valve fails to open and there is no demonstrable flow from the left atrium to left ventricle on colour flow Doppler. Compensatory dilatation of the right ventricle and pulmonary trunk may be present.

Q234	HYPOPLASTIC (L) HEART	Prenatal diagnosis; Termination
Q234	HYPOPLASTIC (L) HEART	Prenatal diagnosis; Termination
Q234	HYPOPLASTIC (L) HEART	Prenatal diagnosis; Termination
Q234	HYPOPLASTIC LEFT HEART	Prenatal diagnosis; Termination

Hypoplastic left heart syndrome can occasionally be associated with chromosomal anomalies, particularly Turner's syndrome but also Trisomy 18 and Trisomy 13.

Q914	TRISOMY 13	Hypoplastic left heart; Prenatal diagnosis; Termination

Coarctation of the Aorta, (Q251)

Coarctation of the aorta is a narrowing of the aortic arch between the origin of the subclavian artery and the insertion of the arterial duct.

A simple coarctation of the aorta is difficult to diagnose on prenatal scan. The most reliable way to assess the aortic arch is in the transverse view in the upper thorax. However, visualization of the aortic arch in longitudinal section is not a usual component of the routine prenatal ultrasound scan. In this view the aortic arch is smaller than normal and smaller than the arterial duct. There may be disproportion between the left and right ventricles and between the aortic arch and pulmonary trunk. However, this is not a reliable diagnostic feature as a slight discrepancy in size between left and right ventricle will be seen in a healthy third trimester fetus.

Coarctation of the aorta is accompanied by extra-cardiac anomalies in 25% of cases. Typical anomalies include those whose embryonic development coincides with the timing and location of aortic arch development and include upper gastrointestinal tract anomalies such as oesophageal atresia and diaphragmatic defect. Monosomy X is also a recognized association.

A total of six cases of coarctation of the aorta were diagnosed in 2015-2016, the majority, (n=4), had the abnormality coded in the primary position.

Q251	COARCTATION AORTA	Live birth; Diagnosed 1st week
Q251	COARCTATION AORTA	Prenatal diagnosis; Live birth
Q251	COARCTATION AORTA	Prenatal diagnosis; Live birth
Q2510	COARCTATION AORTA (PRE-DUCTAL)	Live birth; Diagnosed 1-12 months

Prenatal diagnosis was achieved for 50% of cases.

Q900	TRISOMY 21	Prenatal diagnosis; Live birth; Coarctation of aorta
Q203	TGA	Live birth; Diagnosed 1-4 weeks; VSD; Coarctation

Total Anomalous Pulmonary Venous Return, (TAPVD), (Q262)

Total or partial anomalous pulmonary venous return is present when all or some of the pulmonary veins drain into the right atrium or into the venae cavae that enter the right atrium. Prenatal diagnosis is extremely difficult in the absence of an associated cardiac abnormality. A small left atrium is suggestive. A persistent left superior vena cava may be seen in transverse section directly adjacent to the left atrium on the four-chamber view or as a 4th vessel to the left of the pulmonary trunk on the three-vessel view.

Q262	TOTAL ANOMALOUS PULMONARY VENOUS DRAINAGE	Prenatal diagnosis; ASD; VSD
Q206	ISOMERISM - (L) ATRIAL WITH ASPLENIA	Prenatal diagnosis; TGA; TAPVD

There was a further related case but one that is not included in the EUROCAT Severe Congenital Heart Disease classification.

Q263	PARTIAL ANOMALOUS PULMONARY VENOUS DRAINAGE	Prenatal diagnosis

The above case was a termination of pregnancy at 21 weeks' gestation following the ultrasound diagnosis of multiple abnormalities including AVSD, double-oulet right ventricle, TGA and pulmonary artery stenosis.

OTHER CARDIAC ANOMALIES

Atrial Isomerism/Heterotaxy syndromes, (Q206)

Heterotaxy is defined as an abnormality where the internal thoraco-abdominal organs demonstrate abnormal arrangements across the left-right axis of the body. This broad term includes a wide variety of complex cardiac lesions. Individuals with heterotaxy are broadly stratified into subsets of asplenia/polysplenia syndrome or isomerism of left/right atrial appendages. However, many examples exist where the sidedness of the atrial appendages is not concordant with lung or spleen placement, 'situs ambiguous'.

- Right atrial isomerism: a form of heterotaxy that is also known as asplenia syndrome. The patient effectively has two right sides. There is no spleen present. This form is typically associated with more severe cardiac defects and two tri-lobed lungs with short bronchi.
- Left atrial isomerism/Polysplenia syndrome: this form is usually associated with true left atrial isomerism. Typically, multiple spleens or spleen like nodules can be identified. Lungs are bilaterally bilobed, each with a long bronchus. In many cases the symmetry is far from complete. Individuals with left isomerism have less severe cardiac defects.

Q206	ISOMERISM - (L) ATRIAL WITH ASPLENIA	TGA; TAPVD; Persistent Right aortic arch
Q206	ISOMERISM - (L) ATRIAL WITH POLYSPLENIA	No cardiac defects

Two cases are described in the current dataset. Prenatal diagnosis and live birth was achieved for both cases.

Ventriculo-septal defect, (VSD), (Q210)

The commonest recorded cardiac abnormality in the 2015-2016 data was ventriculo-septal defect, (n=22). These lesions can be located anywhere in the ventricular septum and vary in size. The majority are single but multiple defects can occur. Typically, only the moderate or large defects are seen on prenatal scan. The defects are categorized according to position as peri-membranous, doubly commuted sub-arterial and muscular. Doubly commuted defects are rare and usually only delineated after birth. Ventriculo-septal defects may occur in isolation but are commonly associated with extra-cardiac and chromosomal abnormalities.

About 70% of prenatally diagnosed VSD's are either asymptomatic or close spontaneously within the first year of infant life.

Mesocardia, (Q248)

Cardiac location is influenced by many factors including underlying cardiac malformation, bronchogenic cysts, diaphragmatic hernia and kyphoscoliosis. In mesocardia the heart is centrally located in the chest, (the cardiac axis pints to the midline).

Q248	MESOCARDIA	Prenatal diagnosis; Termination

In the above case ultrasound scan confirmed situs inversus with the stomach on the right side and the heart lying in the midline. There was a large associated AVSD and minimal AV regurgitation. Pulmonary atresia was also present with retrograde filling from the duct. Termination of pregnancy was performed at 20 weeks' gestation. The situs inversus has not been coded in the data.

Malformations of the Respiratory System

A surprising 'light' section of the report this year in that only four abnormalities of the respiratory system are classified under ICD 10 in the primary diagnostic position. All of them were live births.

CONGENITAL MALFORMATIONS OF THE NOSE, (Q30)

Choanal Atresia, (Q300)

This abnormality results from a failure of recanalization of the nasal fossae during fetal development and may be unilateral or bilateral, osseous or membranous, complete or partial. Newborn infants are obligate nose breathers and bilateral choanal atresia is noted at birth by the absence of nose-breathing despite inspiratory effort and variable cyanosis.

Q300	CHOANAL ATRESIA (L)	Male; Diagnosis in 1st week
Q300	CHOANAL ATRESIA BILAT	Female; Diagnosis in 1st week

Choanal atresia is recorded as a secondary malformation in a further case.

Q308	PYRIFORM APERTURE STENOSIS	Male; Diagnosis in 1st week

Congenital nasal pyriform aperture stenosis, (CNPAS), is a rare cause of nasal airway obstruction that mimics choanal atresia in terms of clinical presentation. The pyriform aperture is the narrowest part of the nasal airway.

CONGENITAL MALFORMATIONS OF THE TRACHEA & BRONCHUS, (Q32)

Tracheal Stenosis, (Q321)

Congenital tracheal stenosis, associated with compete tracheal rings, is a rare anomaly that can present as life threatening respiratory insufficiency in neonates. The trachea is essentially a flexible tube made up of a series of 'C' shaped rings of cartilage linked together. The cartilage gives the trachea its structure. When an infant has tracheal stenosis, the rings are fixed and complete, or 'O' shaped. The growth and development of the trachea is consequently restricted.

Q321	TRACHEAL STENOSIS GRADE 3 w COMPLETE TRACHEAL RINGS

The data record a case in a female infant, delivered prematurely at 32 weeks' gestation by emergency caesarean section. There were antenatal concerns regarding fetal growth. It was also felt likely that the pregnancy had initially been a twin gestation with a large but empty second sac. At delivery, a hypocoiled cord was evident. The small placenta showed features consistent with fetal thrombotic vasculopathy and a

second empty – no fetus papyraceus - sac confirmed. The diagnosis of tracheal stenosis was not made until after one month of life. This was, however, a significant obstruction. Grade 3 implies 71-99% obstruction of the tracheal lumen, (Grade 4 is 'no detectable lumen'). There was an associated malformation of the pulmonary artery.

The trachea, filled with fluid, is visible in the coronal plane on antenatal scan. However, whilst the echogenic tracheal cartilage rings can be delineated from the less echogenic surrounding tissue and echo free lumen, a prenatal diagnosis of tracheal stenosis is therefore unlikely.

This infant was intubated, raising the possibility of an acquired, ('traumatic'), tracheal stenosis. However, the presence of complete tracheal rings confirms the diagnosis of a congenital abnormality.

CONGENITAL MALFORMATIONS OF THE LUNG, (Q33)

Congenital Cystic Adenomatoid Malformation, (CCAM), (Q3380)

There were no cases of cystic adenomatoid malformation listed in the data set for 2015-2016.

Abnormalities of Ear, Eye, Face & Neck

Congenital malformations of the head and neck are a wide and heterogeneous group that range in importance and severity from purely cosmetic defects to lethal anomalies. They can be isolated or occur as a component of a sequence, syndrome or chromosomal disorder.

Chapter XVII of the ICD 10 coding system has two sections directly related to face & neck abnormalities. These are 'Congenital Malformations of Eye, Ear, Face and Neck', (Q10-Q18) and 'Cleft Lip & Palate' (Q35-Q37). However facial abnormalities are also classified in many other locations under a variety of systems. This is simply because this region contains parts of almost all organ systems.

CYSTIC HYGROMA, (D1810)

Cystic hygroma is an anomaly of the lymphatic system that appears on ultrasound as a thin-walled multi-loculated cystic mass. The clear majority are located on the posterolateral aspect of the fetal neck although they may occur at other sites. Normally lymph is drained via the thoracic duct to the junction of the subclavian and internal jugular veins. When communication to the venous system is delayed, or obstructed the lymph tissue undergoes cystic dilatation. If the connection with the venous system is 're-established' the cysts may regress and resolve. If the obstruction persists then the cysts may grow to huge proportions and non-immune hydrops develops resulting in intrauterine demise. Nineteen cases are described in the current dataset.[18]

D1810	CYSTIC HYGROMA ® NECK	
D1810	CYSTIC HYGROMA - VERY LARGE	VSD
D1810	CYSTIC HYGROMA - LARGE	
D1810	CYSTIC HYGROMA (MASSIVE)	
D1810	CYSTIC HYGROMA - LARGE	
D1810	CYSTIC HYGROMA - HUGE SEPTATED	Exomphalos
Q790	DIAPHRAGMATIC HERNIA (L)	
Q894	CONJOINED TWINS	
Q8980	CAUDAL REGRESSION SEQUENCE	
Q900	TRISOMY 21	
Q900	TRISOMY 21	
Q900	TRISOMY 21	
Q900	TRISOMY 21	
Q900	TRISOMY 21	
Q900	TRISOMY 21	
Q910	TRISOMY 18	
Q910	TRISOMY 18	
Q960	TURNER SYNDROME	
Q998	UNBALANCED TRANSLOCATION CHROMOSOME 3	

[18] There is a case classified as D1810 that relates to an axillary hygroma.

ABNORMALITIES OF EAR, EYE, FACE & NECK

ANOPHATHALMOS, MICROPTHALMOS & MACROPTHALMOS, (Q11)

Congenital malformations of the eye can be dramatic reflecting early disruption of embryogenesis. When the anterior end of the notochord and surrounding mesoderm are not appropriately induced by the forebrain a spectrum of anomalies such as the absence of an eye (anopthalmia), partial or complete fusion (cyclopia) or small malformed globe associated with a cleft (microphalmos with cysts and coloboma).

Micropthalmos, (Q112)

Microphthalmos, an abnormally small globe, is a clinical spectrum of disease classified as either simple (without co-existent ocular defect) or complex (e.g., colobomatous, cataractous, with retinal detachment, syndromic). The prognosis of microphthalmic eyes depends upon the extent of coexisting ocular abnormality.

There was a single case where microphthalmos is recorded as a secondary malformation.

Q120	CONGENITAL CATARACT ®	Male; Live birth; Diagnosis at birth

CONGENITAL LENS MALFORMATION, (Q12)

Congenital cataracts, (Q120)

Approximately one third of congenital cataracts are a component of a more extensive syndrome or disease. However, the origin a good 30% are unexplained. Metabolic disease tends to be associated with bilateral cataracts. Typical associations include Alports syndrome, Marfan syndrome, Down syndrome, myotonic dystrophy, galactosaemia, trisomy 13 and congenital infections such as rubella, toxoplasmosis, CMV and herpes simplex.

Q120	CATARACT - BILAT	
Q120	CONGENITAL CATARACT ®	Associated micropthalmos, (see above)
Q120	CONGENITAL CATARACT BILAT	
Q120	CATARACT - BILAT	Associated Rieger anomaly, (see below)
Q120	CONGENITAL CATARACT - BILAT	
Q120	CONGENITAL CATARACT (L)	

CONGENITAL MALFORMATION OF ANTERIOR SEGMENT OF EYE, (Q13)

Rieger anomaly, (Q138)

Rieger syndrome, (Axenfeld-Riegar Syndrome), is primarily an eye disorder, although it can also affect other parts of the body. This condition is characterized by abnormalities of the anterior segment. The pupil maybe off-center (corectopia). About half of affected individuals develop glaucoma. Rieger syndrome can also affect other parts of the body. Many affected individuals have distinctive facial features such as hypertelorism; a flattened mid-face with a broad, flat nasal bridge; and a prominent forehead. The condition is also associated

with dental abnormalities, heart defects, hypospadias, anal stenosis, and pituitary abnormalities. Rieger syndrome is inherited as an autosomal dominant trait. Two main types are described. Rieger syndrome type I is associated with a mutation in a gene RIEG1 on chromosome 4 (4q25-q26). The second form, known as Rieger syndrome type II, has been mapped to gene map locus 13q14 and seems to represent a more complex form of the disorder. Patients with Rieger syndrome type II present with, in addition to the usual signs and symptoms, an enlarged head (hydrocephalus), cardiac defects, more hearing defects and kidney abnormalities.

This was a male infant delivered at term. The diagnosis of bilateral cataracts and Reiger anomaly was made in first week of life. No other associated anomalies are listed. There was no family history of note.

OTHER CONGENITAL MALFORMATIONS OF THE EYE, (Q15)

Childhood glaucoma is an unusual eye disease and significant cause of childhood blindness. It is caused by disease related abnormal increase in intraocular pressure. The multiple potential causes fall into one of two categories and may be primary or secondary to some other disease process. Primary congenital glaucoma results from abnormal development of the ocular drainage system. Ten percent of primary congenital glaucomas are present at birth, and 80 percent are diagnosed during the first year of life.

Q150	CONGENITAL GLAUCOMA - BILAT	Female; Diagnosis at 1-12 months
Q8708	PIERRE ROBIN SEQUENCE	Male; Live birth at term; Diagnosis at 1-12 months

CONGENITAL HEARING LOSS

Congenital hearing loss is a relatively common problem occurring in approximately 2-4/1000 live births. Early identification and intervention can prevent linguistic, educational, and social repercussions. Intervention at or before six months allows a child with impaired hearing to develop normal speech and language.

Abnormalities of hearing are classified in different ways in the current data. Firstly, as a neurological disorder under the coding for ‘Conductive and sensorineural hearing loss including congenital deafness’, (H90). This coding seems to presume that no obvious physical defect is evident.

H919	CONGENITAL DEAFNESS	Male; Term delivery; Diagnosis 1-4 weeks

Then there are the cases that where there is a defined physical anomaly which are more appropriately listed under ‘Congenital malformations of the ear causing impairment of hearing’, (Q16)

ABNORMALITIES OF EAR, EYE, FACE & NECK

CONGENITAL MALFORMATIONS OF EAR CAUSING IMPAIRMENT OF HEARING, (Q16)

Congenital absence, atresia and stricture of the auditory canal, (Q161)

Two cases of atresia of the auditory canal are listed, both in association with microtia. Atresia of the auditory canal is a significant abnormality and it is perhaps surprising that it is listed as the secondary diagnosis to a simple deformity of the pinna. Quite simply absence or deformity of the pinna is easier to recognize.

Q172	MICROTIA ®	Female; Term delivery; Diagnosis at birth
Q172	MICROTIA - BILAT	Female; Term delivery; Diagnosis at birth

Auricular deformities such as Microtia, (Q172), are found in the setting of various syndromes and chromosomal abnormalities such as Trisomy 18. They can assume a variety of forms. Auricular tags are most commonly located in front of the external auditory canal. The primordium of the external ear is located at the side of the neck in early development. If the lower jaw is underdeveloped the auricle does not undergo a normal ascension and retains its embryonic position at the level of the head and neck junction. It is very difficult to appreciate these lesions on ultrasound scan but if evident a diligent search should be made for additional abnormalities.

Congenital Malformations of the inner ear, (Q165)

Includes anomalies of the membranous labyrinth and organ of Corti.

Q165	HYPOPLASTIC COCHLEAR NERVES	Female; Term delivery; Diagnosis at 1-4 weeks;

OROFACIAL CLEFTS, (Q35 – Q37)

Cleft lip, with or without cleft palate, and cleft palate alone are collectively referred to as orofacial clefts, (OFC's). Cleft lip and palate are among the more common congenital malformations. The causes of orofacial clefting remain largely unknown. Some 70% of OFC's are multifactorial. The remaining cases may be associated with known teratogens, chromosomal abnormality or single gene defects. Smoking and obesity are modifiable risk factors that are consistently associated with OFC's.

Unilateral clefts arise when the maxillary process fails to reach and fuse with the medial nasal process. Bilateral clefts develop in the upper lip when the maxillary processes on both sides fail to fuse with the median nasal process. The degree of cleft formation may be equal or different on both sides. A median cleft lip is probably caused by a lack of mesenchymal tissue in the central portion of the lip. Cleft palate is characterized by incomplete fusion of the secondary palate and affect the soft and hard palate or only the soft palate. Most would deny cleft palate laterality as this defect is due to the failure of the palatal shelves to fuse in the midline.

Clefts are mainly isolated lesions but are also found in association with various syndromes and chromosomal abnormalities, particularly Trisomy 13 and 18.

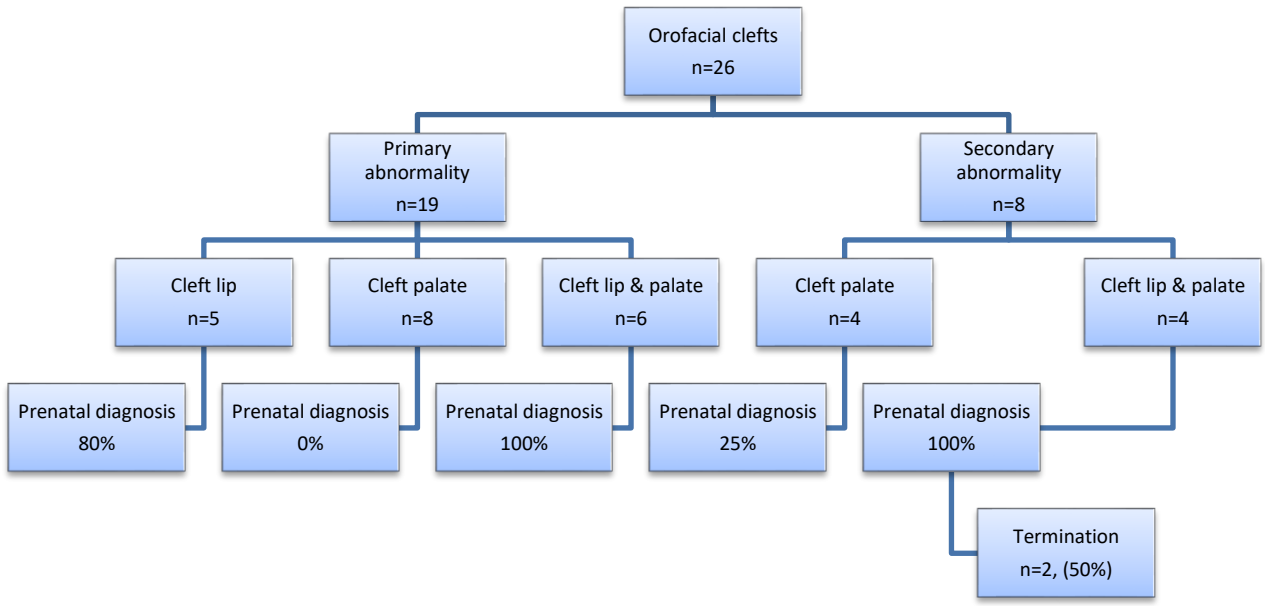
Cleft lip and palate can be diagnosed on prenatal ultrasound scan in a coronal or sagittal scan through the face or in a transverse scan at the level of the maxilla. Large clefts are conspicuous but a small cleft may be easily overlooked: with a small lip cleft, the coronal scan shows only a narrow defect in the upper lip.

A total of 26 cases are recorded of cleft lip, cleft palate or both.

Overall 52.6% of cases of primary orofacial clefting were diagnosed prenatally, (Figure 4.5). It is difficult to comment on the accuracy of prenatal diagnosis when considering orofacial clefting as a secondary abnormality. The 'point of diagnosis' in these cases relates to the primary coded abnormality.

Prenatal detection rates are higher for OFC's associated with malformations in other systems than for isolated clefts. Termination of pregnancy is more common when the cleft is associated with other anomalies. There were two terminations of pregnancy and both foetuses had significant primary malformations, (hypoplastic left heart and severe ventriculomegaly).

Figure 4.5: Overview of Prenatal Diagnosis of Cleft Lip & Palate



PIERRE ROBIN SEQUENCE, (Q8708)

Pierre Robin sequence is characterized by micrognathia, glossoptosis, (posteriorly placed tongue), and clefting of the soft palate. Hypoplasia of the mandibular area prior to the 9th week of gestation causes the tongue to be posteriorly located, presumably preventing closure of the posterior palate

Q8708	PIERRE ROBIN SEQUENCE	Male: Diagnosis at birth
Q8708	PIERRE ROBIN SEQUENCE	Male; Diagnosis 1-12 months; Cleft soft palate; Cong. glaucoma

Gastrointestinal Abnormalities

The gastrointestinal tract is formed from anatomically and functionally distinct regions that may be subject to a variety of errors of embryological development. Patterns of malformation include abnormal lumenization, (e.g. stenosis and atresia), duplications, abnormal rotation and fixation and abdominal wall defects.

CONGENITAL MALFORMATIONS OF THE OESOPHAGUS, (Q39)

Oesophageal Atresia, (Q391, Q3911)

Oesophageal atresia, the anomalous closure of the oesophagus often associated with a trachea-oesophageal fistula, is a relatively common anomaly with an incidence of approximately 1:3000 live births. It arises following an error in the differentiation of the primitive foregut into the oesophagus, trachea and lung between 4 – 6 weeks' gestation.

Q391	OESOPHAGEAL ATRESIA + TOF	Male; Live birth; Diagnosis at birth; ASD

Diagnosis on prenatal ultrasound examination is difficult. The suspicion of an oesophageal atresia is raised by the presence of polyhydramnios and a small or absent gastric bubble. The detection of a fluid filled gastric bubble does not exclude the anomaly particularly if a trachea-oesophageal fistula, (TOF), maybe present. Observation of fetal swallowing movements in these circumstances will demonstrate alternate filling and emptying of the proximal blind oesophageal pouch.

Associated abnormalities are common and should be excluded. The detection of a fluid-filled gastric bubble does not exclude the anomaly since fluid can enter the stomach through the low TOF that is usually present.

Oesophageal atresia also occurs as a feature of the VACTERL syndrome.

Q8726	VACTERL ASSOCIATION	Prenatal diagnosis; Live birth
Q8726	VACTERL	Prenatal diagnosis; Live birth

VACTERL is an acronym for vertebral defects, anal atresia, cardiac anomalies, trachea-oesophaeal fistula with oesophageal atresia, renal dysplasia and limb abnormalities. The first case of 'VACTERL Association' was a normal delivery at term. Antenatal scan had demonstrated unilateral renal agenesis, (which is therefore the recorded 'point of diagnosis'). The diagnosis of oesophageal atresia was made following delivery and had not been suspected antenatally.

The other case was an induction of labour at 37 weeks' gestation on an account of a decline in liquor volume and concern about fetal growth in a baby with an antenatal diagnosis of fetal abnormality. There had been evidence of severe lower urinary tract obstruction which decompressed spontaneously at around 16 to 18 weeks' gestation. However, the fetal kidneys continued to appear abnormal and there were concerns about

chronic renal damage and pulmonary hypoplasia. Following successful induction and a normal delivery of a male infant several other abnormalities were diagnosed including a tracheoesophageal fistula.

CONGENITAL ABSENCE, ATRESIA & STENOSIS OF THE SMALL INTESTINE, (Q41)

Obstructions of the intestinal tract do not usually become evident until the late 2nd trimester. They appear sonographically as unusual intra-abdominal cysts located at various sites depending on the level of the atresia. The development of polyhydramnios is also dependent on the level of closure. Duodenal atresia has a reported incidence of 1:10,000 live births. The condition results from a failure of recanalization of the duodenum during early embryonic life. The ultrasound hallmark is the 'double-bubble sign' of two adjacent fluid filled sacs in the upper abdomen. Duodenal atresia is frequently accompanied by polyhydramnios. Over 50% of fetuses with duodenal atresia have associated cardiac, renal, musculoskeletal or CNS anomalies.

Q410	DUODENAL ATRESIA	Male; Live birth; Prenatal diagnosis; No associated anomaly

Jejunal and ileal atresia can be a consequence of revacuolization/recanalization during intestinal development but may also be secondary to post-embolic or post-thrombotic ischaemia, volvulous or intussusception. Ileal and jejunal atresia usually appear as multiple cystic masses within the fetal abdomen. Polyydramnios may occur but is less likely to be seen the more distal the atresia develops.

E840	CYSTIC FIBROSIS	Female; Live birth; Diagnosis < 1 week; Ileal atresia

CONGENITAL ABSENCE, ATRESIA & STENOSIS OF THE LARGE INTESTINE, (Q42)

Atresia and stenosis of the Rectum, (Q421) & Imperforate Anus, Anal Stenosis & Anorectal Atresia, (Q423)

These abnormalities are associated with a variety of perineal appearances including complete absence of the anus or anterior stenosis and anal fistula. Anal atresia results from a failure of perforation of the embryonic anal membrane. They are often seen in association with abnormalities of the renal tract.

Q421	RECTAL STENOSIS	Male; Live birth at term; Diagnosis in 1st week of life
Q423	IMPERFORATE ANUS	Male; Live birth; Diagnosis at birth; Renal hypoplasia

A further six cases are classified in the secondary position.

Q641	EXSTROPHY BLADDER	Male; Termination at 23 weeks
Q792	EXOMPHALOS - MASSIVE	Termination at 12 weeks
Q794	PRUNE BELLY SYNDROME	Male; Termination at 16 weeks
Q8980	CAUDAL DYSPLASIA PATTERN	Male; Termination at 15 weeks
Q900	TRISOMY 21	Male; Live birth at 34 weeks; Diagnosis at birth
Q210	VSD - MULTIPLE	Male; prenatal diagnosis; Live birth

GASTROINTESTINAL ABNORMALITIES

OTHER CONGENITAL MALFORMATIONS OF THE INTESTINE, (Q43)

Hirschsprung's Disease, (Q431)

Hirschsprung's disease is due to an absence of parasympathetic ganglion cells in the myenteric submucosal plexus of the rectum: parasympathetic neuroblasts normally migrate into the bowel during the 9th to 12th weeks of embryonic development. This disorder sometimes extends to the colon. It occurs predominantly males with an incidence of 1:5000 births.

Q431	HIRSCHSPRUNG'S DISEASE	Male; Live birth at term; Diagnosis in 1st week of life
Q431	HIRSCHSPRUNG'S DISEASE	Male; Live birth at term; Diagnosis in 1st week of life

Hirschsprung's disease typically presents with abdominal distension and failure of passage of meconium within the first 48hrs. Marked dilatation of the large bowel may be seen on prenatal ultrasound examination but dilated fluid filled bowel segments are often seen in healthy fetuses in the 3rd trimester. Recognized associations include multiple endocrine neoplasia, Waardenburg's syndrome & Down syndrome. However, no associated abnormalities were seen in the two cases described above.

Congenital Malformations of Intestinal Fixation, (Q433)

This grouping includes a variety of conditions of the small and large bowel.

During normal development, the foregut, midgut and hindgut herniate out of the abdominal cavity where they undergo a 270^0 counter clockwise rotation around the superior mesenteric vessels. Following this the bowel returns to the abdominal cavity with fixation of the duodenal-jejunal loop to the left of the midline and the caecum to the right lower quadrant. Intestinal malrotation refers to any variation in this process of rotation and fixation. The most common presentation of incomplete rotation is midgut volvulus.

Q433	MALROTATION	Female; Diagnosis 1-4 weeks
Q4330	MALROTATION DUODENUM	Male; Diagnosis 1-4 weeks

In a further two cases a congenital malformation of intestinal fixation was described on post mortem examination following termination of pregnancy.

Q794	PRUNE BELLY SYNDROME	Male; Termination
Q8785	ANGELMAN SYNDROME	Female; Termination

The specific finding in the case of Angelman syndrome was of a non-fixed right colon with the ileo-caecal region centrally placed.

GASTROINTESTINAL ABNORMALITIES

Ectopic Anus, (Q435)

Anterior ectopic anus is a common condition that is very easily missed. In anterior ectopic anus, the anal opening is usually of normal size and only mildly displaced. Most children come to medical attention because of the severe constipation that is associated with this disorder. To facilitate diagnosis an anal position index has been described.

Q435	ECTOPIC ANUS (ANTERIOR)	Male; Live birth; Diagnosis at birth
Q435	ECTOPIC ANUS - SLIGHTLY ANTERIOR	Male; Live birth; Diagnosis in 1st week of life
Q435	ECTOPIC ANUS - ANTERIOR	Male; Live birth; Diagnosis 1-12 months

CONGENITAL MALFORMATION OF GALLBLADDER, BILE DUCTS & LIVER, (Q44)

The gallbladder develops during the 4th embryonic week as a compact endodermal outgrowth of the hepatic rudiment. Bile production commences between 13-16th weeks. Since bile production commences at an early stage the gallbladder can be recognized on antenatal scan as an oblong cystic organ in the right hepatic lobe.

Biliary atresia, in which one or more of the bile ducts are abnormally narrowed or blocked, has a prevalence of 1:16,000 births, (UK). It is more common than female infants. The causes are not well understood. The initial symptoms of biliary atresia are indistinguishable from those of neonatal jaundice.

Q442	ATRESIA BILE DUCT	Female; Live birth; Diagnosis in 1st week of life

An unspecified malformation of the liver, (Q447), was associated with a case of Meckel-Gruber syndrome. This is likely to relate to hepatic fibrosis a well-recognized feature of this syndrome that also includes polycystic kidneys and cephalocoele.

Q6190	MECKEL-GRUBER SYNDROME	Female; Termination

Genitourinary System

Renal tract abnormalities may be isolated or components of a recognizable syndromes. The ICD10 classification divides the abnormalities into renal agenesis and reduction defects, cystic kidney disease and congenital obstruction defects. Fetal renal tract anomalies will usually be detected at the routine 20-week scan.

CONGENITAL MALFORMATION OF OVARIES, FALLOPIAN TUBES & BROAD LIGAMENT, (Q50)

Ovarian Cyst, (Q501)

An ovarian cyst will typically appear on prenatal scan as a sharply circumscribed cystic mass in the lower to mid-abdomen. An ovarian cyst cannot confidently be distinguished from a mesenteric cyst on prenatal scan.

Q501	OVARIAN CYST	Prenatal diagnosis; Live birth
Q501	OVARIAN CYST - LARGE ®	Prenatal diagnosis; Live birth

CONGENITAL MALFORMATION OF UTERUS & CERVIX, (Q51)

Congenital Absence of the uterus, (Q510)

Congenital absence of the uterus was an incidental finding at post-mortem following termination of pregnancy for bilateral renal agenesis.

Q601	RENAL AGENESIS - BILAT	Prenatal diagnosis; Termination

OTHER CONGENITAL MALFORMATIONS OF THE FEMALE GENITALIA, (Q52)

Urogenital Sinus Anomaly, (Q528)

An unexpectedly difficult vaginal delivery at 32 weeks' gestation because of a grossly distended abdomen in a female infant led to the diagnosis of hydrometrocolpos. This abnormality occurs in 1:6000 newborn girls and is typically due to a stenotic urogenital sinus. However, hydrometrocolpos can also result from other conditions including imperforate hymen, midline vaginal septum and vaginal atresia.[19]

Q528	UROGENITAL SINUS ANOMALY	Preterm delivery at 32 weeks

The above case, from a consanguineous marriage, was associated with several other abnormalities including accessory fingers and toes.

[19] Witters I et al., Genet Couns 2012; 23: 513-7

HYPOSPADIAS, (Q54)

Displacement of the uretheral meatus ventrally and proximally from the tip of the penis. It is classified according to the position of the meatus on the penis. The shortening of the ventral side of the penis found in hypospadias can result in penile curvature known as chordee. The diagnosis was made at birth for all primary malformation cases.

Q540	HYPOSPADIAS - SUB-CORONAL
Q540	HYPOSPADIAS - CORONAL
Q541	HYPOSPADIAS - PROXIMAL PENILE
Q548	HYPOSPADIAS (SIGNIFICANT) - MIDSHAFT
Q548	HYPOSPADIAS (MODERATE) - MIDSHAFT

Hypospadias is also classified in the secondary position in 3 further cases.

Q3690	CLEFT LIP ® (& GUM)
Q620	HYDRONEPHROSIS ®
Q8717	RUSSELL-SILVER SYNDROME

The overall number of cases is less than usually anticipated for this common condition.

OTHER CONGENITAL MALFORMATIONS OF MALE GENITAL ORGANS, (Q55)

Congenital absence and aplasia of penis, (Q555)

Aphalia is a congenital malformation in which the phallus, (clitoris or penis) is absent. The term most commonly refers to the condition when a male is born without a penis. It is an extremely rare developmental anomaly. It is believed to result from either the absence of the genital tubercle, or its failure to develop. The urethra of an affected child opens on the perineum. The scrotum, testes and testicular function are usually normal.

Q555	APHALIA	Male; Prenatal diagnosis; Live birth at 33 weeks

This case was associated with malformations of both bladder and urethra, (Q647), but these are not specifically described in the data. Management issues are technical, ethical and social particularly regarding appropriate and realistic gender assignment.

RENAL AGENESIS & OTHER REDUCTION DEFECTS OF THE KIDNEY, (Q60)

These are typically the result of failure of the ureteric bud to develop so that the ureter and kidney are absent. If unilateral the child will live a full and healthy life provided the other kidney is normal. Bilateral agenesis is lethal and is usually diagnosed when profound oligohydramnios is seen on antenatal scan.

Unilateral Renal Agenesis, (Q600)

Unilateral renal agenesis has an incidence of 1:1000 births and can be sporadic or inherited as an autosomal dominant trait. The left kidney is more commonly absent. There is an association with anomalies of the reproductive tract. Compensatory hypertrophy of the contralateral side may not be seen in utero.

Q600	ABSENT KIDNEY ®	Live birth
Q600	ABSENT KIDNEY (L)	Termination; Renal dysplasia

Unilateral renal agenesis is not usually of any major health consequence if the other kidney is healthy. However, it is associated with an increased incidence of abnormality of the development of the female reproductive tract which may present as infertility.

Q8726	VACTERL ASSOCIATION	Male; Prenatal diagnosis; Live birth
Q0521	L/S MYELOMENINGOCELE	Female; Prenatal diagnosis Live birth;

Bilateral Renal Agenesis, (Q601)

Bilateral renal agenesis is classified as the primary abnormality in two instances.

Q601	RENAL AGENESIS - BILAT	Prenatal diagnosis; Termination at 18 weeks
Q601	RENAL AGENESIS - BILAT	Prenatal diagnosis; Termination at 21 weeks

The latter case was associated with congenital absence of the uterus, (Q510).

Bilateral renal agenesis is described as a secondary finding, along with imperforate anus, in a case of massive exomphalos evident on booking scan.

Q792	EXOMPHALOS - MASSIVE	Prenatal diagnosis; Termination at 12 weeks

Renal Hypoplasia, (Q603, Q604)

Bilateral renal hypoplasia is seen in a male infant delivered at term in association with imperforate anus.

Q423	IMPERFORATE ANUS	Live birth at term

CYSTIC KIDNEY DISEASE, (Q61)

Multicystic Dysplastic Kidney, (Q614, Q6140, Q6141)

This sporadic condition is thought to be caused by atresia of the ureter or uretero-pelvic junction during the meta-nephric stage of development. It is characterized by multiple cysts of varying sizes that do not interconnect with each other or the renal collecting system. The cysts are seen within a framework of

echogenic dysplastic renal tissue. Generally, one kidney is affected and bilateral involvement is rare. The changes may affect the entire kidney or just segments. Cystic dysplastic renal disease is usually sporadic but it may be a feature of several syndromes including trisomy 13, trisomy 18 and Meckel.

Q613	POLYCYSTIC KIDNEY DISEASE - BILAT	Male; Prenatal diagnosis; Live birth
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY ®	Male; Prenatal diagnosis; Live birth
Q6140	DYSPLASTIC KIDNEY (L)	Male; Prenatal diagnosis; Live birth
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY (L)	Male; Prenatal diagnosis; Live birth
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY (L)	Male; Prenatal diagnosis; Live birth
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY ®	Male; Prenatal diagnosis; Live birth
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY ®	Male; Prenatal diagnosis; Live birth
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY (L)	Female; Prenatal diagnosis; Live birth
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY ®	Female; Prenatal diagnosis; Live birth
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY	Male; Prenatal diagnosis; Live birth
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY (L)	Female; Prenatal diagnosis; Live birth
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY ®	Male; Prenatal diagnosis; Live birth
Q6190[20]	MECKEL-GRUBER SYNDROME	Female; Prenatal diagnosis; Termination

Meckel- Gruber syndrome is an autosomal recessive lethal malformation. Dysplastic kidneys are prevalent in over 95% of all identified cases. Occipital encephalocele is present in 60% to 80% of all cases, and post-axial polydactyly is present in 55% to 75% of the total number of identified cases. Hepatic fibrosis is a recognized feature, (see above) and bowing or shortening of the limbs is also common. In this case post-mortem demonstrated normal fetal growth. There were external dysmorphic features of a large anterior fontanelle, low set ears, micrognathia and retrognathia. Internally there was small defect on the skin and bone over the occiput, mild renal tubal dilation and possible liver tissue abnormality and mild ventriculomegaly. The couple had unfortunately experienced a previous loss. On that occasion the fetus had several anomalies which included a membranous cyst in the 4th ventricle in the brain, mild dilatation of the lateral ventricles, cystic dysplasia in the kidneys and a subtle ductal plate malformation in the liver.

Cystic kidney disease is also recorded as a secondary abnormality in six further cases.

Q6300	DUPLEX KIDNEY (BILAT)	Male; Prenatal diagnosis; Live birth
Q794	PRUNE BELLY SYNDROME	Male; Prenatal diagnosis; Termination
Q8726	VACTERL[21]	Male; Prenatal diagnosis; Live birth
Q8785	ANGELMAN SYNDROME	Female; Prenatal diagnosis; Termination
Q914	TRISOMY 13	Male; Prenatal diagnosis; Live birth
D821	DI GEORGE	Male; Prenatal diagnosis; Live birth

[20] Q6190 is specific to Meckel-Gruber syndrome, (BPA extension of ICD 10).

[21] The term VACTERL is an acronym where V=vertebral abnormality; A=anal atresia; C=cardiac defects; T=tracheal anomalies including trachea-oesophageal fistula; E=oesophageal atresia; R=renal and/or radial abnormality and L=other limb defects.

CONGENITAL OBSTRUCTIVE DEFECTS OF RENAL PELVIS & MALFORMATION OF URETER, (Q62)

This ICD 10 category includes a variety of abnormalities of the renal and urinary system including, congenital hydronephrosis, atresia and stenosis of the ureter, agenesis of ureter and congenital PUJ obstruction.

Congenital hydronephrosis (Q620)[22]

Renal pelvis dilatation (pyelectasis) is a commonly recognized problem at antenatal scan.[23] It is defined as pelvic dilatation that does not involve the renal calices. While there can be many conditions that lead to hydronephrosis, the most common causes are obstructions that reduce the ability of urine to flow out of the kidney and into the bladder. Many children who are diagnosed with hydronephrosis before they are born will have the condition resolve on its own without medical intervention. Various 'cut-off' measurements have been suggested but these have little clinically significance and in general only an AP measurement of greater than 10mm warrants further postnatal follow-up.

If enlargement of the renal pelvis exceeds 15mm then it is classified as hydronephrosis. In these circumstances, there is calyceal dilatation. Attempts must be made to define the underlying cause. Infants with a continuing abnormality on post-natal assessment may go on to have functional nuclear medicine studies.

Q620	HYDRONEPHROSIS (L)	
Q620	HYDRONEPHROSIS (L)	
Q620	HYDRONEPHROSIS ®	
Q620	HYDRONEPHROSIS ®	Hypospadias
Q620	HYDRONEPHROSIS (L) - MASSIVE	PUJ Obstruction
Q620	HYDRONEPHROSIS ®	Ureterocoele
Q620	HYDRONEPHROSIS (L)	Ureterocoele
Q620	HYDRONEPHROSIS (L)	Ureterocoele
Q620	HYDRONEPHROSIS ®	Ureterocoele

Hydronephrosis is classified as a secondary abnormality in one further case.

Q6300	DUPLEX KIDNEY ®	Female; Prenatal diagnosis; Live birth

Congenital PUJ Obstruction, (Q6210)

The most common cause of obstruction (blockage) in the urinary tract in children is a congenital obstruction at the point where the ureter joins the renal pelvis – the ureteropelvic junction, (UPJ or PUJ). Most PUJ obstructions are identified long before birth by prenatal scan. Urine is produced by the fetus at a rate that

[22] Reported only where major, (cases defined as a renal pelvis at or above 10 mm after birth). Coders should specify in written text if the hydronephrosis is unilateral or bilateral

[23] Ultrasound 'soft' markers can be coded using a reference list developed by BINOCAR. These codes are used exclusively with BINOCAR's additional antenatal variables and should not be used for anomalies.

exceeds the amount able to drain out of the renal pelvis into the ureter. This causes accumulation of urine within the kidney and dilatation of the renal pelvis which is clearly visible on scan.

Q6210	PUJ OBSTRUCTION (L)	Female; Prenatal diagnosis; Live birth
Q6210	PUJ OBSTRUCTION - BILAT HYDRONEPHROSIS	Male; Prenatal diagnosis; Live birth
Q620	HYDRONEPHROSIS (L) - MASSIVE	Male; Prenatal diagnosis; Live birth

OTHER CONGENITAL MALFORMATIONS OF THE KIDNEY, (Q63)

Duplex Kidney & Collecting System, (Q630)

These terms cover a wide range of duplication variants. The ureter usually begins to branch where it approaches the metanephros. If it divides some distance caudal to the metanephros the kidney is divided into two hemi-kidneys, usually fused together with a 'waist'. Usually the upper hemi-kidney has two main calices and the lower one usually has three. The classic complete duplex kidney follows the 'Weigert-Meyer' rule of "the upper moiety ureter inserts more inferiorly and medially than the lower moiety ureter". The upper moiety ureter is often associated with an ureterocoele. The lower moiety ureter has a shorter more vertical course and is therefore more prone to vesico-ureteric reflux and uretero-pelvic junction obstruction.

Q6300	DUPLEX KIDNEY ®	Female; Prenatal diagnosis; Live birth
Q6300	DUPLEX SYSTEM ®	Female; Prenatal diagnosis; Live birth
Q6300	DUPLEX KIDNEY ®	Female; Prenatal diagnosis; Live birth
Q6300	DUPLEX KIDNEY (BILAT)	Male; Prenatal diagnosis; Live birth
Q6300	DUPLEX KIDNEY ®	Female; Prenatal diagnosis; Live birth

Abnormally Sited Kidney, (Q631, Q632)

These are relatively common abnormalities that are often discovered incidentally.

Ectopic Kidney, (Q632)

The incidence of renal ectopia is 0.2%. Pelvic kidneys represent persistent failure of the metanephros to rise up in the fetal body. Hence the kidney remains in the pelvis. Most ectopic kidneys demonstrate a degree of malrotation.

Q6320	PELVIC KIDNEY ®	Male; Prenatal diagnosis; Live birth
Q6320	ECTOPIC PELVIC KIDNEY ®	Male; Prenatal diagnosis; Live birth
Q6320	PELVIC KIDNEY (L)	Male; Prenatal diagnosis; Live birth

The incidence of associated anomalies is generally considered to be low. However pelvic kidney is a secondary feature in three further cases.

Q8785	ANGELMAN SYNDROME	Female; Prenatal diagnosis; Termination
Q3690	CLEFT LIP (R) - CONGENITAL HEALED	Male; Prenatal diagnosis; Live birth
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY ®	Male; Prenatal diagnosis; Live birth

OTHER CONGENITAL ABNORMALITIES Q64

Bladder Exstrophy, (Q641)

This abnormality is usually explained by the formation in early fetal life of an abnormally large cloacal membrane extending up towards the umbilicus preventing ingrowth of the tissue that would otherwise form the muscle and skin of the abdominal wall. In its severest form the bladder opens like a flattened ulcer on the abdomen. There is usually an associated prolapse of the rectum. The symphysis pubis is widely separated.

Q641	EXSTROPHY BLADDER	Male; Prenatal diagnosis; Termination

In the case above the anomaly scan had raised concern about the fetal abdominal wall. The cord insertion was normal but beneath the cord insertion there was abnormal tissue everting from the abdomen and no normal bladder filling was seen during the scan. Both kidneys were normal, as was the liquor volume. The genitalia were male but abnormal. Owing to the gestational age, feticide was required prior to medical termination of pregnancy.

Posterior Urethral Valves, (Q642, Q6420)

Posterior urethral valves are the most common cause of lower urinary tract obstruction in the male neonate. The disorder is of variable severity. The condition arises around the 4th week of gestation as the Wolffian ducts fuse with the developing cloaca. A pair of sail-shaped valves develops adjacent to the verumontanum with appearances not unlike valves in a vein. Consequences are bilateral hydronephrosis and hydroureter, hypertrophy of the bladder detrouser and a dilated prostatic urethra.

Q6420	POSTERIOR URETHRAL VALVES	Male; Live birth; Diagnosis 1-12 months
Q6420	POSTERIOR URETHRAL VALVES	Male; Prenatal diagnosis; Live birth
Q6420	POSTERIOR URETHRAL VALVES	Male; Prenatal diagnosis; Live birth
Q6420	POSTERIOR URETHRAL VALVES	Male; Prenatal diagnosis; Live birth
Q6420	POSTERIOR URETHRAL VALVES	Male; Prenatal diagnosis; Live birth
Q6420	POSTERIOR URETHRAL VALVES	Male; Prenatal diagnosis; Live birth

The apparently late diagnosis of posterior urethral valves, (1-12 months), has already been discussed.

Posterior urethral valves were also seen as a secondary abnormality in two further cases.

Q794	PRUNE BELLY SYNDROME	Male; Prenatal diagnosis; Termination
Q031	DANDY WALKER MALF	Male; Prenatal diagnosis; Live birth

Patent Urachus, (Q6441)

Embryologically the umbilicus is a 'busy' place being the exit site for umbilical vessels and conveying important structures necessary to the development of gastrointestinal and urogenital tracts. The urachus is a structure that connects the dome of the bladder to the anterior abdominal wall at the level of the umbilicus. Patent in early development but gradually obliterated so that a solid core of tissue, the median umbilical ligament, remains. Rarely the urachus may remain patent allowing urine to escape at the umbilicus. This is most commonly seen in association with obstruction at the neck of the bladder or urethra.

Q6441	PATENT URACHUS	Female; Live birth; Diagnosis at birth

Musculoskeletal Abnormalities

Skeletal abnormalities are either malformations or dysplasia. Malformations include amelia, polydactyly, syndactyly and ectrodactyly. Dysplasias are less common and are characterized by generalized defective development of bone and cartilage. Ultrasonically it is not possible to give a precise pathological diagnosis of dysplasias but in general two main groups are recognized. Firstly, short limbs with severely defective ossification with or without fractures will be seen in severe osteogenesis imperfecta or hypophosphatasia. Secondly short limbs with or without spinal deformity are features of thanatophoric dysplasia, achondrogenesis, Jeune syndrome, (asphyxiating thoracic dystrophy) and Jarco-Levin syndrome amongst others.

CONGENITAL DEFORMITIES OF THE HIP, (Q65)

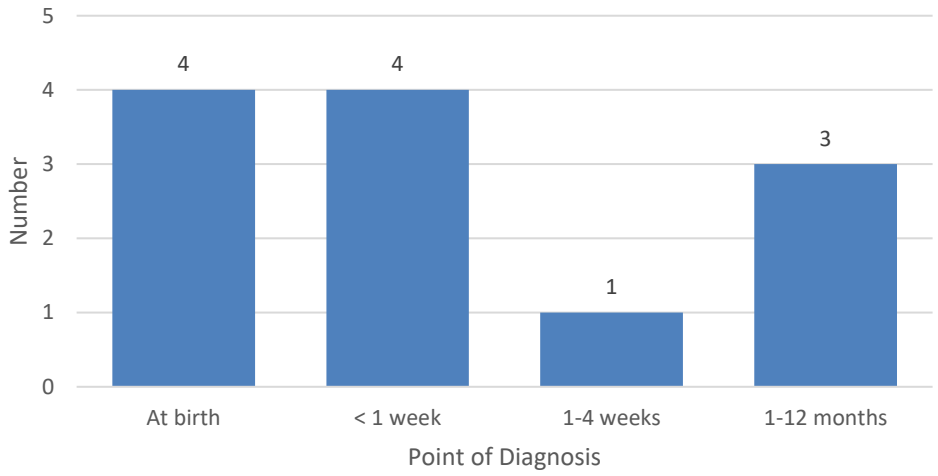
Developmental Dysplasia of the Hip, (Q658)

Dislocated hips are associated with joint laxity and acetabular dysplasia. Postural features often play a role in their causation. They are commonest in female infants, term deliveries, breech presentation and the left hip. Diagnosis is typically made at birth by specifically testing the hips

Q6580	DDH (L)	Male
Q6580	DDH ®	
Q6580	DDH (L)	
Q6580	DDH ®	
Q6580	DDH (L)	
Q6580	DDH (L)	
Q6580	DDH (L)	
Q6580	DDH ®	Male
Q6581	DDH - BILAT	
Q6581	DDH - BILAT	Male
Q6581	DDH - BILAT	
Q6581	DDH - BILAT	
Q780	OSTEOGENESIS IMPERFECTA	
Q8726	VACTERL	Male

A total of 14 cases are listed in the 2015-2016 data. Developmental dysplasia of the hip was recorded as a primary diagnosis in all but two incidences. The observed Female:Male ratio in this series was 5:2.

Figure 4.6: Point of diagnosis for primary diagnosis of developmental dysplasia of the hip, (n=12)



CONGENITAL DEFORMITIES OF THE FEET, (Q66)

Talipes Equinovarus, (Q660)[24]

This condition, which has a wide spectrum of severity, is characterized by adduction of the forefoot and midfoot, adduction of the heel or hind foot and a fixed plantar flexion, (equinus), of the ankle. The foot therefore points downwards and inward but is rotated outward axially. The male: female predisposition is about 2:1. The anomaly is not a single entity and may be considered as extrinsic, (deformation), of intrinsic (true malformation). Talipes may also be unilateral or bilateral, isolated or complex.

Q660	TEV - BILAT	Diagnosis at birth
Q660	TEV (L)	Diagnosis at birth
Q660	TEV (L)	Diagnosis at birth
Q660	TEV (L)	Diagnosis at birth
Q660	CTEV ®	Prenatal diagnosis
Q660	TEV (L)	Prenatal diagnosis
Q660	CTEV ®	Prenatal diagnosis
Q660	TEV - BILAT	Prenatal diagnosis
Q660	TEV (L)	Prenatal diagnosis
Q660	TEV - BILAT	Prenatal diagnosis
Q660	CTEV - BILAT	Prenatal diagnosis
Q660	CTEV - BILAT	Prenatal diagnosis
Q660	TEV ®	Prenatal diagnosis
Q660	TEV BILAT	Prenatal diagnosis

[24] Talipes associated with neuromuscular diagnosis or a syndrome such as arthrogryposis multiplex congenital, myotonic dystrophy or diastrophic dysplasia are excluded from this coding.

Complex talipes can be chromosomal, neurological, musculoskeletal or syndromic. The most commonly associated chromosomal anomaly is trisomy 18. Most cases with complex aetiologies will be bilateral.

Talipes is recorded as an associated abnormality in a further 4 cases

Q900	TRISOMY 21	Live birth
Q938	UNBALANCED DELETION CHROMOSOME 4 - 4p14	Termination
Q998	UNBALANCED TRANSLOC CHROMOS 7	Termination
Q039	VENTRICULOMEGALY - SEVERE	Termination

POLYDACTLYL, (Q69) AND SYNDACTYLY, (Q70)

The hands are fully differentiated in the human embryo by the end of the 8th week. When the finger buds have completed growth in length they are still joined by webs which break down by progressive cell death until the normal proximal web configuration is reached. Failure of cell death results in syndactyly, the commonest congenital hand abnormality. The appearance of abnormality depends on the tine of interference with the developing part. Deformities such as reduplications (partial as in bifid thumb or complete with extra digits) and inversions ('mirror hand') are likely to be related to specific gene defects.

Q691	DUPLICATED THUMB (L)
Q691	ACCESSORY THUMB ® (WASSEL TYPE 2)
Q691	BIFID THUMB WITH 2 NAILS (L)
Q691	ACCESSORY THUMB ®
Q691	DUPLICATED THUMB ®
Q691	DUPLICATED THUMB (L)
Q692	DUPLICATION GRT TOE (L)
Q692	POLYDACTYLY - 6 TOES BILAT
Q704	POLYSYNDACTYLY - ACCESSORY GREAT TOE (L)

Polydactyly and syndactyly are seen in association with a number of other conditions.

Q8980	CAUDAL DYSPLASIA PATTERN
Q914	TRISOMY 13
Q213	TETRALOGY OF FALLOT - TRUNCUS VARIANT
Q528	UROGENITAL SINUS ANOMALY
Q691	DUPLICATED THUMB (L)
Q7130	ABSENT FINGER 5TH (L)
Q8720	HOLT ORAM SYNDROME

MUSCULOSKELETAL ABNORMALITIES

REDUCTION DEFECTS OF THE UPPER (Q71) AND LOWER, (Q72) LIMBS

There have been many attempts to categorize the complex clinical manifestations relating to reduction defects of the limb, (particularly by Swanson). The absence of a consistent classification system may be a consequence of a lack of understanding of the pathogenesis of these abnormalities. Unfortunately, the ICD 10 listings are based on the affected limb without relation to underlying pathology.

It is therefore difficult to present this data in a meaningful way. However, an attempt has been made to make the information clearer, although still not consistent with the more recent OMT Classification of Hand & Upper Limb Anomalies as approved by the IFSSH Scientific Committee on Congenital Conditions.

Major limb defects are usually diagnosed at routine 2nd trimester ultrasound imaging. Risk factors include pre-gestational diabetes, drug exposures, (e.g. valproic acid, methotrexate, misoprostol), ethnicity, smoking, early chorionic villus sampling, single gene defects, and chromosomal abnormalities, (particularly when bilateral). Infants born after IVF show an increased risk for limb reduction defects.

Limb deficiencies are characterized by either the total or partial absence of the skeletal structure of the limbs or different degrees of limb hypoplasia. Limb deficiencies may be longitudinal, transverse or intercalary. Interference with the development of blood supply is the most likely mechanism in the appearance of many congenital limb deformities.

Longitudinal limb deficiencies, (Q714-Q716, Q724-Q727), refer to the partial absence of a limb extending parallel to the long axis of the limb. They typically involve specific components of the limbs: preaxial (first ray: thumb or radius in the arms or first toe or tibia in the leg); postaxial (fifth ray: fifth finger or ulna in the arm, fifth toe or fibula in the leg); or central components (typically third or fourth rays in the hand or foot such as lobster-claw hand).

Three longitudinal limb deficiencies are coded as secondary abnormalities.

Q8680	FETAL VALPROATE (LIKELY)	Clubhand; Reduction defect ulna
Q8720	HOLT ORAM SYNDROME	Reduction defect ulna
Q8726	VACTERL	Clubhand

‘Clubhand’, ‘radial club hand’ or ‘radial longitudinal deficiency results in radial deviation of the wrist and shortening of the forearm. It is variable in presentation from an isolated thumb anomaly to complete absence of the radius.

In transverse limb defects, (Q710, Q712, Q713, Q720, Q722, Q723), there is complete or partial absence of distal structures of a limb in a transverse plane at the point where the deficiency begins. The proximal structures remain intact. They may be described as ‘congenital amputations’.

Q712	ABSENT FOREARM & HAND (L)	Prenatal diagnosis
Q712	ABSENT FOREARM ® w THUMB & FINGER STUMPS AT END	Prenatal diagnosis
Q712	RUDIMENTARY PROX ULNA & RADIUS	Prenatal diagnosis
Q7130	ABSENT FINGER 5TH (L)	Diagnosed at birth
Q718	HYPOPLASIA DISTAL PHALANGES 4 FINGERS	Diagnosed at birth
Q718	FOREARM TRANSVERSE GROWTH ARREST (L)	Prenatal diagnosis
Q7230	ABSENT TOES 2ND-4TH ®	Diagnosed at birth
Q7230	HYPOPLASTIC TOES (L)	Diagnosed at birth

Transverse limb defects were also reported as secondary abnormalities in the three cases already described with longitudinal limb deficiencies.

Q8680	FETAL VALPROATE (LIKELY)	Shortening of upper limb
Q8720	HOLT ORAM SYNDROME	Absent hand & fingers
Q8726	VACTERL	Shortening upper limb

Holt Oram syndrome was first described in 1960. Upper limb abnormalities with associated cardiac anomalies. Asymmetric, the left side more often affected than the right. Autosomal dominant with complete penetrance but variable expression. Often severe phocomelia, deformed carpal bones, clinodactyly, syndactyly, radial synostosis and deformed sternum.

Intercalary cases, (Q711 & Q721), are where there is complete or partial absence of the proximal or mid segments of a limb but preservation of distal limb structures. There were no cases of intercalary limb deficiency recorded in the current cohort.

OTHER CONGENITAL MALFORMATIONS OF THE LIMBS, (Q74)

This grouping and its subcategories includes a variety of abnormalities: everything from accessory carpal bones, macrodactylia and triphalangeal thumb to cleidocranial dysostosis and arthrogryposis multiplex congenital.

Q8980	CAUDAL DYSPLASIA PATTERN	Malformation of upper limb (unspecified)
P351	CONGENITAL CMV INFECTION	Congenital malformation of limb (unspecified)

Arthrogryposis, (Q743)

Arthrogryposis is not a diagnosis but a description that refers to several pathological processes resulting in limb immobilization and multiple congenital joint contractures. It is therefore a rather heterogenous grouping of conditions both syndromic, (e.g. Larsen syndrome, Freeman-Shelden syndrome and Multiple Pterigium syndrome) and non-syndromic. Therefore, it may not be surprising to find that two different codes have been used to classify arthrogryposis in the current data, 'Q743' and 'Q870E'. Sometimes these codes are used to differentiate between a presentation with primary involvement of the limbs and more complex abnormality where limb deformity is combined with other congenital anomalies.

There were two cases in the 2015-2016 data where arthrogryposis is recorded.

Q743	ARTHROGRYPOSIS	Male; Prenatal diagnosis; Termination
Q870E	PENA-SHOKEIR	Female; Prenatal diagnosis; Termination

Pena-Shokeir syndrome, (arthrogryposis multiplex congenital and pulmonary hypoplasia), is a rare, early lethal disorder with an estimated incidence of 1: 12,000. Approximately one hundred cases have been reported. It was first identified by Pena and Shokeir in 1974 but although early descriptions resulted in the eponym it has recently been suggested that Pena-Shokeir is not a specific unitary diagnosis or syndrome, but rather a description of a clinically and genetically heterogeneous phenotype from variable aetiology, resulting from the reduction of movements in the uterus due to an intrinsic pathology regardless of the cause, and was subsequently included among the phenotypes associated with the fetal akinesia/hypokinesia deformation sequence.

In this instance concerns were first raised at the 20 weeks fetal anomaly scan when bilateral talipes and persistently clenched hands were seen throughout the scan. These findings persisted on several scans. Edward's syndrome was suspected and amniocentesis performed although the fetal karyotype was normal. The scan findings deteriorated with progressive scans and minimal movement was seen. The pregnancy was terminated at 25 weeks' gestation. Prior to termination significant polyhydramnious was becoming evident suggesting that fetal swallowing was now affected.

OTHER CONGENITAL MALFORMATIONS OF THE SKULL AND FACE BONES, (Q75)

Craniosynostosis, (Q750)

Craniosynostosis results from premature closure of one or more of the skull sutures. It affects about 1:2500 children. Craniosynostosis causes distortion of the shape of the skull owing both to failure of bone growth at the prematurely closed suture site and to compensatory overgrowth at the sutures that remain open. The different types of craniosynostosis are classified by which sutures have closed prematurely.

Q750	SCAPHOCEPHALY	Female; Live birth at term; Diagnosis at birth

Scaphocephaly is the most common of the craniosynostosis conditions and is characterized by a long, narrow head.

OTHER CONGENITAL MALFORMATIONS OF SPINE AND BONY THORAX, (Q76)

This is a broad classification under ICD10 and includes fusion of the spine, absence of vertebrae, hemi-vertebrae, malformation of the lumbo-sacral joint and supernumerary vertebrae. It also includes sacral agenesis.

Q768	JARCHO-LEVIN (LIKELY)/SPONDYLOCOSTAL DYSPLASIA	Female infant; Live birth;

Jarcho-Levin syndrome is a rare genetic disorder characterized by fusion of the vertebra and malformations of the ribs. Consequently, the chest cavity is too small to accommodate the growing lungs. Infants born with Jarcho-Levin syndrome have short necks, limited neck motion due to abnormalities of the cervical vertebrae and short stature. In most cases, infants with Jarcho-Levin syndrome experience respiratory insufficiency and are prone to repeated respiratory infections that result in life-threatening complications. There are apparently two forms of Jarcho-Levin Syndrome that are inherited as autosomal recessive genetic traits and termed spondylocostal dysostosis type 1 (SCDO1) and spondylocostal dyostosis type 2 (SCDO2).

Disorders of the spine are also classified as secondary abnormalities in four further cases. These were predominantly disorders of the vertebrae including hemivertebrae.

Q203	TGA	Hemivertebrae
Q213	TETRALOGY OF FALLOT - TRUNCUS VARIANT	Sacral agenesis
Q262	TOTAL ANOMALOUS PULMONARY VENOUS DRAINAGE	Cong. abnormality vertebrae
Q300	CHOANAL ATRESIA BILAT	Abnormal vertebrae

Sacral agenesis, as listed above, is often seen as part of the caudal regression sequence.

Caudal Regression Sequence, (Q8980)

Caudal regression sequence is a disorder that impairs the development of the lower (caudal) half of the body. Areas affected include the lower back and limbs, the genitourinary system and the gastrointestinal tract. The bones vertebrae of the lower spine, particularly the sacrum, are frequently misshapen or missing. Scoliosis is common and the lower limbs are typically underdeveloped. Abnormalities in the genitourinary tract are extremely varied. Defects include unilateral renal agenesis, horseshoe kidney, bladder extrophy, ureteral duplication, hypospadias, cryptorchidism in the male and rectovaginal fistula in the female. Individuals with caudal regression syndrome may have malrotation of the large bowel and imperforate anus.

Caudal regression sequence occurs sporadically. The condition is likely to be caused by the interaction of multiple genetic and environmental factors resulting in a combination of abnormal mesoderm development and decreased blood flow to the caudal areas of the fetus. Caudal regression sequence is estimated to occur in 1 to 2.5 per 100,000 newborns but is much more common in infants born to diabetic mothers, (up to 1:350 newborns), particularly if the diabetes is poorly controlled. Indeed, the female infant with tetralogy of Fallot and associated sacral agenesis, (listed above), was delivered to an older mother with diabetes.

Q8980	CAUDAL DYSPLASIA PATTERN	Termination of pregnancy at 15 weeks' gestation
Q8980	CAUDAL REGRESSION SEQUENCE	Termination of pregnancy at 17 weeks' gestation

Two cases are described where the diagnosis was evident from the booking ultrasound examination. In the first case post mortem confirmed a male fetus with biometric measurements consistent with gestation but several congenital abnormalities including spina bifida, imperforate anus, horseshoe kidney, kyphoscoliosis,

hypoplastic bladder and an absent left hypogastric artery. There were also some minor abnormalities of the right hand listed in the post-mortem report but not coded.

With the second case the booking scan had demonstrated that although the lower limbs were present they were highly flexed and held in an abnormal position underneath the baby. There was also a clear posterior and lateral cystic hygroma. Amniocentesis was to show a normal male chromosome compliment. Post mortem examination following termination of pregnancy was to also reveal a double outlet right ventricle. On radiology, there was segmentation anomalies in keeping with caudal regression. The abdomen was short and there was a small pelvis with hyper-flexed legs.

OSTEOCHONDRODYSPLASIA WITH DEFECTS OF GROWTH OF THE TUBULAR BONES & SPINE, (Q77)

Asphyxiating Thoracic Dysplasia (Jeune), (Q772)

Asphyxiating thoracic dystrophy, also known as Jeune syndrome, is an inherited disorder of bone growth characterized by a narrow chest, short ribs, shortened bones in the arms and legs, short stature, polydactyly. Additional skeletal abnormalities can include unusually shaped clavicles and pelvic bones, and cone-shaped ends of the long bones in the arms and legs. Many infants with this condition are born with an extremely narrow, bell-shaped chest that can restrict the growth and expansion of the lungs. Life-threatening problems with breathing result, and people with asphyxiating thoracic dystrophy may live only into infancy or early childhood.

Q772	ASPHYXIATING SHORT RIB THORACIC DYSPLASIA	Male; Preterm; Live birth

This condition is inherited in an autosomal recessive pattern. Mutations in at least 11 genes have been found to cause asphyxiating thoracic dystrophy. Genetic changes in the IFT80 gene were the first to be associated with this condition. Mutations in the genes associated with asphyxiating thoracic dystrophy impair IFT, which disrupts the normal assembly or function of cilia. Thus, cilia are missing or abnormal in many kinds of cells.

Hypochondroplasia, (Q774)

This is a form of short limbed dwarfism. Hypochondroplasia is a rare inherited dysplasia causing short stature not unlike a mild form of achondroplasia. It can be difficult to diagnose. Features, other than short stature, include macrocephaly, lordosis, disproportionate arms and legs with short but broad hands and feet, limitation of elbow movement but hypermobility of other joints. It is due to a mutation of FGFR3 gene on chromosome 4p16.3.

Q774	HYPOCHONDROPLASIA	Female infant; Live birth; Prenatal diagnosis at 34 weeks

OTHER OSTEOCHONDRODYSPLASIAS, (Q78)

Osteogenesis Imperfecta, (Q780)

Osteogenesis imperfecta is a heterogenous condition characterized by disproportionate dwarfism and multiple fractures of the long bones of the extremities. Four types are distinguished. Type II is the most severe and not compatible with life. The main features on scan are shortened and deformed limbs with multiple fractures. The head is typically large and shows defective ossification of the calvaria.

Q780	OSTEOGENESIS IMPERFECTA	Live birth; Diagnosis at birth
Q780	OSTEOGENESIS IMPERFECTA	Live birth; Diagnosis at birth
Q780	OSTEOGENESIS IMPERFECTA - SEVERE	Live birth; Prenatal diagnosis; Micrognathia; Cleft
Q780	OSTEOGENESIS IMPERFECTA	Prenatal diagnosis; Termination
Q7800	OSTEOGENESIS IMPERFECTA - SEVERE	Prenatal diagnosis; Termination

In a case of severe osteogenesis imperfecta short bowed long bones were noted at the 20-week anomaly scan. The lower limbs seemed to be affected more than upper limbs. No other malformations were evident. Chest shape and circumference was normal. Free fetal DNA testing for thanatophoric dysplasia and achondroplasia was performed and returned as negative. Fetocide was undertaken prior to termination at 23 weeks' gestation. At post-mortem a moderately macerated male fetus showed evidence of osteopenia, irregularity and buckling of long bones. A diagnosis of osteogenesis imperfecta was finalized.

Abdominal Wall Defects

ICD 10 codes Q790-Q799 are 'Congenital Malformations of the Musculoskeletal System, NEC' and include congenital diaphragmatic hernia, exomphalos, gastroschisis and amniotic rupture sequence which are collectively considered here as 'Abdominal Wall Defects'.

CONGENITAL DIAPHRAGMATIC HERNIA, (CDH), (Q790)

The diaphragm is formed from the septum transversum, pleuroperitoneal membranes and the oesophageal mesentery. It forms between the 8th and 10th week and fusion is normally complete before the intestines return to the abdominal cavity. The pleuroperitoneal canal in the fetus closes as the diaphragm is formed. Persistence of this 'canal' may be the main cause of CDH. Typically, there is a posterolateral 'Bochdalek' hernia through the pleuroperitoneal canal. Approximately 80% of CDH occur through the left diaphragm and approximately 30% of patient have an intact peritoneal sac partially confining the content of the hernia in the chest. The time of herniation into the chest is likely to be the most important factor influencing the degree of pulmonary hypoplasia.

Ultrasound enables the diagnosis of CDH to be made prenatally on routine second trimester fetal anomaly scan. Suspicions regarding the diagnosis are often raised when a cystic structure is visualized at the level of the four-chamber view. However, it is well recognized that the ultrasound diagnosis may not occur until the 3rd trimester. Some cases are not recognized until after delivery.

Whilst the prenatal diagnosis of congenital diaphragmatic hernia is well established the outcome continues to be poor. Polyhydramnios is a predictor of poor outcome as is left heart under-development, the presence of intrathoracic liver and early gestation at diagnosis. In the presence of a karyotype abnormality or lesions associated with genetic syndromes the prognosis obviously depends on the underlying aetiology. The principal cause of death with CDH is the associated pulmonary hypoplasia and pulmonary hypertension. All cases are associated with an abnormality of gut rotation although this may not necessarily be classified in our data. The left side predominates

Q790	DIAPHRAGMATIC HERNIA (L)	Live birth
Q790	DIAPHRAGMATIC HERNIA	Live birth
Q790	DIAPHRAGMATIC HERNIA (L)	Live birth
Q790	DIAPHRAGMATIC HERNIA (L)	Live birth; Preterm at 29 weeks
Q790	DIAPHRAGMATIC HERNIA (L)	Live birth; Preterm at 32 weeks
Q790	DIAPHRAGMATIC HERNIA (L)	Termination
Q790	DIAPHRAGMATIC HERNIA (L)	Termination; AVSD; Aortic atresia; Cystic hygroma

GASTROSCHISIS, (Q793)

Gastroschisis results from the herniation of small bowel into the amniotic cavity through a small defect in the right para-umbilical region. Attachment of the umbilical cord is normal. The small bowel is always herniated but large bowel, pancreas and stomach can occasionally be found in the eviscerated organs. It is

usually an isolated abnormality and the prognosis is generally good but depends on the condition of the bowel at birth and a small proportion will experience significant morbidity.

The antenatal detection of gastroschisis is uniformly good. The features are easily recognized on prenatal ultrasound scan.

Q793	GASTROSCHISIS	Prenatal diagnosis; Live birth
Q793	GASTROSCHISIS	Prenatal diagnosis; Live birth
Q914	TRISOMY 13	Prenatal diagnosis; Live birth; Multiple abnormalities

There appears to have been a worldwide rise in gastroschisis over the last few decades. The pathogenesis is poorly understood. Young maternal age and smoking are the only factors that are consistently associated with this condition.

The last case listed above is therefore unusual in that gastroschisis is seen in association with an aneuploidy. This infant, delivered at 37 weeks to an older mother, had a number of associated abnormalities including VSD, cleft lip & palate, polydactyly and cystic renal disease.

EXOMPHALOS (OMPHALOCOELE), (Q792)

The gut normally returns to the abdominal cavity by the 10th week of gestation. Omphalocoele results when this process fails. It has an incidence of 1:5000 live births. The defect comprises a herniation of intra-abdominal contents within the umbilical stalk covered by a layer of peritoneum and amnion. The severest consequences are associated with failure of the closure of the lateral fold at 4 weeks' gestation resulting in a very large abdominal wall defect which may include bladder extrophy. After post-natal repair of the omphalocoele a defective anterior abdominal wall remains as normal apposition of the rectus muscles does not occur.

The primary abnormality is an anterior abdominal wall defect involving the umbilical cord. The contents may include peritoneal fluid, bowel liver and spleen. Associated anomalies are observed in 30% of cases and are predominantly cardiac in nature. Karyotypic abnormalities, particularly Trisomy 18, are said to be present in 10-20% of cases.

Four cases of exomphalos are listed in the primary position.

Q792	EXOMPHALOS	Prenatal diagnosis; Live birth
Q792	EXOMPHALOS MINOR	Prenatal diagnosis; Live birth
Q792	EXOMPHALOS	Prenatal diagnosis; Live birth
Q792	EXOMPHALOS - MASSIVE	Prenatal diagnosis; Termination; Indeterminate sex; Renal agenesis

The latter case was an early medical termination at 12 weeks' gestation. Multiple anomalies had been detected at the booking scan. Subsequent PCR excluded trisomy 13, 18, & 21 but a full karyotype could not be obtained.

Exomphalos is a secondary diagnosis in a further four cases.

Q8730	BECKWITH-WIEDEMANN SYNDROME	Macroglossia; Live birth
Q910	TRISOMY 18	Termination
Q998	UNBALANCED TRANSLOCATION CHROMOSOME 3	Cystic hygroma; Termination
D1810	CYSTIC HYGROMA - HUGE SEPTATED	Termination

Beckwith- Wiedemann syndrome is the result of abnormalities within the short arm of chromosome 11, (11p15). It is an 'overgrowth syndrome' and is recognized in 1:15,000 live births. Typical features include macrosomia, macroglossia, midline abdominal wall defects, (such as exomphalos), neonatal hypoglycaemia and a risk of hepatoblastoma.

It is likely that the final case listed was in fact associated with chromosomal abnormality. However, this was a termination of pregnancy at 12 weeks' gestation and there seems to be no record of genetic assessment of the fetal tissue.

PRUNE BELLY SEQUENCE, (Q794)

Prune-belly syndrome describes the association of hypotonic abdominal wall, large hypotonic bladder with dilated ureters, renal dysplasia and genital abnormalities. It may be considered a malformation sequence due to intrauterine abdominal wall distention. Such distention is usually due to an obstructive uropathy, (e.g. obstruction of the urethra leads to megacystis and bilateral megaureters), but other causes could lead to the morphological features of the syndrome in the absence of urinary involvement.

The incidence varies from 1:35,000 to 1:50,000 live births. The overwhelming majority of affected infants are male, (97%). There is a wide spectrum of severity. Congenital heart anomalies are reported in 10% of cases. Absence of the prostate and cryptorchidism are common in males. Affected females typically have associated genital abnormalities including vaginal atresia, rectovaginal or rectovesical fistulas and bicornuate uterus.

The overall prognosis is poor. There is a 20% risk of stillbirth and only 50% of children survive the first 2 years of infant life. Pregnancy termination may be considered.

Q794	PRUNE BELLY SYNDROME	Prenatal diagnosis; Termination

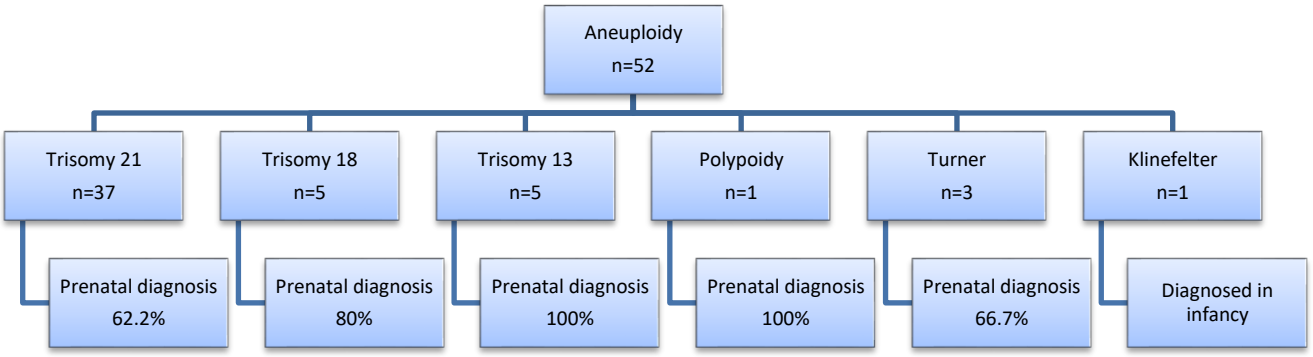
The above case in a male fetus was diagnosed prenatally and was a consequence of posterior uretheral valves. Associated abnormalities included imperforate anus, multicystic dysplastic kidneys, VSD and a malformation of intestinal fixation.

Chromosomal Abnormality

A chromosomal abnormality is recorded for 60 cases. The majority, (n=57, 95%) are listed in the primary diagnostic position.

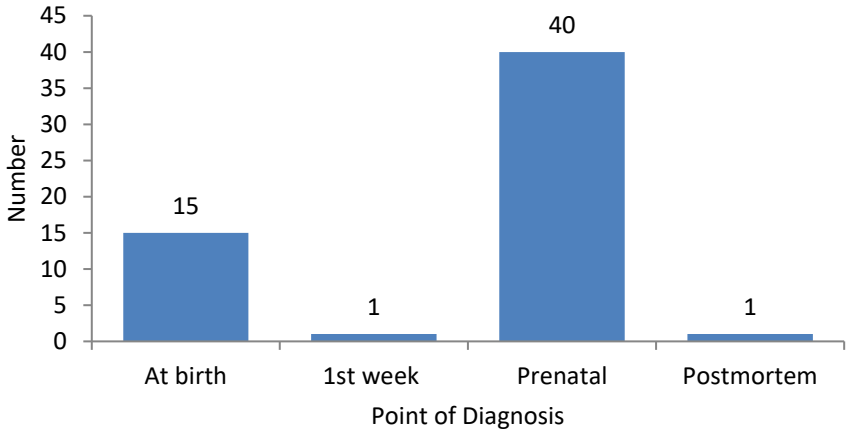
Figure 4.7: Overview of Prenatal Diagnosis of Primary Chromosomal Abnormality, (n=52).

(Excluding unbalanced translocations and partial deletions)



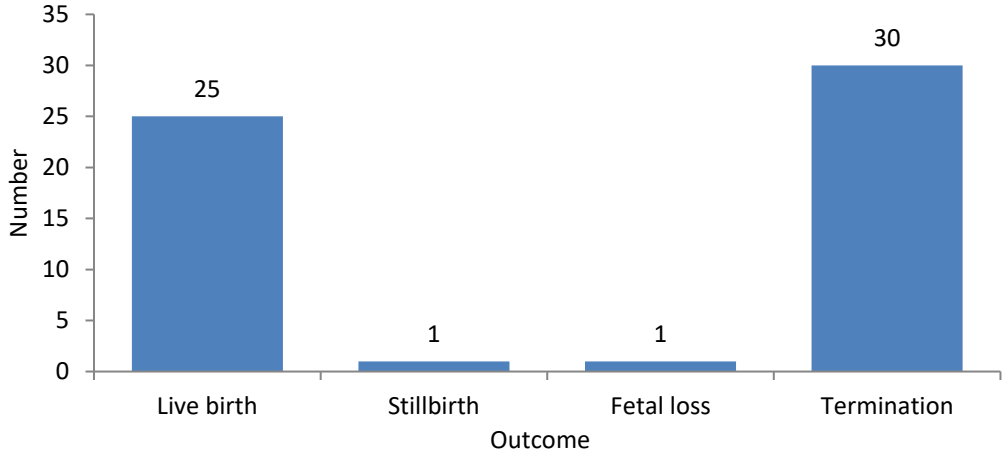
Seventy percent of all primary chromosomal abnormalities were diagnosed prenatally, (Figures 4.7 & 4.8). Sixteen cases, (28%), were diagnosed within the first week of infant life.

Figure 4.8: Point of diagnosis of Primary Chromosomal Abnormality, (n=57)



Termination of pregnancy is the predominate outcome, (n=30, 52.6%). When a prenatal diagnosis of chromosomal abnormality is made termination of pregnancy is performed in 75% of cases.

Figure 4.9: Outcome of pregnancy for Primary Chromosomal Abnormality, (n=57)



TRISOMY 21 (DOWN SYNDROME), (Q900, Q909)

Trisomy 21 is one of the most common congenital anomalies. There is a well-defined phenotype, intellectual delay and major and minor structural anomalies – most commonly cardiac and gastrointestinal. Infants tend to be small and have a low birthweight. Advanced maternal age is the most significant established risk factor.

A total of 37 cases were associated with Trisomy 21. Mean maternal age was 37 years, (range 22 – 45 years).It was always recorded as the primary abnormality. Nineteen cases, (51%), were live born. The remaining eighteen cases were all terminated following prenatal diagnosis, (Figure 4.10).

Associated anomalies included trachea-oesophageal fistula, cystic hygroma, VSD, ASD, AVSD, congenital hydrocephalus and exomphalos.

There were fourteen cases of Trisomy 21 where prenatal diagnosis was not achieved, (Figure 4.11). All women in NHS GG&C are offered screening for Trisomy 21. Information is available through the PNBS system regarding this screening process including those mothers who were offered yet declined prenatal screening and where screening was performed but a diagnostic test was declined. This additional data is reported separately through the annual NHS GG&C Public Health Screening Report and is therefore not included here.

Figure 4.10: Outcome of pregnancies associated with Trisomy 21, (n=37)

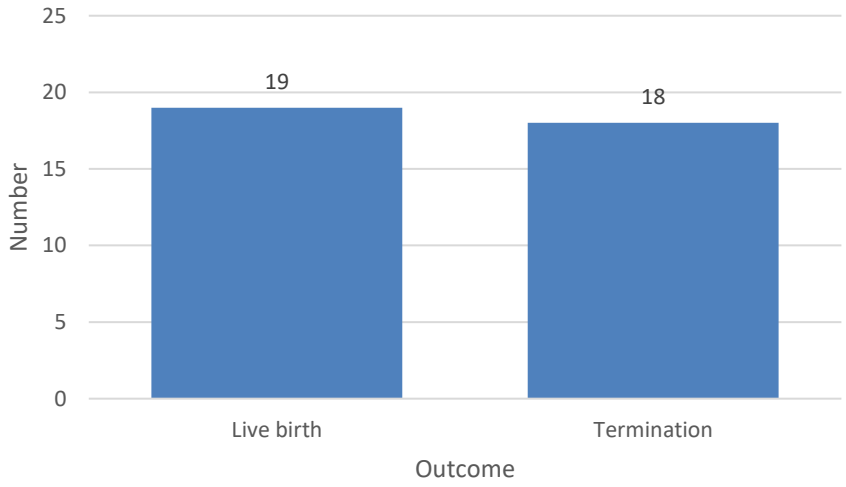
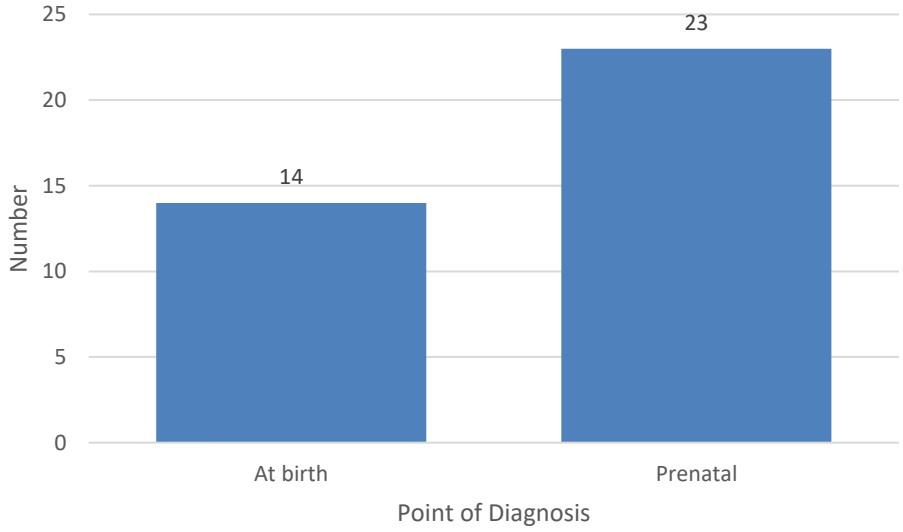


Figure 4.11: Point of diagnosis for Down syndrome, (n=37)



TRISOMY 18, (Q910)

Trisomy 18, also called Edwards syndrome, is a chromosomal condition associated with abnormalities affecting several body systems. The condition is increasingly diagnosed in prenatal life. Typically, ultrasound examination will reveal signs of intrauterine growth retardation associated with features such as neural tube defect, exomphalos, congenital heart defects and polyhydramnios.

There were five cases of Trisomy 18, (Edward's syndrome), listed in the data.

Q910	TRISOMY 18	Live birth; Diagnosed at birth; VSD; PDA
Q910	TRISOMY 18	Prenatal diagnosis; Live birth; Oesophageal atresia; VSD; Rocker-bottom foot[25]
Q910	TRISOMY 18	Cystic hygroma; Termination
Q910	TRISOMY 18	Cystic hygroma; Termination
Q910	TRISOMY 18	Exomphalos; Termination

Most affected pregnancies ended as termination. However, there were two live births. In the first case induction for IUGR resulted in the delivery of female infant. She was to be an early neonatal death. There were no structural abnormalities amenable to antenatal detection, the VSD was small. Subsequent review demonstrated that biochemical screening for Trisomy 18 would have detected this case but is not currently available within NHS GG&C.

In the other case Trisomy 18 was detected antenatally but the parents elected to continue.

TRISOMY 13, (Q914, Q915)

Trisomy 13, also called Patau syndrome, is a chromosomal condition associated with severe intellectual disability and physical abnormalities in many parts of the body. Like trisomy 18 this condition is often diagnosed through a recognizable pattern of dysmorphism and malformation. Individuals with trisomy 13 often have heart defects, brain or spinal cord abnormalities, very small or poorly developed eyes, (microphthalmia), extra fingers or toes, a cleft lip with or without a cleft palate, and hypotonia.

Q914	TRISOMY 13	Gastroschisis; VSD; Cleft lip & palate; Polydactyly; Cystic kidney; Early NND
Q914	TRISOMY 13	
Q914	TRISOMY 13	
Q914	TRISOMY 13	Hypoplastic left heart; Double outlet right ventricle
Q914	TRISOMY 13	Di George syndrome; Cardiac malposition

There was one live birth in this group. Concerns were raised at the 20-week anomaly scan with a cleft lip and possible cardiac defect, the left side of the heart was smaller than the right side and there were multiple echogenic cardiac foci. There was also felt to be a small exomphalos. The fingers appeared to be overlapping.

[25] Coded Q668 which means 'Other congenital deformity of feet'. The Paediatric adaptation of ICD 10 would more accurately record 'Rocker-bottom feet' as Q6680.

Harmony™ Prenatal Test suggested a likely trisomy 13. Whilst this test does not have 100% accuracy, trisomy 13 was certainly in keeping with the anomalies detected on ultrasound scan. The pregnancy continued to livebirth of a male infant at 37 weeks' gestation who was unfortunately to be an early neonatal death.

TRIPLOIDY, (Q927)

Triploidy, a complete extra set of chromosomes, is a common chromosomal anomaly in human gestation occurring in 1-2% of all conceptions. Most triploidies abort spontaneously in the 1st trimester. Triploidy accounts for 10% of spontaneous miscarriage. Triploidy may result from either diandric or digynic fertilizations.

In diandry the extra set of chromosomes is of paternal origin either from a meiotic error leading to a diploid sperm or more typically dispermic fertilization, Diandry predominates in cases of triploidy without embryos after nine weeks or in the second trimester with foetuses of relatively normal size and placental features of a partial hydatidiform mole. Digyny, (fertilization of a diploid oocyte) predominates in early miscarriages with embryos before nine weeks or in 2nd trimester loss of a fetus with marked asymmetrical growth retardation.

Q927	TRIPLOIDY	Termination at 16 weeks' gestation

TURNER SYNDROME, (Q960)

Turner syndrome is an aneuploidy, and is also known as 'monosomy X', (45XO). The incidence is roughly 1:2500 live-born girls. Fifteen percent of cases demonstrate some mosaicism. Sometimes a lymphangioma, (cystic hygroma), prompts diagnostic investigation.

Q960	TURNER SYNDROME	Prenatal diagnosis; Live birth
Q960	TURNER SYNDROME	Prenatal diagnosis; Cystic hygroma; Fetal loss
Q963	TURNER MOSAIC SYNDROME	Stillbirth; Diagnosis at post-mortem examination

Most girls and women with Turner syndrome have normal intelligence. Developmental delays, nonverbal learning disabilities, and behavioural problems are possible, although these characteristics vary among affected individuals.

KLINEFELTER SYNDROME, (Q980)

Klinefelter syndrome, (47, XXY), affects 1:1000 males and is typically diagnosed in early adulthood during investigations of infertility. A single case of Klinefelter syndrome is listed.

Q980	KLINEFELTER SYNDROME	Live birth at term; Diagnosis in 1st week of life

DELETIONS, (Q935, Q938)

The varied presentations of Di George syndrome have already been considered. Di George syndrome is classified under ICD 10 as a primary blood disorder but always given the associated abnormality code of 'Q935'. It is perhaps better considered under this coding as a 22g11.2 deletion syndrome.

Di George syndrome is also known as '3rd & 4th Pharyngeal Pouch syndrome' and 'Hypoplasia of the Thymus & Parathyroid' It overlaps clinically with 'Conotruncal Anomaly Face syndrome'. It is characterized by neonatal hypocalcaemia which may present as tetany or seizures. A variety of associated cardiac malformations are recognized and renal anomalies are common.

D821	DI GEORGE SYNDROME	Multiple cardiac abnormalities; Live birth
D821	DI GEORGE	Prenatal diagnosis; Cardiac and renal anomalies; Live birth
D821	DI GEORGE	Prenatal diagnosis; Persistent truncus; VSD; Termination

A further case of an unbalanced 4p14 deletion, (Wolf-Hirschhorn), is listed. Wolf-Hirschhorn syndrome is a contiguous gene deletion syndrome associated with a hemizygous partial deletion of the short arm of chromosome 4. It is characterized by intrauterine growth retardation, facial clefting, 'Greek helmet' facies and diaphragmatic hernia. Prenatal diagnosis has been established after karyotyping for IUGR.[26]

Q938	UNBALANCED DELETION 4p14	Talipes equino-varus; Prenatal diagnosis; Termination

The above case was a singleton pregnancy. Increased nuchal thickening, reduced liquor and abnormal position of both feet had been noted on ultrasound scan. Amniocentesis confirmed a sizeable deletion in the 4p14 position. Termination of pregnancy was performed at 23 weeks' gestation. Post-mortem examination was declined. The deletion appears to have arisen *de novo*.

OTHER SPECIFIED CHROMOSOMAL ABNORMALITIES, (Q998)

As discussed in previous reports the ICD 10 code 'Q998' is used for a collection of chromosomal abnormalities that are not easily categorized elsewhere. The code is used on four occasions in the current data set.

Q998	MILLER DIEKER SYNDROME (17p13 deletion)	Prenatal diagnosis; Live birth
Q998	UNBALANCED TRANSLOCATION CHROMOSOME 3	Prenatal diagnosis; Termination
Q998	UNBALANCED TRANSLOCATION CHROMOSOME 3	Prenatal diagnosis; Termination
Q998	UNBALANCED TRANSLOC CHROMOSOME 7	Prenatal diagnosis; Termination

Quite why Miller Dieker syndrome is not given a code that would allow it to be classified amongst the deletions, (even Q939), is uncertain. Miller–Dieker syndrome, (chromosome 17p13.3 deletion syndrome),

[26] Witters I et al. Ultrasound 2011; 19: 224-226

is a micro deletion syndrome characterized by congenital malformations. The congenital malformation can be genetic random and of unknown origin but the malformation is characterized by lissencephaly. The disorder arises from the deletion of part of the small arm of chromosome 17p (which includes both the LIS1 and 14-3-3 epsilon genes), leading to partial monosomy. This infant, a female delivered at 36 weeks' gestation also had a congenital pulmonary valve stenosis and an abnormality of the aortic valve.

There were two cases where an unbalanced translocation of chromosome 3 were diagnosed. These cases relate to the same mother with both fetuses terminated at 13 weeks' gestation following prenatal diagnosis with CVS. On both occasions an early ultrasound scan had demonstrated a cystic hygroma and small exomphalos. Later genetic studies revealed one of the parents to be a carrier of a pericentric inversion of chromosome 3.

Appendix 1: General Statistics

NHS GREATER GLASGOW & CLYDE MATERNITIES 1ST APRIL 2015 TO 31ST MARCH 2016

Source: GG&C Pregnancy & Newborn Screening System: NHS Greater Glasgow & Clyde Hospitals & Residents.

Maternity Unit	Appointed Referrals Not NHSGGC Residents	Appointed Referrals NHSGGC Residents	Appointed Referrals Total	Bookers Not NHSGGC Residents	Bookers NHSGGC Residents	Bookers Total
Not assigned to a unit	506	299	805	506	299	805
Princess Royal Maternity Hospital (PRM)	1,491	4,235	5,726	1,353	3,871	5,224
Royal Alexandra Hospital (RAH)	365	3,517	3,882	330	3,241	3,571
Queen Elizabeth University Hospital*	576	6,488	7,064	531	6,016	6,547
Total	2,938	14,539	17,477	2,720	13,427	16,147

*Previously the Southern General Hospital

GG&C BIRTHS 1ST APRIL 2015 TO 31ST MARCH 2016

Source: Child Health Universe Extract run 15th August 2016

Area	Live Births	Stillbirths
Clyde	3,174	48
Greater Glasgow	9,249	
Total	12,423	12,471

Appendix 2: Case Prevalence

CASE PREVALENCE COMPARISON, (PER 10,000 BIRTHS) ‡

Abnormality	Prevalence in Primary Position	Prevalence in any Position	EUROCAT Prevalence Data
Amniotic Band Sequence	N/A	N/A	0.51
CCAM (Q338)	N/A	N/A	0.95
Bilateral Renal Agenesis (Q602)	1.60	2.41	1.18
Congenital Cataract, (Q120)	4.81	4.81	1.23
Hirschprung's Disease, (Q431)	1.60	1.60	1.24
Turner syndrome, (Q914-917), (Q960-969)	2.41	2.41	2.24
Craniosynostosis, (Q750)	0.80	0.80	2.39
Hypoplastic Left Heart, (Q234)	3.21	4.01	2.66
Congenital Diaphragmatic Hernia, (Q790)	5.61	5.61	2.76
Gastroschisis, (Q793)	1.60	2.41	2.85
Exomphalos, (Q792)	3.21	6.41	3.00
Fallot's Tetralogy, (Q213)	4.81	4.81	3.45
Transposition of Great Arteries, (Q203)	3.21	4.81	3.52
Coarctation of Aorta, (Q251)	3.21	4.81	3.85
Atrioventricular Septal Defect, (Q212)	N/A	7.22	4.09
Edwards syndrome, (Q910-913)	4.01	4.01	5.13
Hydrocephalus, (Q030-Q039)	2.41	3.21	5.77
Developmental Dysplasia of the Hip, (Q65)	9.62	11.22	8.07
Cleft Lip/Palate, (Q352-Q279)	14.43	20.84	8.77
NTD's, (Q000, Q010-Q019, Q051-Q059)	20.04	20.85	9.66
Hypospadias, (Q549)	4.01	6.41	18.01
Down syndrome, (Q900-Q909)	29.67	29.67	22.10

‡Denominators: The congenital anomaly surveillance tool that has been used to compile the data within this report is restricted to mothers' resident within the geographically defined area of NHS GG&C at the time of birth. To allow comparison with the EUROCAT prevalence data the appropriate denominator for the prevalence data is therefore the total live births and stillbirths for that area between 1st April 2015 and 31st March 2016 which is 12,471. Data was extracted on 15th August 2016.

*Source for comparison data: EUROCAT Website Database. The EUROCAT prevalence data quoted is for 2007-2011.

Appendix 3: Prenatal Detection Rates

PRENATAL DETECTION RATES: COMPARISON WITH 'ESTABLISHED' DATA

Primary Abnormality	Observed Prenatal Detection Rate	Expected Detection Rate*	EUROCAT Observed
Anencephaly	100%	98%	96.7%
Spina Bifida	93.75%	90%	82.9%
Congenital Diaphragmatic Hernia, (Q790)	100%	60%	58.0%
Cleft Lip, (Lip alone OR Lip & palate)	100%	75%	
Cleft Lip, Cleft Palate, Cleft Lip & Palate	52.6%		50.7%
Gastroschisis	100%	98%	91.6%
Exomphalos	100%	80%	83.0%
Bilateral Renal Agenesis	100%	84%	88.1%
Talipes Equino-varus	71.4%		39.8%
Serious Cardiac Abnormalities (EUROCAT defined)		50%	
Transposition of Great Vessels, (Q203)	50%		41.4%
Atrioventricular Septal Defect, (Q212)	100%		
Fallot's Tetralogy	16.7%		
Ebstein's Anomaly	N/A		
Hypoplastic Left Heart, (Q234)	100%	61%	71.9%
Hypoplastic Right Heart, (Q226)	N/A		
Coarctation of the Aorta, (Q251)	50%		
Trisomy 21	62.2%	95%	63.8%
Trisomy 18	80%	95%	90.9%
Trisomy 13	100%	95%	90.9%

*Ward P & Soothill P. Fetal Anomaly ultrasound scanning: the development of a national programme for England. TOG 2011; 13: 211-217.

The widespread use of ultrasound has led to the erroneous belief that all major and many minor structural fetal abnormalities can be detected before birth. Indeed, some major malformation such as anencephaly are rarely missed on routine ultrasound. However prenatal diagnosis of some abnormalities is highly dependent on the resources and skills available e.g. if screening for CHD is limited to the examination of the four-chamber view, major abnormalities such as transposition of the great arteries and tetralogy of Fallot will not be detected. Isolated cleft palates are extremely difficult to identify and problems such as anal and rectal atresia are simply not amenable to prenatal diagnosis, (nor are many dysmorphic features).