AGE RELATED ASSESSMENT OF THE STATUS OF CLINICAL CARE OFFERED TO CHILDREN WITH DOWN SYNDROME AT KENYATTA NATIONAL HOSPITAL

A dissertation submitted in partial fulfillment of the requirements for the award of the Masters Degree in Paediatrics and Child Health of the University of Nairobi.

Candidate: Dr. Benard Munyao (MB Ch.B – UON)

H58 / 67523 / 13

12th June, 2016

DECLARATION

I hereby solemnly declare that this dissertation is my original work, and to the best of my knowledge, has not been submitted elsewhere for examination.

Signed.....Date.....

Dr Benard Munyao (MB ChB)
Department of Paediatrics and Child Health, University of Nairobi

This dissertation is being submitted with our full approval as University supervisors:

Signed.....Date.....

Professor Jowi Christine Yuko (MB ChB, M. Med paeds, paediatric Cardiology)

Associate professor,
Department of Paediatrics and Child Health, University of Nairobi

Signed..... Date.....

Dr Daniel M Njai (MB Ch B, M.Med paeds)

Senior lecturer
Department of Paediatrics and Child Health, University of Nairobi

TABLE OF CONTENTS

ACKNOWLEDGEMENTS

I wish to convey my sincere thanks to Prof Christine Jowi and Dr Daniel Njai, my supervisors, for their constant encouragement and counsel which has enabled me to carry out this study to completion.

I thank the entire faculty of the Department of Paediatrics and Child Health for their support and positive critique and provision of an enabling environment for this study. I thank the staff or paediatric, neurology, physiotherapy and speech therapy clinics for their cooperation during data collection.

My family was always there for me during this time. I sincerely thank them.

Above all I thank God for good health and strength He gave me throughout the study period.

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ASD	Atrial Septal Defect
CHD	Congenital Heart Disease
HLA	Human Leukocyte Antigen
IQ	Intelligence Quotient
KNH	Kenyatta National Hospital
SPSS	Statistical Package for Social Sciences
VSD	Ventricular Septal Defect

ABSTRACT

Background: Down syndrome, a common chromosomal disorder is the leading cause of learning disabilities in children. The median survival of individuals with Down syndrome has increased considerably in developed countries, but this may not be the case in developing counties. Despite clear international guidelines on the follow-up and management of down syndrome children,their care and follow up locally remains haphazard.

Objective: To evaluate the status of care and clinical evaluation of children with Down syndrome at Kenyatta National Hospital.

Methods: This was a Descriptive Cross-Sectional study involving children with Down syndrome from birth to 18 years in paediatric wards and outpatient clinics at Kenyatta National Hospital. We administered guided questionnaire and reviewed their documented files on continuity of care given to them. Data was coded and entered into SPSS version 23.0. We employed descriptive statistics like means and proportions to analyze the sociodemographic characteristics of the respondents. Cross-tabulations with chi-square correlation was used to establish the relationship between variables like status of evaluation, diagnosis at evaluation and care given to the children.

Results: Out of the 101 children recruited for the study, 60 (59.4%) were males. The mean age of the respondents was 2.56 years (range 7 weeks-15 years). The primary caregiver was the mother in 94.1% of cases. Majority of the children were not done thyroid assessment (63%), cardiac assessment (49%) and ophthalmological assessment (91%).For those who had been evaluated for congenital anomalies, most evaluation was done at less than 1 year of life. Only 7.1% had normal milestone development. Of the 92.9% who had delayed milestones, 60% were on follow up at physiotherapy and speech therapy clinics.

Conclusion: This study has found a significant proportion of children with Down syndrome who are not followed up or evaluated as per the known guidelines. We recommend more education of clinicians to ensure these children get care to avoid long term complications which are associated with high mortality and morbidity.

1.0 INTRODUCTION AND LITERATURE REVIEW:

1.1 Definition and Epidemiology:

Down syndrome (DS) is a genetic disorder resulting from extra chromosomal material chromosome 21. The resultant syndrome causes varying degrees of intellectual retardation and developmental delays, coupled with a myriad of medical problems[1].

In Europe, DS accounts for approximately 8% of all registered cases of congenital anomalies. Worldwide, about 10 in 10, 000 live births are afflicted by DS, and the prevalence continues to rise. Some socio-cultural variables affect the prevalence of DS. For instance, in countries where abortion is illegal (Like Ireland and United Arab Emirates), more cases of DS are reported, whereas in France, the prevalence is low due to termination of pregnancies suspected to have the condition. A recent report put the prevalence of DS in The Netherlands at 16 per 10, 000 live births[2, 3]. Likewise, DS has been increasing reported in the United Kingdom but there has been no overall change in the live birth prevalence of down syndrome[4].

Some of the factors associated with the increasing incidence and prevalence of DS are increasing maternal age and improved survival rates for infants with Down syndrome which have outweighed the effects of prenatal diagnosis followed by the termination of pregnancy and a declining general birth rate[5]. In Kenya the prevalence of Down syndrome is not known. This may be attributed to early deaths and challenges in diagnosis. Maternal age affects the chances of having a pregnancy with Down syndrome. At age 20, the chance is one in 1441; at age 30, it is one in 959; at age 40, it is one in 84; and at age 50 it is one in 44[5]. Nevertheless, studies have shown that about 70% of cases of DS are born to women 35 years and younger, possibly due to the fact that they tend to have more children.

1.11 Risk factors and pathophysiology of DS

Down syndrome is a trisomy, with three copies of the genes on chromosome 21, rather than the usual two[1]. This condition is not inherited in a Mendelian fashion, with the parents of the affected individual being normal. If parents have a child with DS, they have a risk of 1% of having a second child with the syndrome. if both parents are found to have normal karyotypes[1].

Trisomy 21

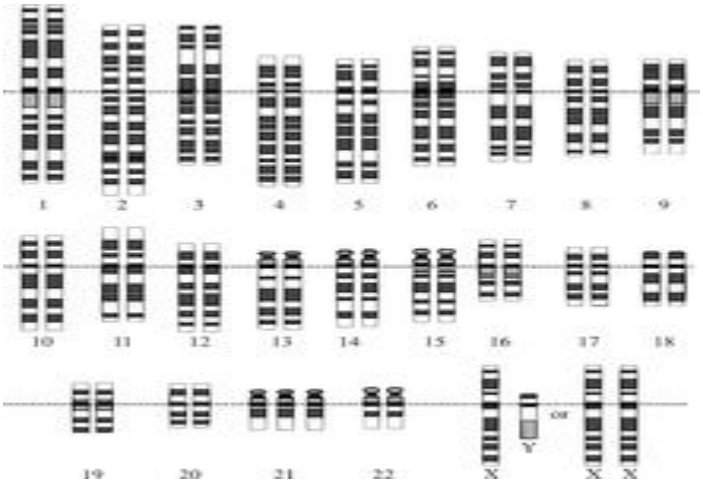


Figure 1: Karyotype for trisomy Down syndrome; showing three copies of chromosome 21

1.12Translocation

The extra chromosome 21 material may result from a Robertsonian translocation in 2–4% cases.[6] In a Robertsonian translocation, one arm of chromosome 21, typically the long arm may be attached to chromosome 14. In a male affected with Down syndrome, it results in a karyotype of 46XY,t(14q21q).This may be a denovo mutation, or inherited from mother or father, though the parent may have normal phenotype; however, during production of egg or sperm cells, a higher chance of creating reproductive cells with extra chromosome 21 material exists. Consequently, the chance of having a child with DS is about 15% when the mother has this genotype, and 5% when the father is affected.

1.2 Clinical features

1.2.1 Newborn assessment

When some unique characteristics are observed in a child, they can influence the decision to do karyotype testing, which is the gold standard for diagnosis of DS. One of the striking factors that may prompt testing is hypotonia[7]. Other common findings include a simian fold, congenital heart disease, gastrointestinal anomalies and cataracts.[8]

As the child advances in age, the attendant features include growth delays, facial anomalies like those of neonates and learning impairment. Young adults with DS have below average IQ. One study found the average IQ to be 50, equivalent to mental age of an 8-9 year old.

1.3 Complications in Down syndrome

This condition is characterized by psychomotor development and a myriad of features of dysmorphism [4]. Victims are at an increased risk of multisystemic congential disorders such as gastrointestinal, cardiac, endocrine, neurological and skeletal anomalies. Celiac diseases and hypothyroidism are more common in DS than in the general population. Survival for individuals with DS has increased over the years, from 25 years three decades ago to 49 years in current reports in the United States.

A study looking at death certificates of DS individuals found that congenital cardiac and respiratory disorders were the commonest causes of death. Malignancies accounted for less mortality, with the exception of leukaemia and testicular cancer, which are highly prevalent in Down syndrome.[5]

The life expectancy of children with DS has improved vastly in recent times. For instance, there was a substantial drop in infant mortality rate in children with DS from 7.07% in 1992 to 4% in 2003 in a study in the Netherlands. The general infant mortality rate in the same population was found to be 0.48%[8]. This fall is attributed to improved surgical treatment of cardiac gastrointestinal anomalies. The risk of mortality is highest in the first year of life. There still remains room for further reduction of morbidity and mortality associated with DS. This is hedged on the proper treatment of respiratory and neonatal complications of DS.

With the increase in life expectancy of DS, there is expected to be a substantial growth of the total population of individuals with DS, and many will transition into adulthood. To improve the care of these children, there is need to place emphasis on preventive programmes and adopt evidence-based medical guidelines for their care.

Table 1: Prevalence of different complications in Down Syndrome[9]

Complication	Prevalence (%)	Most Common
Congenital heart defects	44–58	Atrioseptal defects 54%, ventricular septal defects 33%, pulmonary hypertension 14%
Vision disorders	38–80	refractive error 43-70%,strabismus 20-47%
Hearing disorders	38–78	chronic rhinorrhea and middle ear diseases
Obstructive sleep apnoea syndrome	57	
Wheezing airway disorders	30–36	Respiratory syncitial virus infections
Congenital defects of gastrointestinal tract	4–10	Tracheoesophageal fistula,esophageal atresia,doudenal stenosis,hirshprung,constipation
Coeliac disease	5–7	
Obesity	30–35	
Transient myeloproliferative disorder	10	Acute myeloid leukemial,acute lymphocytic leukemia,myelodysplastic syndromes
Thyroid disorders	28–40	congenital hypothyroidism,hashimoto thyroiditis
Atlanto-axial instability	10–30	
Urinary tract anomalies	3.2	hydrouretus
Skin problems	1.9–39.2	alopecia,seborreic dermatitis
Behaviour problems	18–38	emotional instability,obsessive compulsive disorders,depression

1.31 Visual disorders

Visual problems are very common in children with DS, affecting roughly 50% of the children. Proper vision is critical in the development of a child and for proper adaptation to the environment.

Dysmorphic features of structures around the eyes are common in DS; these include epicanthal folds, narrowed or slanting of palpebral features, the mongoloid slant and Brushfield spots (38–85%). Vision disorders prevalent in DS include strabismus (20–47%),

nystagmus (11–29%), congenital cataract (4–7%), acquired cataract (3–15%), blepharitis (7–41%), refractive errors (43–70%) and glaucoma (0.7%).[10, 11]

Keratoconus is rare in childhood but develops later in life in individuals with Down syndrome.[11] An early screening programme, backed by robust guidelines could detect and manage these complications early, with less complications and better quality of life[10].

1.32 Cardiovascular disorders

Worldwide, congenital cardiac defects affect about 44-58% of children with DS, with Atrioventricular septal defect and ventricular septal defect as the commonest forms of abnormalities. One study reported a prevalence of 54% atrioseptal defects and 33%of ventricular septal defects.[4] A serious CHD may exist even in a child with a normal systemic examination. Early detection is crucial in the management of these children and facilitates optimal management and better outcomes for these children, with fewer complications.

The surgical correction of significant defects usually takes place at the age of 2–4 months, though it is sometimes performed earlier (e.g. in cases of Tetralogy of Fallot). An elevated incidence (5.2–13.7%) of persistent pulmonary hypertension of the neonate (PPHN) with Down syndrome has recently been established, and there should be a specific focus on this condition after birth Early assessment of the cardiac condition of neonates with Down syndrome should always be performed by echocardiography in the first month of life.[1, 3, 12]

1.33 Ear, nose and throat disorders

Ear disorders are more prevalent in individuals with DS, compared to the general population. These problems have a positive correlation with developmental delay. Midface hypoplasia is common in children with Down syndrome and consists of abnormalities of the nasopharynx, abnormal Eustachian tube anatomy, abnormal tooth development and agenesis of the teeth. Because of hypotonia and macroglossia, children with DS are likely to suffer chronic rhinorrhoea and chronic otitis media.

Unlike in the general population, allergy and atopy are not the underlying causes of chronic rhinitis in children with Down syndrome.[13] Other immune disorders predispose them to upper airway infections instead.[4] Hearing loss, even in its mildest form, has detrimental effects on educational, language and emotional developments, significantly affecting a child's articulative skills. This calls for early and regular assessment of hearing, active search for chronic ear disease and prompt treatment.[15]

Sleep disorders are common in DS, and have been reported in approximately half of them. These have been associated with macroglossia, glossoptosis, adenotonsillar enlargement and enlargement of lingual tonsils. There is a poor correlation between parental impressions of sleep problems and polysomnography results.[8] Baseline polysomnography is critical in children between 3-4 years of age.

1.34 Respiratory disorders

Respiratory problems account for majority of hospital admissions in children with Down syndrome. Respiratory syncytial virus (RSV) is more common, and poses a greater risk of hospitalization and mortality in children with this condition.[14] Recurrent wheeze is very common among children with Down syndrome (it is found in up to 36%) and is related to previous RSV infection and to other factors such as tracheamalacia.[14]

The clinical picture may mimic asthma but is not equivalent to asthma. These respiratory problems can in turn become exacerbated because of the existence of CHD with haemodynamic instability and as a result of hypotonia, both known characteristics of Down syndrome. Other causal factors include airway anomalies like tracheolaryngomalacia, pulmonary anatomical changes like pulmonary hypoplasia, and subpleural cysts. Subpleural cysts are common in individuals with Down syndrome (up to 36%) but are difficult to detect on plain chest films—CT imaging is needed to detect them.[4] Furthermore, an association with abnormal lung growth and lung hypoplasia is found in children with Down syndrome. RSV prophylaxis with human monoclonal antibodies in children with Down syndrome with CHD is common, but in a child without CHD, the prophylaxis has to be considered because of their risk of the more frequent and serious infections associated with RSV.[14]

1.35 Gastrointestinal tract disorders

Gastrointestinal malformations have been reported in up to 10% of children with DS, and are a major cause of morbidity in infancy. Common disorders include trachea-oesophageal fistula, esophageal atresia, pyloric stenosis and duodenal atresia. Congenital megacolon affects up to 3% of children, while ano-rectal malformations have been reported in 1-4%. Compared with normal children, DS predisposes children to these malformations, with an increased risk of 25-30%. Coeliac disease is also common in DS, which confers a risk ten times higher than the general normal population.[17]

It is important to screen and actively look for cases of celiac disease so as to institute proper management to prevent common complications such as failure to thrive, anaemia, osteoporosis and malignancies. Human Leukocyte Antibody (HLA)-DQ2 and HLA-DQ8 typing is recommended in the first year of life, and this can be done by buccal swabs instead of blood. This has the benefit of excluding children with negative HLA-DQ2 /DQ8 results from further screening, and provides reassurance of the absence of celiac disease. Beginning three years of age, IgA anti-endomysium and anti-tissue transglutaminase antibodies should be employed in testing for celiac disease.[17, 18]

An aberrant right subclavian artery, whose risk is increased in DS (19-36%) is associated with compression of the oesophagus and dysphagia. Moreover, impaired oral motor function, gastro-oesophageal reflux or congenital disorders have to be considered as a cause in feeding problems in children with Down syndrome.[19, 20] Hypotonia and Hirschprung disease are risk factors for chronic constipation in these children[12].

Due to potential benefits to the immune system and psycho-emotional growth, and development of oral motor system, parents should be advised to breastfeed children with DS [4]. Swallowing, drinking and chewing can be difficult in these children because of hypotonic muscles and poor co-ordination.

1.36 Haemato-oncological and immunological disorders

Up to 66% of neonates with DS may have thrombocytopenia, while 33% have polycythaemia[21]. Thrombocytopenia has to be distinguished from pre-malignancy states like leukaemia, while polycythaemia may herald respiratory complications.

The risk of acute myeloid and lymphoblastic leukaemias is increased in DS and vigilance must be exercised when screening these children. Myeloid leukaemia in children with Down syndrome is heralded by a preleukaemic clone (transient myeloproliferative disorder), which may disappear spontaneously but may need treatment when symptoms are severe.

The common age at onset of leukaemia is 5[21]. Children with Down syndrome have impaired T- and B-lymphocyte physiology, predisposing them to infections. Conversely, the risk of allergy in children with DS is lower than that of the normal population[13, 14, 22].

1.37 Endocrine disorders

Neonates with DS have a left shift in thyroid stimulating hormone and thyroid hormonal profiles. The benefit of thyroid hormone replacement in children with DS has not been ascertained by large scale studies[23].

Thyroid disorders have been reported in up to 28–40% of children with Down syndrome, and they increase in frequency, up to 54%, as the children age.[15, 23] These disorders include congenital hypothyroidism which affects up to 4%, primary hypothyroidism, Hashimoto thyroiditis and compensated hypothyroidism. Grave's disease may occur in up to 2% of children. These thyroid antibodies are the second most frequently present, and when present, they can cause manifest hypo-or hyperthyroidism within 2 years in almost 30%, but these antibodies are as such not primary related to abnormal thyroid function.

Frequent testing of these children can unmask hypothyroidism because of frequent development of antibodies to thyroid cells. When both are normal in the first decade of life, there is a low probability of hypothyroidism in the second decade. Diabetes mellitus is more common in DS, although the causal mechanisms are not well elucidated.

1.38 Orthopaedic disorders

Laxity of ligaments, joint hypermobility and hypotonia are hallmark features of DS skeletal disorders[18]. Several studies have reported a prevalence of 8-63% of craniocervical instability, while atlanto-axial instability occurs in up to 30% of victims. These abnormalities have implications in medical management of these patients. For instance intubation needs to be performed with extra caution. These children should be supervised during sports, as neck injuries can lead to devastating consequences.

Individuals with DS have a characteristic gait, with external rotation of the hips, knees in flexion and valgus, and externally rotated tibias. In childhood, pes planovalgus is often seen, and in cases where marked pronation of the foot creates problems with stable ambulation, active support is warranted.

Acquired hip dislocation affects around 30% of DS children and should be considered in a limping child.Further, patellofemoral instability is reported to occur in 10–20% of children with Down syndrome; while the risk of slipped capital femoral epiphysis is increased in DS and is associated with poor prognosis. Once they start ambulating, these joint abnormalities become apparent, typically at 2-3 years of age.[25, 26] The delay in motor development in children with Down syndrome is more pronounced than the delay in mental development.

Hypotonia significantly hampers motor development and causes postural instability, and also negatively affect static and symmetrical movement patterns, compensatory movement strategies and leads to less motional variability. Limitations in the functional activities of 5 to 7-year-old children with Down syndrome seem to be more related to the level of motor ability than to the level of performance of mental ability.[27] Early initiation of physical and occupational therapy is adviced to spur motor development and acquisition of motor skills. These exercises confer confidence and muscular strength.

1.39Urinary tract disorders

Down syndrome significantly increases the risk of urinary tract anomalies. Coupled with delayed psychomotor development, they have voiding disorders as well as delayed toilet training. Structural problems in the genitor-urinary tract which are associated with DS include hydronephrosis, hydroureter, renal agenesis and hypospadias. While no guidelines are available for screening of urinary tract, paediatricians should make efforts to screen for them using available tests.[28]

No specific guidelines towards the attitude in delay in daytime and nighttime continence in children with Down syndrome; besides the standard treatment, visual instruction is helpful as well as showing them how to do. The advice is to start training at the moment the child can sit properly and understand the items stool, urine and toilet.

1.40 Dermatologic problems

The dermatologic manifestations of DS present during the troublesome period of adolescence.[3] Common among them are alopecia areata (2.9–20%), vitiligo (1.9%), seborrhoeic eczema (8–36%), folliculitis (10.3–26%) and syringoma (12.3–39.2%). Other rare dermatologic disorders include elastosis perforans serpiginosa and milia-like idiopathic calcinosis cutis.[22, 27]

Though one study reported a relatively high prevalence of atopic eczema (56.5%), recent studies have reported lower prevalence of 1.4–3%. A possible explanation for this disparity is development of new and different diagnostic criteria for atopic dermatitis. This observation also notes a lower allergy risk in children with Down syndrome, which is in concordance with the studies on allergic rhinitis.[13, 22, 29]

1.41 Neuro-behavioural disorders

Neuro-cognitive development is retarded in DS, and intelligence quotient noticeably decreases in the first decade of life. This development plateaus during adolescence and persists in adulthood. They manifest with mild to moderate mental impairment, and their IQs range from 35-70. Only in rare cases is severe cognitive impairment seen in Down syndrome.[12] Counterproductive behaviour and avoidance tactics hamper learning and language production. Delayed verbal short-term memory and expressive language indicate the need for a special approach to teaching these children to speak (for example, learning to speak by first learning to read).[3, 15]

Because of poor motor co-ordination in oropharyngeal musculature, articulation is affected. Furthermore, DS predisposes to pronounced neuro-behavioural and psychiatric problems, found in 18% to 38%. Frequent manifestations include antisocial behavior such as attention deficit hyperactivity disorder (6.1%), conduct/oppositional disorder (5.4%) or aggressive behaviour (6.5%), and obsessive–compulsive disorders. More than 25% of adults with Down syndrome have a psychiatric disorder, most frequently a major depressive disorder (6.1%) or aggressive behaviour (6.1%).[3, 15]

Autistic disorders and their associated spectra have been reported in up to 7% of children with DS. This condition mimics many other neuro-cognitive disorders inherent in DS, making diagnosis difficult.

Epilepsy is seen in 8% of children with Down syndrome, with 40% occurring in infancy and often presenting as infantile spasms. Alzheimer's disease which is associated with Down syndrome appears later in life, not in childhood.[3]

1.5 Guidelines for evaluation of children with Down syndrome

In 2011, the American Academy of Pediatrics updated their previous 2001 guidelines on caring for children with Down syndrome. Several members of the Down syndrome Medical Interest Group assisted in the revision of the guidelines and this document has replaced the 1999 DSMIG medical guidelines.

Evaluate for:

Heart defects (~50% risk)-all infants with Down syndrome should receive an echocardiogram regardless of physical exam findings at birth to 3 months of age and atleast another at the age of 4 months to 12 months with no annual echocardiograms unless there is a heart defect that needs follow up

Feeding problems- Any infant with slow feeding, choking with feeding, recurrent pneumonia or persistent respiratory symptoms should receive a radiographic swallowing assessment as early as from birth to 3 months of age with subsequent tests done if there is a complication being followed up

Visual testing for eye problems especially cataracts should be done asearly as from birth to 3 months and a second testing at 4-12 months with subsequent testing done every 3 years if no complications where detected early.

Hearing tests should be done as early as from birth to 3 months to detect congenital hearing loss and repeated at 4-12 months with follow up tests annualy.

Gastrointestinal problems investigated as early as from birth to 3 months,celiac disease is common in genetic syndromes such as Down syndrome and may present early in life with gastrointestinal complitations such as abdominal distension,diarrhea,vomiting and even constipation,other complications include: Constipation.-If present, evaluate for limited fluid intake, hypothyroidism or GI tract malformation, including Hirschsprung disease. Gastroesophageal reflux.

Duodenal atresia or anorectal stenosis.

Children presenting with respiratory symptoms such as stridor, wheezing or noisy breathing should be evaluated from the begining of presention and managed as per the complications they have with no mandatory annual tests required

Hematologic abnormalities.-A complete blood count is recommended shortly after birth to check for leukemoid reactions, or transient myeloproliferative disorder and there after a total blood count should be done annually to monitor any abdomalities

Congenital hypothyroidism or hyperthyroidism.- Obtain TSH and a free thyroxine level at 4-12 months of age and anually.

Genetic counseling should be performed as early as before delivery in well equipped centres that can do amniocentesis and detect Down syndrome,in other centres it should be done immediately after birth and a karyotype result available

At 3- 4 years of age they should have a polysomnogram study done to assess the sleep pattern and detect sleep apnea which is associated with pulmonary hypertension and later right heart failure if not intervened early

Speech and swallowing problems should be managed as early as from birth to 3 months,4 to12 months and every year till coordination of swallowing and speech are well established.

The DS interest group in u.k and Ireland have come up with a screening tool for DS patients which guides the clinician on what to do at a particular time.

Table 2: Follow up/screening schedule for children with Down syndrome 0–18 years[30]

	Timeline for medical assessment of children with Down syndrome			
	0– 3 months	4– 12 months	Every year	Note
Genetic counseling	+			Once, after birth
Cardiac Ultrasound	+	+		Follow-up depends on the heart defect
Vision	+	+		Every 3 years
Hearing	+	+	+	
Obstructive sleep apnea			+	Polysomnography at 3–4 years
Periodontal			+	Dental agenesis
Constipation	+	+	+	
Coeliac disease	+			Every 3 years TGA, once HLA-DQ2 and 8[b]
Growth/Overweight			+	Specific Downcurves-length/weight
Haematology	+		+	TMD at first, leukaemia mainly first 5 years
Thyroid function		+	+	
Hips/Patellae	+	+	+	
AAI			+	neurologic screening, care during intubation
Physiotherapy	+	+	+	Most impact in first 4 years
Skin			+	
(Pre)Logopaedic	+	+	+	Until speech is well established

Whereby the full meaning of abbreviations is:
TGA-tissue transglutaminase antibodies
HLA DQ2-Human leucocyte antigen beta 2 allel
TMD-Transient myeloproliferative disorder

Standards of care; Health supervision and evaluation at various stages of life in children with Down syndrome (American Academy of Paediatrics guidelines)[12]

a) From birth to 1 month (Neonatal period)

Even before birth, thorough history and prenatal information is crucial in making a diagnosis of DS. Physical examination remains the most sensitive test in detecting salient features of DS, especially in the initial days of life. This should then trigger blood or buccal tissue investigation for chromosomal studies, which are confirmatory tests.

Empathy should be employed in divulging information to the parents/caregivers in a private and supportive setting. Proper guidance and counseling should be employed by healthcare givers in handling the parents. The process of counseling entails explaining the condition, its causes or risk factors, manifestations and possible complications. Any questions should be handled with empathy, and where necessary, referrals should be made. They should also explain to the parents about hypotonia, feeding difficulties and sleep difficulties at this stage.

The neonate should be evaluated as follows:

- Heart defects (50% risk). An early echocardiographic screening is crucial in diagnosing or ruling out presence of congenital heart defects. As soon as a diagnosis is made, appropriate referral should be made to a paediatric cardiologist as early as possible.
- Parents should be taught how to handle neonates with feeding difficulties like choking, recurrent pneumonias, failure to thrive, and necessary referrals done.
- A careful ophthalmological examination to look for a red reflex, which can be a pointer to congenital cataracts. Involvement of a paediatric ophthalmologist in the neonatal period is important.
- Objective testing should be done to look for hearing loss. This includes brainstem auditory evoked response and otoacoustic emissions.
- Physical examination should be done to rule out duodenal atresia and anorectal atresis/stenosis. Chronic constipation should point to Hirschprung disease, which should be thoroughly investigated.
- Early referral to a paediatric pulmonologist should be made for those with recurrent wheezing, stridor and respiratory infections.

- A full blood count should be done in the first month of life to check for leukamoid reactions or transient myeloproliferative disorder (TMD). These conditions may signal an increased risk for leukaemias.
- Thyroid stimulating hormone should be done to check for congenital hypothyroidism.

b) Standard of care from 1 month to 1 year of life (Infancy)

At every visit, thorough physical evaluation should be carried out. If earlier screened for hearing loss, a re-screening should be done at 6 months. At least once in the first 6 months, discuss with parents about obstructive sleep apnoea, including heavy breathing, snoring, frequent night awakenings, day time sleepiness, apnoeic pauses and refer appropriately. There should be referral to a paediatric ophthalmologist within 6 months for evaluation for cataracts, strabismus and nystagmus. Repeat thyroid profile at 6 months, then annually.

Continuous monitoring for cardiac defects is important. The clinician should be on the lookout for tachypnoea, feeding difficulties and poor weight gain. For large cardiac defects, surgical repair is recommended at 4 months of age to avoid complications.

Neurological evaluation and monitoring should be done to rule out seizures, infantile spasms and other complications.

Immunization for influenza in addition to other scheduled vaccines should be given.

c) Standard of care from 1 year to 5 years (Early childhood)

Like other ages, proper physical evaluation at every visit is essential/

- Review hearing loss especially in children with recurrent serous otitis media.
- Check vision and use developmentally appropriate subjective and objective criteria at each visit. An annual ophthalmologic review should be performed.
- Atlantoaxial instability is common in Dow syndrome and can lead to spinal cord injury in case of subluxation. If present, an early referral to paediatric neurosurgeon should be done.
- Thyroid stimulating hormone should be assayed annually.
- Advise on gluten sensitivity. Look for features of celiac disease like diarrhea, protracted constipation, failure to thrive and anaemia. Advise on gluten-free diet, and obtain tissue transglutaminase immunoglobulin A (IgA).

- Discuss obstructive sleep apnoea with parents. Refer all children by age 4 years to a sleep laboratory review for a polysomnogram.
- Maintain cardiology and neurology review.
- Review early interventions such as physiotherapy, occupational therapy and speech therapy.
- Discuss with parents behavioural and social progress and refer appropriately to a psychiatrist.
- Ensure the child gets annual influenza vaccine. In case of chronic cardiac/pulmonary disease, give 23-valent pneumoccal vaccine (PPS23) at 2 years of age and above.

d) Standard of care for 5-13 years of age (Late childhood)

At this age, the child should continue clinic visits with physical examination. Monitoring for BMI and diet should be done. There should be annual ear check-up, 2 yearly ophthalmological evaluation, annual thyroid stimulating hormone evaluation and neurological evaluation. Cardiac assessment should be individualized based on history of defects. Parents should be counseled on the risk of spinal injury if child engages in some sports.

e) Health supervision from 13 to 21 years or older (Adolescence to early adulthood)

- At the beginning of adolescence, hemoglobin and TSH levels should be measured annually. Annual audiologic and audiometric assessment should be done by a qualified audiometrist. Screening for celiac disease should be done, and where possible, gluten free diet instituted.

- If there is a history of congenital heart defects, then cardiology follow-ups should be done based on expert advice. During these follow-ups, issues of obstructive sleep apnea, including snoring, restless sleep, day time sleepiness, night time awakening, behavior problems, and sleep position should be discussed. Where indicated, a referral to a sleep specialist should be sought early. Obesity, being a risk factor for sleep apnoea should be addressed early.

- Musculoskeletal laxity may predispose children to sports injuries. Parents should be counseled on the risk of spinal cord injury. Neurologic monitoring for seizures should be instituted and adhered to regularly.

- There should be ophthalmologic evaluation every 3 years. Check for onset of cataracts, refractive errors, and keratoconus, which can cause blurred vision, corneal thinning, or corneal haze and is typically diagnosed after puberty.

- Even in the absence of congenital heart defects, vigilance should be exercised to rule out acquired mitral and aortic valvular disease in older victims. If a DS patient presents with increasing exertional dyspnoea, orthopnoea, pedal swelling or sleep disturbances, an echocardiogram should be obtained.

- Transition to adulthood is troublesome and comes with issues of guardianship, moving away from home and financial planning. These issues should be planned and addressed early during adolescence before young adulthood starts. Potential adult morbidities including apparent tendency toward premature aging and increased risk of Alzheimer disease may also be discussed. Monitor growth patterns, especially BMI, and counsel regarding healthy diet and a structured exercise program.

- Schooling is an important consideration, and the adolescent should be placed in appropriate schools, as well as acquisition of vocational life skills.

- Whereas DS is not inherited in a Mendelian fashion, it is important to advice the female patient that she is at an increased risk of getting a child with DS.

- Continue to assess, monitor, and encourage independence with hygiene and self-care. Provide guidance on healthy, normal, and typical sexual development and behaviors. Emphasize the need for understandable information, and encourage opportunities for advancing comprehension of sexuality. Discuss the need for

contraception and prevention of sexually transmitted diseases and the degree of supervision required. Advocate for the least invasive and least permanent method of birth control and be familiar with local law and resources to assist the family in their decision-making regarding questions about sterilization.Make recommendations and provide or refer for routine gynecologic care if not already provided.

1.6 Study Justification and utility

The population of children with Down syndrome is on the rise but the current clinical care and management of this children is haphazard. Therefore proper medical care should be given to these patients with multiple medical complications. An assessment of care given to these patients with the aim of making our own treatment/care guidelines is a major step in health care promotion of these patients.

Since prenatal screening for congenital malformations is not routinely carried out in our setting,then the number of Down syndrome cases is expected to rise. Currently there are no medical guidelines in Kenya on how to take care of these patients which remains to be a neglected group of people with special medical and social needs.

OBJECTIVES

Broad objective

To profile the clinical care of children with a clinical diagnosis of Down syndrome on follow up in paediatric outpatient and inpatient departments at Kenyatta National Hospital.

Specific objectives

1. To assess the clinical care offered to children with Down Syndrome
2. To correlate the clinical care with known guidelines for care of Down syndrome patients.

2. METHODOLOGY

2.1 Study Design

This was a Descriptive Cross-Sectional study. We administered pre-designed questionnaires to guardians of patients attending the outpatient clinics at Kenyatta National Hospital and admitted patients meeting the inclusion criteria. We evaluated the care of these patients according to the known complications of DS: Cardiovascular, Ophthalmological, Endocrine and Respiratory. We obtained further information on the state of care of these patients by abstracting information from the patient medical records.

2.2 Study population

The patients comprised children aged 0-12 years with Down syndrome attending Kenyatta National Hospital as outpatients/inpatients during the period.

2.3 Study location

This study was conducted in Kenyatta National hospital (KNH) which is a national referral and teaching hospital. DS patients attend paediatric, neurology, physiotherapy and speech therapy clinics. The principal investigator and research assistants recruited patients from these clinics during these clinics, as well as inpatient paediatric wards for any patients admitted during the study period.

2.4 Selection and enrollment of participants

2.4.1 Inclusion criteria

The following were included in the study:

- All patients with the clinical diagnosis (Phenotypic) and/or karyotype test done and positive from birth to 12 years visiting Kenyatta hospital as outpatients or inpatients
- All patients whose guardians consented to be part of the research study

2.4.2 Exclusion criteria

The following children were excluded from the study:

- Patient with no file/documentation of their diagnosis
- If guardian decline to consent

2.5 Sample size calculation

The sample size was determined using the Fishers formula for determination of sample size. The formula is as below.

$$n = \frac{Z^2 * p * q}{d^2}$$

- *n*= Sample Size
- *N= Population size taken at 136*
- *z* = statistic for a level of confidence
- *p* = Expected Proportion(0.5)
- *d* = Study Precision taken as 5% therefore d is 0.O5

$$n = \frac{1.96^2 * 0.5 * 0.5}{0.05^2}$$

$n = 384$

Since the population is less than 10,000 then the sample size after finite correction ($n^{'}$) will be calculated as follows;

$$n^{'} = \frac{384}{1 + \frac{384 - 1}{136}} = 101$$

A total of 101 children were sampled

2.6 Study Procedure

Study participants were recruited from the outpatient clinics (paediatric, neurology, physiotherapy and speech therapy clinics). We consecutively recruited patients in the clinics during the study period.

Data collection was done with the help of pre-designed questionnaires. The research team consisted of principal investigator, two trained research assistants and a data clerk.

2.6.1 Data collection for outpatients

During clinic days, we obtained medical records of patients to be reviewed on that particular day, and identified files of patients with DS. We then recruited the patients with the help of nurses and registrars in the clinics. Caregivers were given adequate information about the study. Informed consent was obtained from the caregivers, while assent was obtained from the children. The investigator and research assistants filled the questionnaires as the caregivers provided answers. At the same time, additional information was abstracted from the patient files.

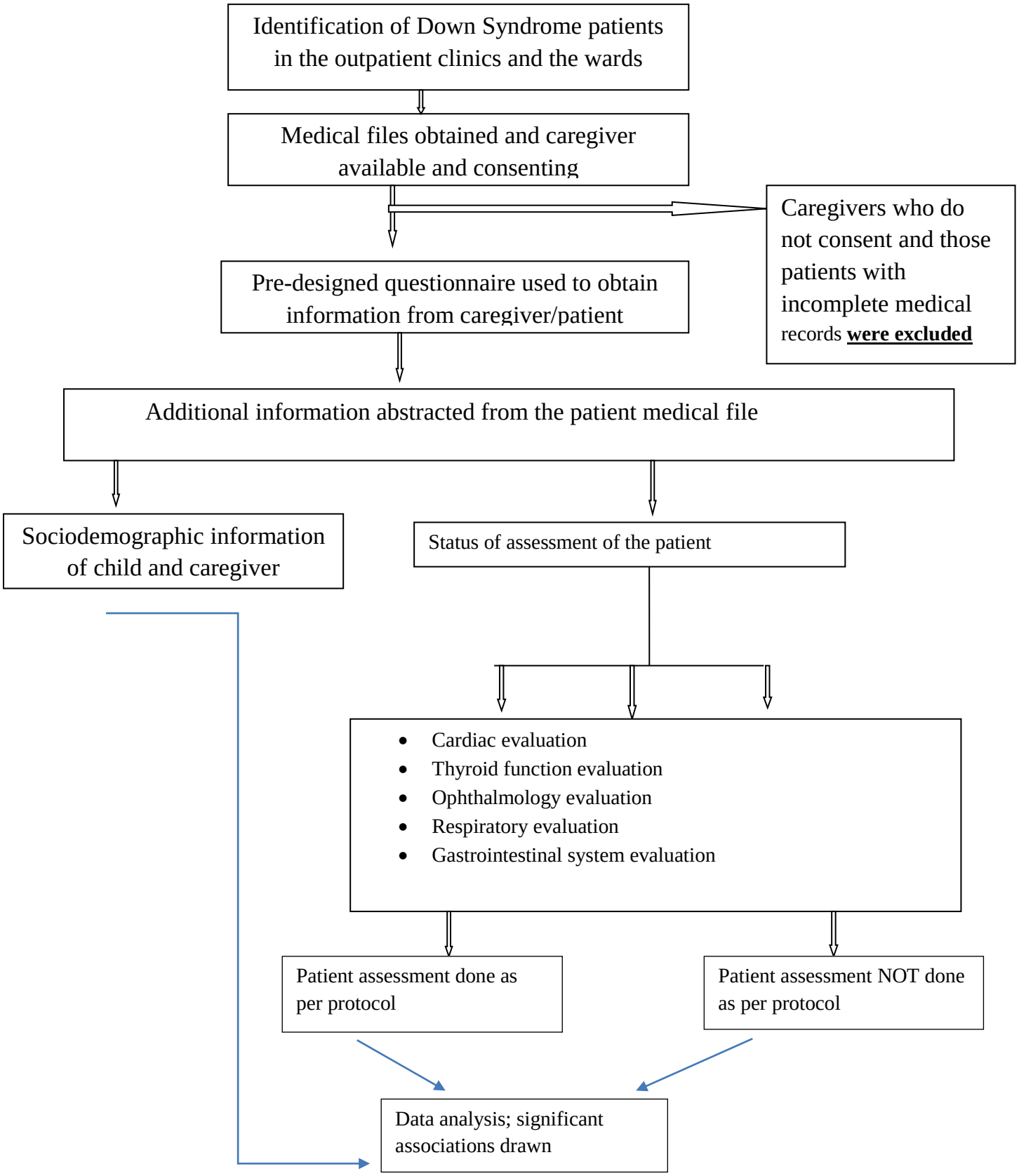
2.6.2 Data collection for inpatients

Every alternate day during the study period, the principal investigator visited all the paediatric, medical and surgical wards and identified admitted patients with DS using the admission register.

For those who met the inclusion criteria, caretakers were given information on the study and gave informed consent. The investigator and research assistants filled the questionnaires as the caregivers provided answers. At the same time, additional information was abstracted from the patient files.

CONCEPTUAL FRAMEWORK OF THE STUDY PROCEDURES

(figure-2)



2.7 Data management and analysis

The data collected in questionnaire was serialized and unique identifiers input before data entry. The data was entered in to SPSS, IBM version 23.0 for editing, cleaning and analysis. Data was presented in form of tables and graphs while proportions amongst different categories were graphically expressed as pie charts. Quantitative variables were summarized using means with standard deviations and medians with minimum and maximum limits of respective ranges defined. Chi-square statistics were deployed to assess and establish association towards clinical care of DS.

2.8 Ethical considerations

Permission was sought from the Kenyatta Hospital Ethics Research Committee to collect and analyze data collected in the study as part of this Dissertation. The purpose of the study was carefully explained to the caregivers and informed consent obtained in all cases. We observed strict confidentiality during the study. No personal identification like names, phone numbers or hospital numbers were recorded during data collection.

RESULTS

a) Socio-demographic characteristics

A total of 101 children we studied during the period December 2015 to February 2016. The mean age was 2.55 years (minimum age was 7 weeks, maximum 15 years). Sixty children (59.4%) were males, while 41 (40.6%) were females. Table 1 below summarizes the sociodemographic characteristics of the children and their caregivers. All the children had a clinical diagnosis of DS. Only 30 children (29.7%) had a karyotype done, which confirmed DS.

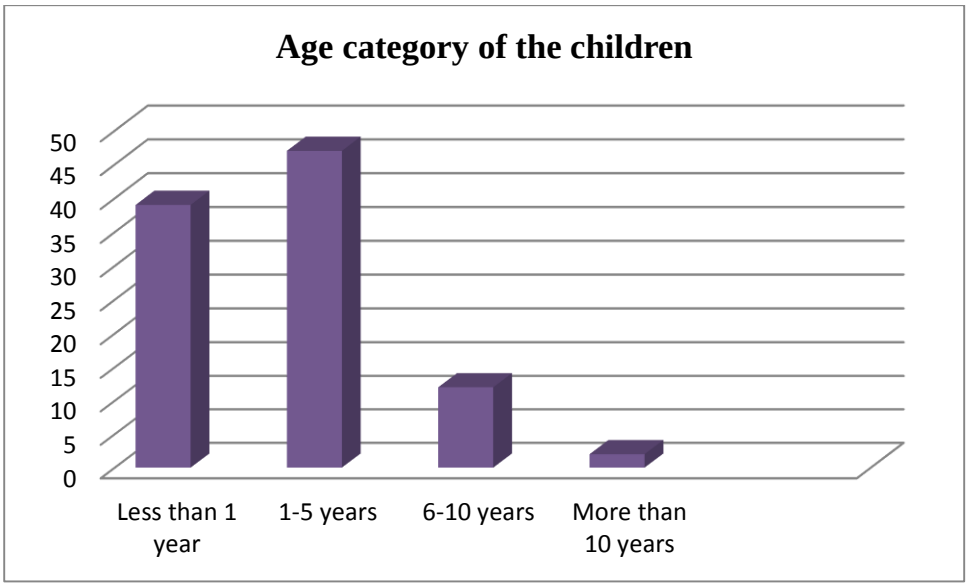
The mean age of the primary caregivers was 34 years. Most caregivers (94.1%) were biological mothers of the children.

Table 2; Sociodemographic characteristics of children and their primary caregivers

Characteristic		**N**	**%**
Gender			
Male		60	59.4%
Female		41	40.6%
Level of education of child			
Not yet in school		12	12.0%
Pre-school		57	56.4%
Primary school		32	31.6%
Primary caregiver			
Mother		95	94.1%
Father		2	1.9%
Others		4	3.9%
Guardian level of education	No education	3	3.0
	Primary	19	18.8
	Secondary	38	38.6
	Tertiary	40	39.6

Most children (46.5%) fell in the age category of 1-5 years, with few (2.0%) over 15 years of age. The graph below illustrates the age categories of children evaluated during the study period.

Figure 3 showing the age profile of children on follow up for Down Syndrome included in this study



b) Age related evaluation for complications of Down Syndrome

We found that majority of children were not done thyroid evaluation (63.4%), cardiac assessment (48.5%), ophthalmological assessment (91.1%). The commonest age at evaluation of possible complications of DS was 4-12 months.

Guardians were not informed, or aware of why there was no evaluation of the children as per the guidelines. There was a high prevalence of respiratory complications among these children (68.4%), $p<0.04$. 24.7% of children reported frequent diarrhoea and constipation. There was no record of evaluation for possible Hirschprung disease in these children.

i) Thyroid evaluation

Only 37 (36.6%) of the children had been evaluated for thyroid abnormalities. Out of these, 8 (7.9%) were found to have hypothyroidism, and 5 were on treatment with levothyroxine. When the rest were asked why the child was not on treatment, 4 reported that they were not informed of the need for follow-up and treatment, while 1 cited lack of finances. From the medical records, thyroid profile was done mostly at 4-12 months of age (51.3%).

ii) Cardiac assessment

Cardiac assessment was done in 52 patients (51.5%). The commonest age at assessment was less than 1 year of age (95.7%). Echocardiography was used in cardiac evaluation for 44 cases (84.6%), while electrocardiography was performed in 2 cases (3.8%). The rest (11.5%) had both echocardiography and electrocardiography performed.

Out of the 44 children who had echocardiography done, 12 (11.9%) had a cardiac lesion. Most were found to have atrial septal defects (6, 50%), 4 had ventricular septal defects while 2 had atrioventricular septal defects. There was no record of surgical intervention for the cardiac lesions found.

Figure 4 showing the diagnostic modality used in assessing cardiac lesions among children with DS on follow up at Kenyatta National Hospital

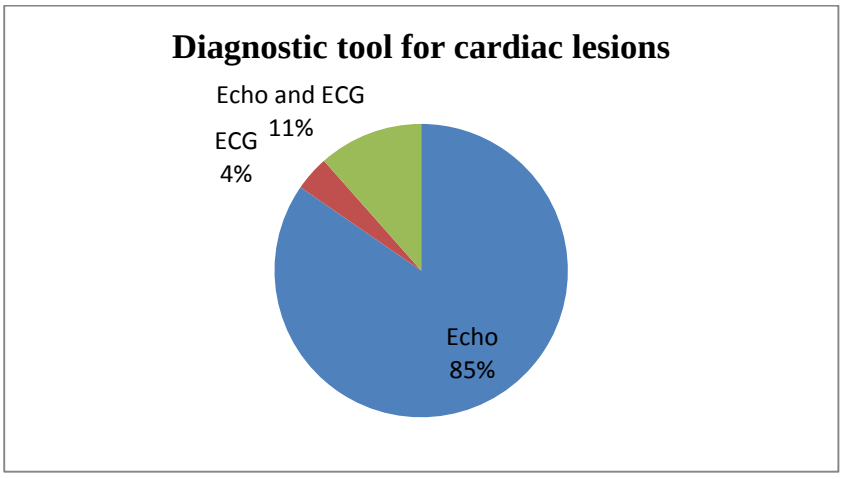
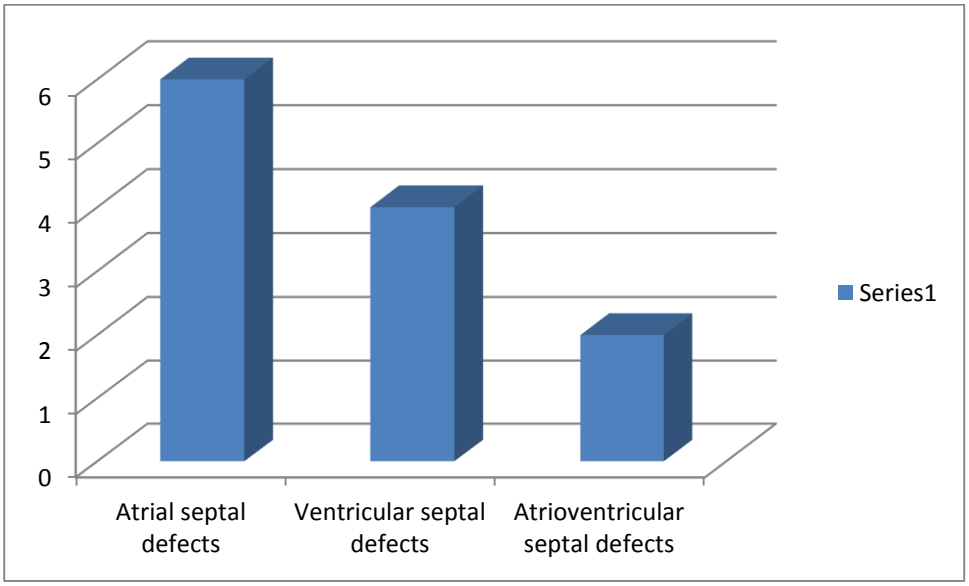


Figure 5 showing the cardiac abnormalities diagnosed by echocardiography among children with DS at Kenyatta National Hospital



iii) Ophthalmological evaluation

Ophthalmology assessment was done in only 9 (8.9%) of the children. The age at evaluation was distributed equally at less than 3 months, 4-12 months of life and above 1 year (each at 3.3%). 2 patients (1.9%) were found to have congenital cataracts, but no surgical operation was done on them.

iv) Respiratory assessment

Sixty seven (66.3%) of the children studied reported a history of cough, difficulty in breathing or wheeze. Most of these respiratory symptoms were reported at 4-12 months of age (61.2%). 77.1% of the children had two or more episodes of respiratory symptoms per year.

v) GIT assessment

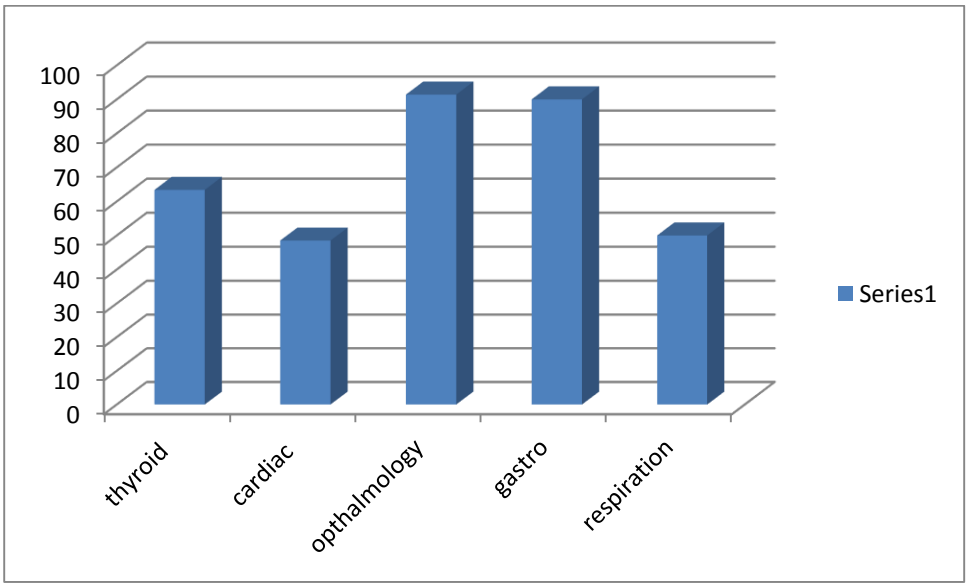
Gastrointestinal system assessment was done in 10 patients (9.9%). There was no record of any structural abnormalities of the gut like Hirschprung disease. 33 children (32.7%) had a

history of frequent diarrhoea and constipation.No child was assessed for possibility of Coeliac Disease among all children seen at the clinic.

Table 4: Systemic evaluation in children with Down Syndrome under various age categories seen at Kenyatta National Hospital

System	Assessment done (%)		Age category at assessment (%)			Abnormality found
	Yes	No	≤3months	4-12 months	>1yr	
Thyroid	36.6	63.4	40.6	59.5		Hypothyroidism-7.9%
Cardiac	51.5	48.5	41.3	54.3	4.3	Cardiac lesion-11.9%
Ophthalmology	8.9	91.1		100		Cataracts-22.2% (n=2)
Gastrointestinal system	9.9	90.1		100(n=10)		None reported

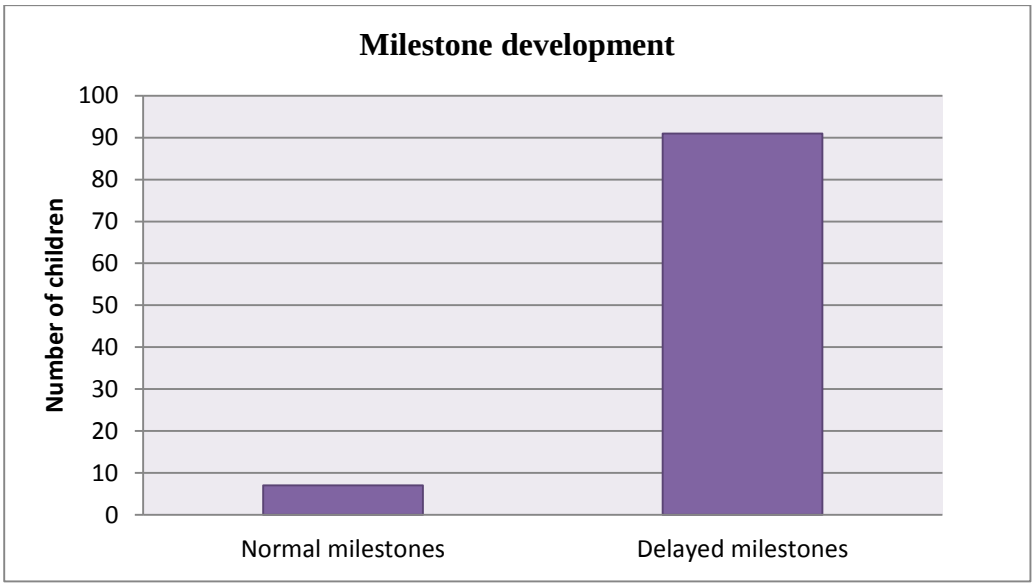
Figure 6; graph showing percentage of children not evaluated



c) **Evaluation of children for developmental milestones**

Out of the 101 children studied 56 (55.4%) were on follow up at the physiotherapy and speech therapy clinics for delayed milestones. Only 7 (6.9%) had normal milestone development, while 94 (93.1%) had delayed milestones ($p<0.002$). For those children not on follow up, caregivers cited lack of finances (8.9%), were not informed on need for follow up (62.2%) or medicines were not available (13.5%).

Figure 7 showing the proportion of children with normal and delayed milestones



Proportion of children not assessed for systemic complications of Down Syndrome

As reflected in Table 4 and figure 6 above, 63.4% of children did not undergo thyroid assessment, 41.3% not undergone cardiac assessment, 91.1% not undergone ophthalmology and 90.1% did not undergo gastrointestinal evaluation. This represents a missed opportunity for early diagnosis and management of the complications arising from DS.

DISCUSSION

The present study has revealed missing gaps in the follow up of children with Down syndrome a condition which ideally should be diagnosed in utero via amniocentesis and early intervention done. since we diagnose it at birth or even later in our setting,the challenges/complications of Down syndromes will present. This condition, which is thought to occur in 1 in 800 to 1000 live births[31] presents with a constellation of abnormalities which require careful assessment and follow up for the wellbeing of the children. The need for institutionalization of these children is now lower, and parents/caregivers should be referred for early therapy to minimize developmental delay and for proper health supervision. In our Kenyan population, despite a relatively high prevalence of DS, there are no guidelines on the follow up of these children.

We found more boys than girls being followed up for Down syndrome in this study. This reflects the population dynamics, with boys being more than girls in the local population. Further, the mean age of the caregivers, who were mostly mothers (94.1%), was 34 years,which differs slightly with the literature showing maternal ages more than 35 yrs. Previous studies have identified a clear link between increasing maternal age with DS[5], which is thought to be due to increased number of chromosomal errors with increasing maternal age. Most of the caregivers had secondary education (38.6%) and tertiary education (39.6%). This possibly means that mothers who spend more time in school are more likely to have children with DS because of the increased age.

Thyroid function assessment was done in only 36.6% of the children, and 7.9% were found to have hypothyroidism. Thyroid disorders are common in DS, occurring in 28-40% of the children[15, 23]. Since thyroid abnormalities in DS increase with age, it is advisable that serial thyroid function tests are performed during follow up of the children. The common thyroid disorders include congenital hypothyroidism and compensated hypothyroidism. The latter is

commoner, occurring in 25.3-32.9% of cases, and is characterized by mild elevation in TSH, with normal or low T4. Thyroid hormones are critical for brain growth and musculoskeletal function. Hypothyroidism, which is common in Down syndrome, may underlie delayed milestones and hypotonia which are commonly seen. It is therefore imperative that all children on follow up for Down syndrome have their thyroid functions checked.

Out of the 101 children included in this study, 51.5% had cardiac assessment, with echocardiography being the commonest mode of screening in 84.6% of cases. There is strong recommendation in literature for early screening for cardiac defects in Down syndrome, preferably in the first month of life[1, 3,12]. This is because congenital heart disease is very common in Down syndrome, estimated to occur in 44-58% of the patients worldwide[4]. Ventricular septal defects and atrial septal defects are the most common abnormalities seen in these patients. Early diagnosis is necessary as it will lead to optimal management and prevent complications such as pulmonary hypertension. Surgical correction, the preferred method of treating congenital heart disease should be performed at 2-4 months of life. In our study, there was no record of surgical correction of the anomalies detected on echo.

Ophthalmological assessment was done in only 9 (8.9%) of the patients. Congenital cataracts were diagnosed in 2 patients (1.9%). There was no record of surgical correction of the condition. This represents a missed opportunity of up to 90% of patients in the diagnosis of visuo-ocular disorders. Studies have shown that up to 50% of patients with DS have ocular abnormalities. These include strabismus, nystagmus, congenital and acquired cataracts and blepharitis[10, 11]. Visual screening is vital, especially in detecting congenital cataracts, which can be corrected to prevent blindness.

We observed a high prevalence of respiratory symptoms in the study population, with 66.3% of the children having respiratory symptoms like recurrent wheezing, cough and difficulty in

breathing. This is in agreement with previous researchers, who show that respiratory problems account for majority of hospital admissions in children with Down syndrome [14]. Recurrent wheeze, which is not asthmatic in aetiology, is a common complication, occurring in up to 36% of the children, due to respiratory syncytial virus and tracheamalacia[14]. Respiratory symptoms may be complicated by the presence of congenital heart diseases and anatomical abnormalities of the respiratory system like pulmonary hypoplasia and subpleural cysts[4]. There is great need for constant follow up and prophylaxis with human monoclonal antibodies for respiratory syncytial virus, especially for children with confirmed congenital heart disease.

Gastrointestinal assessment was done in 9.9% of the children. 32.7% of all the children had a history of frequent constipation, diarrhoea and vomiting. There was no record of structural abnormality like Hirschprung disease. Vomiting and constipation may be early signs of the presence of duodenal atresia, pyloric stenosis, annular pancreas, imperforate anus and trachea-esophageal fistula[17]. Another common abnormality is celiac disease, with a reported incidence of 7-16.7% in some populations[32,33]. It is important to rule out hypotonia and hypothyroidism as the causes of the constipation.

Most of the children (93.1%) had delayed milestones. Only 55.4% were on follow up for delayed milestones in the physiotherapy and speech therapy clinics. For the 44.6% who were not on follow up, caregivers cited lack of finances and inadequate or inappropriate information as the reasons. Most of the developmental delay of these children is linked to hypotonia. Further, it has been found that among 5-7 year olds, limitations in activity are more associated with motor impairment and not mental disability. This calls for more aggressive physiotherapy to ensure better sudomotor development of these children. Typically, children with Down syndrome are in the low range of intelligence quotient. However, severe mental retardation is rare in Down syndrome [12]. Special approaches to

teaching and speech therapy need to be adopted to facilitate their growth[3, 15]. Autistic disorders, which are reported in up to 7% of children with Down Syndrome, should also be put into consideration when selecting therapy for these children.

STRENGTHS AND LIMITATIONS OF THE STUDY

This study has numerous strengths: it is the first study looking at the assessment done to children with Down Syndrome among children in Kenya. It has therefore identified the missed opportunities and gaps in the care given to children with Down Syndrome. Data was collected from caregivers and augmented by information from medical records. This precludes the possibility of collecting incorrect information from the records or caregivers.

This study had some limitations. We relied on medical records and recall from caregivers on the evaluation done on the children. Poor record keeping, loss of records from patient files and recall bias from caregivers might have slightly compromised the quality of the data we collected.

CONCLUSION AND RECOMMENDATIONS

1. This study has found missed opportunities in the management and follow up of children with Down syndrome at the referral hospital.
2. Majority of the children were not done thyroid, ocular, gastrointestinal, cardiac or respiratory assessment as shown in figure 6.
3. Over 44% of the children were not on follow up for physiotherapy and speech therapy for delayed milestones.
4. Down syndrome is associated with increased mortality and morbidity, hence the need for strict adherence to guidelines for these children.

We recommend that:

1. Clinicians, nurses and other healthcare workers be sensitized on the need for high index of suspicion to diagnose the condition early. Further, there is need to start interventions early to improve the outcomes of children with the condition.
2. Tailored guidelines are instituted on the assessment of the children, based on age. These can be borrowed from existing guidelines and modified to suit the needs of children in Kenya.
3. Training is intensified on early referrals of children diagnosed with Down syndrome for the associated complications. The care of these children should be a multidisciplinary approach
4. Adoption of screening tools and for instance the DS Interest Group tool[30] if possible modify it depending on the available resources, this would greatly improve the survival and outcomes of children with Down syndrome.

REFERENCES

1. Wiseman FK, Alford KA, Tybulewicz VL, Fisher EM. Down syndrome--recent progress and future prospects. Hum Mol Genet. 2009 Apr 15;18(R1):R75-83.

2. Collins VR, Muggli EE, Riley M, Palma S, Halliday JL. Is Down syndrome a disappearing birth defect? J Pediatr. 2008 Jan; 152(1):20-4, 24.

3. Roizen NJ, Patterson D. Down's syndrome. Lancet. 2003;361:1281–1289.

4. Weijerman ME, van Furth AM, Vonk Noordegraaf A, van Wouwe JP, Broers CJ, Gemke RJ.Prevalence, neonatal characteristics, and first-year mortality of Down syndrome: a national study. J Pediatr. 2008 Jan;152(1):15-9.

5. Irving C, Basu A, Richmond S, Burn J, Wren C. Twenty-year trends in prevalence and survival of Down syndrome. Eur J Hum Genet. 2008 Nov;16(11):1336-40.

6. Nelson LD, Siddarth P, Kepe V, Scheibel KE, Huang SC, Barrio JR, Small GW.Positron emission tomography of brain β-amyloid and τ levels in adults with Down syndrome. Arch Neurol. 2011 Jun;68(6):768-74.

7. Rex AP, Preus M. A diagnostic index for Down syndrome. J Pediatr. 1982;6:903–906.

8. Wouwe JP, Siderius EJ, Borstlap R, Nijenhuis TA, Hirasing RA. Optimal medical care for children with Down syndrome and their parents. Ned Tijdschr Geneeskd. 2001 Aug 25;145(34):1617-21.

9. Weijerman ME, van Furth AM, van der Mooren MD, van Weissenbruch MM, Rammeloo L, Broers CJ, Gemke RJ. Prevalence of congenital heart defects and persistent pulmonary hypertension of the neonate with Down syndrome. Eur J Pediatr. 2010 Oct;169(10):1195-9.

10. Stephen E, Dickson J, Kindley AD, Scott CC, Charleton PM.Surveillance of vision and ocular disorders in children with Down syndrome. Dev Med Child Neurol. 2007 Jul;49(7):513-5.

11. Wong V, Ho D. Ocular abnormalities in Down syndrome: an analysis of 140 Chinese children. Pediatr Neurol. 1997;16:311–314.

12. American Academy of Pediatrics. Committee on Genetics.American Academy of Pediatrics: Health supervision for children with Down syndrome. Pediatrics. 2001 Feb;107(2):442-9.

13. Mannan SE, Yousef E, Hossain J. Prevalence of positive skin prick test results in children with Down syndrome: a case-control study. Ann Allergy Asthma Immunol. 2009 Mar;102(3):205-9.

14. Bloemers BL, van Furth AM, Weijerman ME, Gemke RJ, Broers CJ, van den Ende K, Kimpen JL, Strengers JL, Bont LJ. Down syndrome: a novel risk factor for respiratory syncytial virus bronchiolitis--a prospective birth-cohort study. Pediatrics. 2007 Oct; 120(4):1076-81.

15. Crissman BG[1], Worley G, Roizen N, Kishnani PS.Current perspectives on Down syndrome: selected medical and social issues. Am J Med Genet C Semin Med Genet. 2006 Aug 15;142C(3):127-30.

16. Biko DM, Schwartz M, Anupindi SA, Altes TA.Subpleural lung cysts in Down syndrome: prevalence and association with coexisting diagnoses. Pediatr Radiol. 2008 Mar;38(3):280-4.

17. Yang Q, Rasmussen SA, Friedma JM. Mortality associated with Down's syndrome in the USA from 1983 to 1997: a population-based study. Lancet. 2002;359:1019–1025.

18. Bertrand P, Navarro H, Caussade S, Holmgren N, Sánchez I. Airway anomalies in children with Down syndrome: endoscopic findings. Pediatr Pulmonol. 2003 Aug; 36(2):137-41.

19. Freeman SB, Torfs CP, Romitti PA, Royle MH, Druschel C, Hobbs CA, Sherman SL. Congenital gastrointestinal defects in Down syndrome: a report from the Atlanta and National Down SyndromeProjects. Clin Genet. 2009 Feb; 75(2):180-4.

20. Roofthooft MT, van Meer H, Rietman WG, Ebels T, Berger RM.Down syndrome and aberrant right subclavian artery. Eur J Pediatr. 2008 Sep;167(9):1033-6.

21. Zwaan MC, Reinhardt DR, Hizler J, Vyas P. Acute leukemias in children with Down syndrome. Pediatr Clin North Am. 2008;55:53–70.

22. Schepis C, Barone C, Siragusa M, Pettinato R, Romano C. An updated survey on skin conditions in Down syndrome. Dermatology. 2002;205(3):234-8.

23. Gibson PA, Newton RW, Selby K, Price DA, Leyland K, Addison GM. Longitudinal study of thyroid function in Down's syndrome in the first two decades. Arch Dis Child. 2005 Jun;90(6):574-8.

24. Cremers MJ, van der Tweel I, Boersma B, Wit JM, Zonderland M. Growth curves of Dutch children with Down's syndrome. J Intellect Disabil Res. 1996 Oct; 40:412-20.

25. Hankinson TC, Anderson RC. Craniovertebral junction abnormalities in Down syndrome. Neurosurgery. 2010;66:A32–A38.

26. Caird MS, Wills BP, Dormans JP. Down syndrome in children: the role of the orthopaedic surgeon. J Am Acad Orthop Surg. 2006;14:610–619.

27. Volman MJ, Visser JJ, Lensvelt-Mulders GJ. Functional status in 5 to 7-year-old children with Down syndrome in relation to motor ability and performance mental ability. Disabil Rehabil. 2007; 29:25–31.

28. Kupferman JC, Druschel CM, Kupchik GS.Increased prevalence of renal and urinary tract anomalies in children with Down syndrome. Pediatrics. 2009 Oct; 124(4):e615-21

29. Madan V, Williams J, Lear JT. Dermatological manifestations of Down's syndrome. Clin Exp Dermatol. 2006;31(5):623–629.

30. Guidelines for basic essential medical surveillance. The Down's syndrome medical interest group UK and Ireland. Available at: http://www.dsmig.org.uk/publications/guidelines.html

31. Baird PA, Sadovnick AD. Life tables for Down Syndrome. Human Genet. 1989; 82:291-2

32. Karlsson B, Gustafsson J, Hedov G, et al. 1998. Thyroid dysfunction in Down's syndrome: relation to age and thyroid autoimmunity. *Archives of Diseases in Childhood* 79(3): 242–5.

33. Csizmadia CGDS, Mearin ML, Oren A, et al. 2000. Accuracy and cost-effectiveness of a new strategy to screen for celiac disease in children with Down syndrome. *Journal of Pediatrics* 137: 756–61.

APPENDICES

Appendix 1: Consent Form

Dear Parent/Guardian,

My name is Dr Bernard Munyao, a Senior House Officer (registrar) at Kenyatta National Hospital. I am carrying out a research study in regards to the clinical care offered to children with down's syndrome at Kenyatta National Hospital.

Purpose of the study: The aim is to understand the current care practices and if any changes should be done regarding what is offered and what is available to improve the quality of health for your child.

Study procedure: I have developed a questionnaire to capture the information and documented details in patient files.

Risks and Discomforts: It does not involve any procedures to be done on the child but incase a child has a specific problem which has never been attended to or needs follow up then a referral shall be made immediately within Kenyatta Hospital. No costs will be implicated, no medications or procedures will be done on the child.

Study benefits: The study outcome will be used to improve the state of clinical care for down syndrome

Compensation: There are no compensations involved.

Confidentiality: The information you will provide shall be treated with utmost confidentiality as required by law and medical ethics. You will not be required to provide any identification information.

Voluntary Participation: Your participation is voluntarily and there is no penalty for declining to answer or participate. You are free to withdraw at any stage of the study without any fear of victimization.

You may contact me on the cell phone number 0727753245 or email bmunyao29@gmail.com or Prof. M. L Chindia (Secretary KNH-UoN-ERC) Kenyatta National Hospital/Ethics Research Committee contact is 0722829101 Ext. 44102

Thank you for your time.

Parent/Guardian's consent

I have read and understood the information provided to me about the research. I voluntarily agree to participate.

Parent/Guardian sign_____ Date:_____

Investigators sign:_____Date:_____

Appendix 2: Study questionnaire

Questionnaire No: _____Interviewer No: _____Date: _____

PARTICIPANT DETAILS

Age	
Sex	Male ☐ Female ☐
Level of education	
Type of the patient	Outpatient ☐ Inpatient ☐
WARD (if answered inpatient)	

GURDIAN DETAILS

Age of gurdian or Ages of both biological parents if available	Gurdian…. Mother….. father……
Sex of guardian	Male ☐ Female ☐
Residence	
Level of education	
Occupation	

Tick as appropriate inside the box. Some interventions put in written as per what is documented in the patient's file

A. Thyroid function test of the patient (to be obtained from patient file)

	Tick response
1. Was thyroid profile level done{confirm with results}	Yes ☐ NO ☐
2. At what age was it done?	3months ☐ 4-12 months ☐ 1-18 years ☐
3. Was hypothyroidism diagnosed?	Yes ☐ NO ☐
4. What treatment was given?	Thyroxine ☐ None ☐
5. What made treatment not be given?	Lack of finances ☐ Medication not available ☐ Guardian not informed ☐

Others _____ _____

B. Cardiac Evaluation

	Tick response
6. Was a cardiac evaluation done?	Yes ☐ No ☐
7. At what age was it done?	3months ☐ 4-12 months ☐ 1-18 years ☐
8. What diagnostic tool was used?	Echo ☐ E.C.G ☐
9. Was a cardiac lesion diagnosed?	Yes ☐ No ☐
10. What heart lesion was detected?	
11. What intervention was /is being done?	Medical: ……... ……... ……...
	Surgical: ……... ……... ……...

C. Ophthalmology Evaluation

	Tick response
12. Was ophthalmology evaluation done?	Yes ☐ No ☐
13. At what age was it done?	3months ☐ 4-12 months ☐ 1-18 years ☐
14. Was/is there an eye complication?	Yes ☐ No ☐
15. What is /was the diagnosis?	

16. What intervention was /is being done?	Medical: ……... ……... ……...
	Surgical: ……... ……... ……...
17. If no intervention, why?	Lack of finances ☐ Medication or surgery not available/not practiced within ☐ Guardian not informed ☐
Others _____ _____ _____	

D. Respiratory System Evaluation

	Tick response
18. Has the child ever had either cough or difficulty breathing or wheeze?	Yes ☐ No ☐
19. At what age was it or has it occurred?	3months ☐ 4-12 months ☐ 1-18 years ☐
20. How many episodes per year?	1 episode ☐ 2 episodes ☐ More than 2 episodes ☐
21. What investigations were done at every visit to hospital?	None ☐ CXR ☐ CT Scan chest ☐
Others for respiratory system investigation	
22. What were/was the diagnosis	

23. What interventions were given during each visit? …………………………………………………………………………………… …………………………………………………………………………………… …………………………………………………………………………………… …………………………………………………………………………………… ……………………………………………………………………………………	
24. Any prophylaxis given for recurrent infections?	Yes ☐ No ☐
25. What medications for prophylaxis?	

E. Diarrhea or Constipation

	Tick response
26. Has the child had diarrhea/ constipation or both ?	Yes ☐ No ☐ Both ☐
27. At what age was it ?	3months ☐ 4-12 months ☐ 1-18 years ☐
28. How frequent per year?	1 episode ☐ 2 episodes ☐ More than 2 episodes ☐
29. What investigations were carried out at every hospital visit? …………………………………………………………………………………… …………………………………………………………………………………… …………………………………………………………………………………… …………………………………………………………………………………… ……………………………………………………………………………………	

30. What was/were the diagnosis made at every visit?

…….....

…….....

…….....

…….....

…….....

……..

31. What interventions were done

1) Medical ……

2) Surgical (hirshprung disease)……..……

3) Diet modification…….

32. If an intervention not done why?	Financial constraint ☐ Intervention not available ☐ Guardian not informed ☐

Others _____

_____

_____

F: Milestone Evaluation/Support (to be obtained from the guardian)

	Tick response
33. Has the child been active/walking/sitting as per the age?	Yes ☐ No ☐
34. If the child has delayed milestones, is the child on follow up at the occupational therapy or physiotherapy	Yes ☐ No ☐
35. If an intervention not done why?	Financial constraints ☐ Facility being far ☐ Guardian not informed
Other reasons_____ _____ _____	