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Review Article

An Overview of Developmental Delay Screening in Saudi Arabia for General Pediatrician

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Received: November 14, 2022; **Published:** November 30, 2022

DOI: 10.31080/ecpe.2022.11.01236

Abstract

Objective: It is difficult to estimate doctors' performance of developmental screening during well child visits in Saudi Arabia as there is no current literature available based on our search. Furthermore, few data exist regarding validated tool for developmental screen in Arabic or middle east practice**.** Well child or routine clinic visit can be an excellent opportunity to pick up early signs of developmental delay in children. As we see more of these children in our general pediatric clinics, it's crucial to pay attention to the early clues of developmental delay so an appropriate referral and intervention can be made. This overview is primarily to shed the light on the importance of developmental screening in general pediatric clinics. we need some modification of approaching developmental delayed child in local practice guidelines in Saudi Arabia.

Method: We reviewed practice guidelines in many places in the world. We summarized the causes, basic investigations and management of common causes of Developmental Delay in a child or young person presented to general pediatric clinic. We looked at different in-use developmental screening tools to detect early signs of developmental delay.

Conclusion: Once early positive surveillance is detected by the physician, basic investigations (include Microarray, Fragile X and metabolic set with Thyroid test), imaging (MRI), vision and hearing screen then referral to community pediatric clinic for further assessment and management is made so early intervention and prevention of recurrence in family can be achieved. This review is applied to children of age 0 - 14 years.

***Keywords*:** *GDD; Global Development Delay; Intellectual Disability*

Abbreviations

DS: Developmental Screen; DM: Developmental Monitoring; GDD: Global Development Delay; ASD: Autistic Spectrum Disorder; AAP: American Academy of Pediatric; CDC: Center for Disease Control; AGS: Ages and Stages Screening Tool; PEDS: Parents' Evaluation of Developmental Status

Introduction

Developmental delay is defined as failure to gain expected milestone that gained by children of similar age category or time frame [1]. Developmental delay can be categorized to subgroups according to the affected developmental areas: gross motor, fine motor/vision, speech, or social/cognitive area. Global delay is diagnosed when two or more areas are affected. Typical diagnosis becomes evident at age 12 - 24 months [2]. Historically, early detection and intervention can help to improve outcome. It is documented that, causes as much as 40 - 80% can be identified. Genetic and metabolic causes can collectively account for 65% of identified causes [3]. This information can impact the preventive counselling massively, especially in country with consanguinity marriage of around 60% like Saudi Arabia [4]. Prevalence of Global development delay is around 16% in one study in Saudi Arabia [5], similar to other estimated international studies [6]. However, some differences in causes present. For example, metabolic disease prevalence reported to be higher in Saudi Arabia compared to international studies [4]. Moreover, parents' knowledge regarding developmental milestones is lacking [7]. Having said that, we need some modification of approaching developmental delayed child in local practice guidelines. If we early detect development abnormality during the brain growth in early childhood, we might help in making new neuronal connections through early intervention as the theory of neuronal plasticity explains [8]. On the other hand, the benefits of early intervention outweigh the parental anxiety created by the early diagnosis.

Developmental screening (DS) is complemented by developmental monitoring (DM) which is out of our scope here in this overview. Developmental screening plus monitoring enhance early referral for intervention by six folds in comparison to either DM or DS alone as shown in one study [9]. Our aim to review current practice/guideline in Saudi Arabia regarding development delay and this overview is primarily to shed the light on the importance of developmental screening in general pediatric clinics. We did open search PubMed, and Google Scholar for development delay clinical practice guidelines. We used key words: GDD, Global Development delay, clinical practice guidelines.

Causes [3,10,11]

The etiology of developmental delay is complex and multifactorial. Majority of the causes of developmental delay is idiopathic. Here are some of the causes discussed below.

Environmental/exogenous causes [12,13]

It is well recognized that multiple environmental factors can affect the child development leading to varying degree of delays. The effect can occur at a single or multiple point during the developmental process in early childhood.

These can be classified further into:

Prenatal causes:

- Early maternal infections during early pregnancy, (e.g. rubella, cytomegalovirus (CMV), toxoplasmosis etc.
- Late maternal infections, (e.g. varicella, HIV, malaria, etc).
- CNS congenital malformations, teratogens and toxins.

Perinatal causes:

- Prematurity, recent studies showed that extreme prematurity (22 - 25 weeks' gestation) is associated with high rates of severe developmental delay [14].
- Hypoxic-ischemic encephalopathy (HIE) and periventricular leukomalacia.

- Intrauterine growth restriction (IUGR).
- Metabolic causes- Hypoglycemia, bilirubin-related neurotoxicity, etc.

Postnatal causes:

- Metabolic: Inborn errors of metabolism - PKU, hypoglycemia, etc.
- Teratogens/toxins - such as lead, mercury, etc.
- Trauma - severe head trauma.
- Postnatal Infections (e.g. neonatal meningitis, encephalitis).
- Maternal psychological state - such as depression, anxiety, etc.
- Maltreatment and domestic violence.
- Child neglect/psychosocial trauma/poverty.
- Malnutrition - especially multivitamins and minerals deficiency, such as iron, folate, Vitamin D, etc.

Genetic [13]

Up to date, there are no known recognized genetic traits for developmental delay. However, developmental patterns are well recognized within some families, including late walking, and talking. These manifestations can also be associated with certain syndromes or neurodevelopmental disorders. Genetics of developmental delay disorders can vary widely from copy number variants (CNV's), insertions, deletions, and duplications. Fragile X syndrome is the most common classic example of a genetic cause for developmental delay associated with high risk for Autism. It is caused by a trinucleotide repeat disorder (CGG) targeting the Fragile Mental Retardation 1(FMR1) gene located on the X-chromosome.

On the other hand, genetic dysregulation in imprinting disorders like Prader-Willi and Angelman syndrome has been recognized as a susceptibility factor for autism spectrum disorder (ASD) in both disorders. Other syndromes with developmental delay and distinct phenotypes can be associated with other genetic abnormalities like trisomies, for example, Down syndrome (trisomy 21), Edward syndrome (trisomy 18) and Patau syndrome (trisomy 13). Other X-linked disorders with gender associated developmental delay include Coffin-Lowry syndrome predominantly in males and Rett syndrome in females [13].

Clinical features [2,10]

Some clinical features are considered as red flags for developmental delay. These can be obtained from family as they report concerns or from examination findings in routine developmental surveillance or screening. We can categorize these features according to the affected areas.

Motor area

Early warning signs: hand fisting beyond 3 months, early rolling less than 3 months, poor head control at 3 months, Early hand preference less than 1 year, persistent of neonatal/primitive reflexes.

Classical/commonest milestones signs: Not sitting by 8 months, not walking by 18 months and any change in tone at any age.

Speech

Speech delay can be either expressive (no babble at 6 months, not saying Mama-Baba at 1 year, no 5 words at 18 months), or receptive delay (does not respond to sounds at any age, not following command at 18 months).

Social/cognitive

Social/cognitive delay manifests as immature behavior, immature play, self-help problems and young sibling overtaking in terms of social skills.

Approach to detect child with developmental delay

Surveillance: Through History, milestones review and detailed examination at each well child clinic visit. We can use the 6 steps for surveillance set by CDC, AAP during each health visit. These include: 1. review checklists/developmental history; 2. asks about concerns; 3. assess strengths and risks; 4. observe the child; 5. document; and 6. share results with others [15].

Screening: Using different validated tools such as parent filling questionnaire e.g. AGS, PEDS or doctors filled e.g. Denver. Screening during specific visits at 9, 18 & 24 months [16].

There are international variations regarding using surveillance or screening tools. In America, Academy of Pediatric recommends routine development screening tool use at age 9, 18 and 30 months [16]. Others such as NICE guideline in the UK; recommends enhanced development support and surveillance for children born prematurely less than 2 years, while they recommend questioner at/after 2 years of age [17,18]. Canadian task force on preventive health care stated there is no evidence that commonly used screening tools would consistently identify otherwise unrecognized cases, but there is evidence that the low specificity of these tools would lead to a high proportion of false positives [19]. It is important to emphasize in cases of motor delay; that the physician should observe other milestones and perform a thorough neurological examination [20]. Having reviewed the different screening tools as mentioned above; we opt to keep it optional to use screening tool or directly going to early intervention and subspecialist referral in line with other local guideline suggest [10]. The main reasons were due to concern for time spent during clinic visits, training required to use screening tool and validation in Arabic speaker communities. All these factors might affect the early identification and delay the referral process that is not yet well established for development delay screen. It is worth mention, in Saudi Arabia primary care services are developing and national interest in child development has increased significantly from higher regulation authorities e.g. 1st national autism screening policy was mandated in 2021.

History [3,10]

- **Past medical history:** Review medical disease, admissions as well as medications given before.
- **Maternal and neonatal history:** Covering maternal medications, radiation, and illness during pregnancy, review perinatal events (APGAR score) and postnatal periods (NICU admission).
- **Family history:** Three generation pedigree, looking for similar conditions, metabolic, neurological, genetic disease, or recurrent miscarriage.
- **Development history:** Careful review of the four milestones domains.
- **Social history:** Review relations in-between family members, parent education, living area and economic status. Check baby and mother interaction during the interview. Look for any psychological disorder signs/diagnosis or drug abuse in the family.

Examination [3,20]:

- **General examination:** Growth parameters and Head circumference.
- Dysmorphic features.
- **Motor development assessment:** Observe child posture, play and interactions.
- **Vision test:** Inspect eyes, observe if fix and following objects, do red reflex, white reflex**.**
- **Hearing test:** Check if responds to audible stimuli or follow commands according to age.
- **Neurological exam (include skin):** Looking for posture, motor tone, primitive reflexes.
- **Gastrointestinal system examination:** For Hepatosplenomegaly.

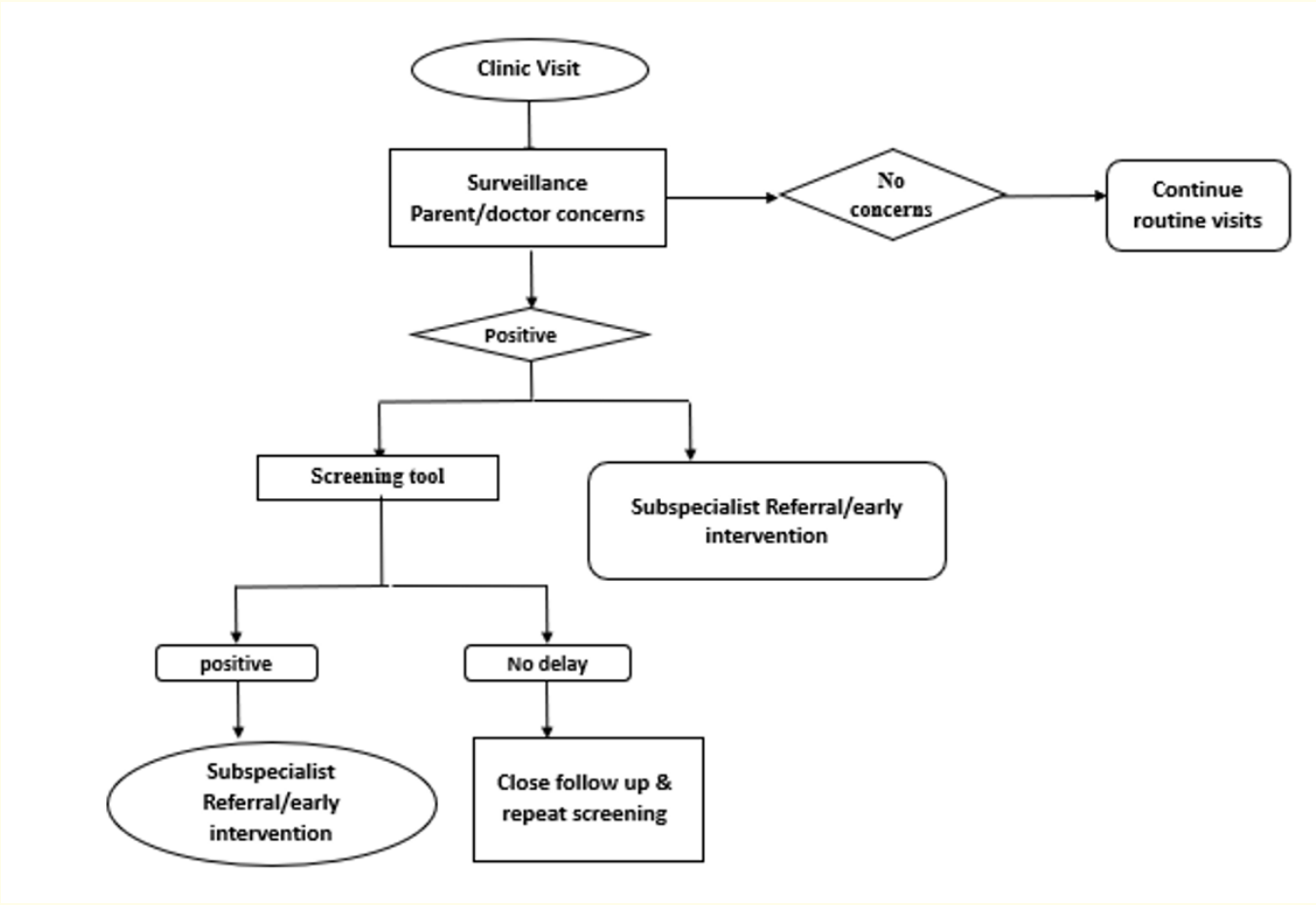

Figure 1: *Approach for detection of development delay in routine clinic visit [21].*

Investigations

Given the high consanguinity community rate 60% [4], 57% [22], genetic diseases work up helps in prevention efforts through family counseling and IVF pregnancy planning. For that reason and based on fast growing genetic/metabolic services in the country we make it as one tier work up given the high incidence of genetic/metabolic disease in the community (One of the highest reported incidence so far worldwide) [23]. It is worth to request an initial genetic test (Microarray and fragile X) as it has a diagnostic yield of 8 - 20% for Microarray in some guidelines review [3], in systematic review article 15 - 20% [13] and in another report 7.8% [24]. Genetic tests might diagnose up to 40% of cases [3]. For more advanced genetic tests such as Whole Exome Sequence, we decide to keep it for subspecialist level.

Work up helps in early management of developmental delay in treatable conditions such as metabolic diseases or hypothyroidism. Metabolic tests were found positive in 25% of the study population [22]. In accordance with recent UK guidelines review, they found doing the metabolic tests at 1st tier work up is cost effective based on long-term cost savings if early diagnosis and treatment are possible [13]. So, we recommend doing a complete metabolic set: Serum Amino acid, acylcarnitine, Bicarbonate, Lactate, Glucose, Ammonia, Pyruvate, CK, Urine glycosaminoglycan, and Urine organic acid [24]. The selection of the metabolic test can be tailored based on child clinical pre-

sentation. Also, we emphasize on reviewing newborn screening results given that Saudi Arabia has a national newborn screen program for 17 diseases. If it is not possible to retrieve the newborn screen result, we recommend doing a new screen. Due to technical difficulty to retrieve newborn screen results (for congenital hypothyroidism) in national level as well as high possibility of acquired hypothyroidism causes, we recommend doing TFT. In a local study MRI brain has been found abnormal in 54% of examinations. Furthermore, the MRI brain helped in establishing a diagnosis in 40% of cases through direct diagnosis or suggested diagnosis confirmed by further diagnosis [25]. Taking these figures into consideration, we recommend MRI brain with initial work up. Hearing is directly linked to speech and literacy development; we recommend a complete assessment for child hearing through audiology referral (Physiologic e.g. OAE or ABR or behavioral method play audiometry) [26]. Vision is important to child motor development; we recommend to screen vision (fixation) through 1st year and ophthalmology referral for instrument-based vision screening if abnormality detected at any age [27]. For Motor delay, it would be helpful to categorize children in the high tone group which will require neuroimaging vs. low tone group whom more information will be obtained from (CK and TFT) [20].

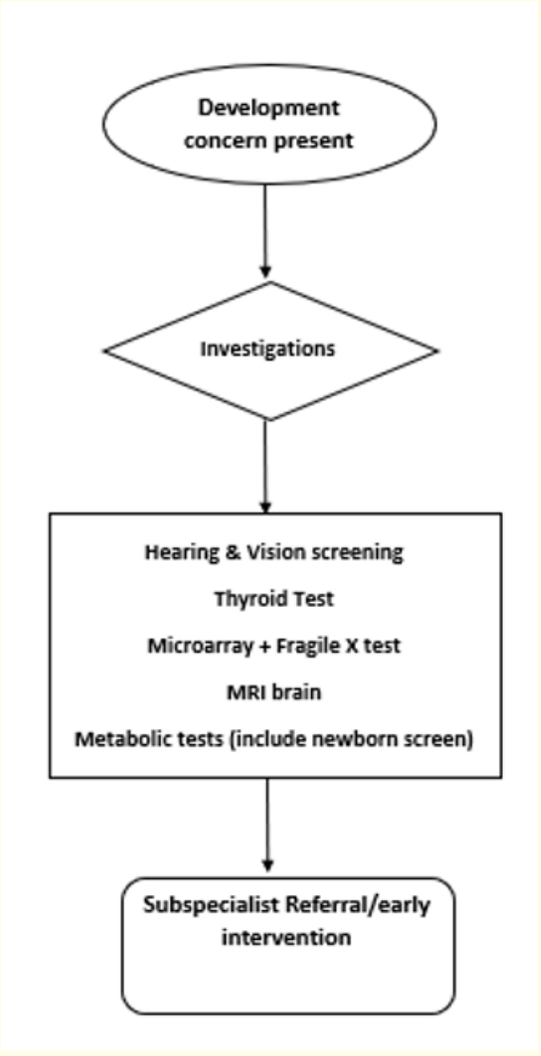

Figure 2: *Summary of investigations algorithm*

Management

We recommend early intervention during and after completion of assessment of a child with global developmental delay. It is important to work on child milestones achievement or correction of sensory loss/motor/speech/cognitive skills during investigation process which may take some time. General referrals include: Developmental subspecialist, neurologist/Geneticist, Psychologist, Special educators & Social services (for government financial support) [28]. Based on the type of development domain delayed, specific referral can be

made. For Motor delay: Occupational/physiotherapy and neurologist. For Social/Cognitive delay: Behavioral therapy and assessment for Special school need. For Speech delay: Speech therapist and assessment for Special school need.

Development Delay Domain		**Motor***	**Social/Cognitive**	**Speech†**
Causes		Genetic: (non-metabolic, metabolic) Environmental/exogenous: (Prenatal, Perinatal, Postnatal)		
Surveillance		Not yet show expected milestones		
	Red Flags	Parents concern		
		Early rolling less than 3 M Hand fisting beyond 3 M Poor head control at 3 M Persistent of neonatal/primitive reflexes after 6 M Early hand preference less than 1 year	Immature behavior Immature play Self-help problems Young sibling overtaking	Behavior problems e.g. temper
Screening Tools		e.g. AGS, PEDS		
Investigations		Hearing and Vision tests Metabolic tests and newborn metabolic screen‡ Thyroid test Genetic tests (Chromosomal Microarray + Fragile X) Neuroimaging		
General referrals		Developmental subspecialist Neurologist/Genetic Psychologist Special educators Social services (for government financial support)		
Specific referrals		Occupational/physiotherapy Neurologist	Behavioral therapy Assessment for Special school need	Speech therapist and assessment for Special school need.

Table 1: *General summary.*

**In motor delay physician observation of milestones and perform of neurologic exam is important.*

†Other specific causes if single speech delay: Developmental such as autism or deafness.

‡Serum amino acid, acylcarnitine, bicarbonate, lactate, glucose, ammonia, pyruvate, CK, urine glycosaminoglycan and urine organic acid. Also, newborn screening review, if not possible do a new screen.

Limitation of the Study

This was review, so it carries risk of bias such as incomplete retrieval of identified research, reporting bias. However, it is purpose to found ground for future researches and guidelines development.

Conclusion

We found one current clinical practice guideline in Arabic [10]. However, this overview shed the light on the importance of developmental screening in general pediatric clinics with subsequent early referral/early intervention to improve outcome in communities with high incidence of genetic diseases. Furthermore, carrying out local studies for Arabic region development screening tool use & outcome relation, and Role of genetic studies/tests (Whole Exome/Genome Sequence) in development delay evaluation for general pediatrician.

Funding Support

This article/research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declarations of Interest

None.

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Volume 11 Issue 12 December 2022