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Research Article

A Unique Experience with Mental and Developmental Retardation: Innovative Medical Therapies for Idiopathic Mental Retardation

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Abstract

Background: Until, 2016, there have been no specialized consultation clinic nor medical treatment services for children with mental and developmental retardation and other childhood psychiatric disorders in Iraq. However, early during the year 2017, a pediatric psychiatry (neuropsychiatry) consultation clinic was established at the Children Teaching Hospital of Baghdad Medical City with aim of providing evidence-based consultations and evidence-based medical therapies and also conducting a pediatric psychiatry training courses. Many of the scientific practices and disease patterns at the pediatric neuropsychiatry clinic were documented earlier through scientific publishing. The aim of this paper is to describe new our experiences with mental and developmental retardation with emphasis on recently used innovative medical therapies for idiopathic mental retardation.

Patients and Methods: During nine months period (from March to December, 2019), eighty patients (55 males and 25 female) with mental and developments retardation were studied at the Children Teaching Hospital of Baghdad Medical City. Their ages ranged from 4 months to sixteen years.

Results: Idiopathic mental retardation accounted for 51%, Down syndrome 8.75, Cornelia De Lang syndrome accounted for 6.25%. Most of the patients especially patients with idiopathic mental retardation were treated based on our previously published experiences with individualized courses of medical therapies with aim of improving the quality of their life by improving adaptive skills including bowel control and spoon feeding, improving cognition and understanding, improving their fine motor skills and with the ultimate aim of making them more educable. However, it was not possible to record the treatment courses of all patients, but it was possible to demonstrate a beneficial effect of treatments in four patients.

Conclusion: In this study, the most common causes of mental and developmental retardation were idiopathic mental retardation accounting for 51%, Down syndrome accounting for (8.75%) and Cornelia De Lang syndrome accounting for 6.25%. The use of innovative multifactorial therapies was helpful in the management of idiopathic mental retardation.

Keywords: *Mental Retardation; Iraq; Innovative Therapies*

Introduction

Until, 2016, there have been no specialized consultation clinic nor medical treatment services for children with mental and developmental retardation and other childhood psychiatric disorders in Iraq. However, early during the year 2017, a pediatric psychiatry (neuropsychiatry) consultation clinic was established at the Children Teaching Hospital of Baghdad Medical City with aim of providing

evidence-based consultations and evidence-based medical therapies, and also conducting a pediatric psychiatry training courses. Many of the scientific practices and disease patterns at the pediatric neuropsychiatry clinic were documented earlier through scientific publishing [1-14]. The patterns of pervasive developmental disorders and mental and developmental retardation in Iraqi children have been determined [4-6,9,11]. The occurrence of pediatric psychiatric disorders that have not been documented in Iraq children has been reported. These disorders include Rett syndrome, Heller syndrome, regressive autism, and Gilles de La Tourette syndrome [2,3,6,10,12]. The content of pediatric psychiatry courses has also been scientifically documented [13]. The use of innovative evidence-based medical therapies with obvious benefits in pervasive developmental disorders and mental retardation has been documented [1,2,4,7,8,14]. The work at the pediatric psychiatric clinic provided evidence that a cure from pervasive developmental disorders including autism and Asperger syndrome is possible [14].

Aim of the Study

The aim of this paper is to describe new experiences with mental and developmental retardation with emphasis on recently used innovative medical therapies for idiopathic mental retardation.

Patients and Methods

During nine months period (from March to December, 2019), eighty patients (55 males and 25 female) with mental and developments retardation were studied at the Children Teaching Hospital of Baghdad Medical City. Their ages ranged from 4 months to sixteen years.

Results

41 patients had idiopathic mental retardation (27 boys and 14 girls), 7 patients had Down syndrome (5 boys and 2 girls), 5 patients had Cornelia De Lang syndrome, 3 patients had kernicterus (2 boys and one girl), 2 male patients had Fragile X-syndrome, 2 male patients with Prader Willi syndrome, two patients had Noonan syndrome (a boy and girl), 2 brothers had Goldberg Shprintzen syndrome, 2 patients with microcephaly (one boy and one girl), two patients had non syndromic agenesis of corpus callosum, Seven patients (4 males and 3 females) each had congenital myotonic muscular dystrophy (Congenital dystrophia myotonica), Townes Brocks Syndrome, the extended Michelin tire baby, Mowat Wilson syndrome, Toriello-Carey Syndrome, Dandy walker syndrome, and familial congenital cataracts. In addition, five patients had newly recognized mental retardation syndromes. Table 1 shows the causes of mental and developmental retardation in this series.

Cause	Number	Sex
Idiopathic mental retardation	41 (51%)	27 males and 14 females
Down syndrome	7 (8.75%)	5 males and 2 females
Cornelia De Lang syndrome	5 (6.25%)	4 males and 1 female
Kernicterus	3	2 males and 1 female
Fragile X-syndrome	2	2 males
Prader Willi syndrome	2	2 males
Noonan syndrome	2	1 male and 1 female
Goldberg Shprintzen syndrome	2	2 males
Microcephaly	2	1 male and 1 female
Non-syndromic agenesis of corpus	2	1 male and 1 female
Congenital myotonic muscular dystrophy	1	1 female
Townes Brocks Syndrome	1	1 female
The extended Michelin tire baby	1	1 male
Toriello-Carey Syndrome	1	1 female
Mowat Wilson syndrome	1	1 male
Dandy walker syndrome	1	1 male
Familial congenital cataracts	1	1 male
New mental retardation syndromes	5	4 males and 1 female

Table 1: *The causes of mental and developmental retardation in a series of eighty Iraqi patients.*

The patients with idiopathic mental retardation included a brother and sister with thalassemia trait and two twin sisters. One boy with idiopathic mental retardation had severe growth retardation and history of renal stone.

Patients with Down syndrome included two infants, a boy and a girl with atrial septal defect. Two boys with Down syndrome had alopecia areata. One of the boys with Down syndrome had mild overweight.

Many of the patients in this series were previously reported including four of the five patients with Cornelia De Lang syndrome [15], the two patients with Noonan syndrome [16,17], the brothers with Goldberg Shprintzen syndrome [18], the two patients with Non-syndromic agenesis of corpus [19] and the patients with congenital myotonic muscular dystrophy (Congenital dystrophia myotonica) [20], Townes Brocks Syndrome [21], the extended Michelin tire baby [22], Mowat Wilson syndrome [23], Toriello-Carey Syndrome [24] and Dandy walker syndrome [25]. The cases of the five patients with new mental retardation syndromes have also been reported [26-31].

Figure 1 shows a boy with Cornelia De Lang syndrome who was not previously reported. Figure 2 shows a patient with Prader Willi syndrome with characteristic facial features and hypogonadism. Figure 3 shows the boy and girl with microcephaly. Figure 4A and 4B shows the two boys with Fragile X-syndrome.

Figure 1: *A boy with Cornelia De Lang syndrome who was not previously reported. He had the characteristic facial features which include synophrys.*

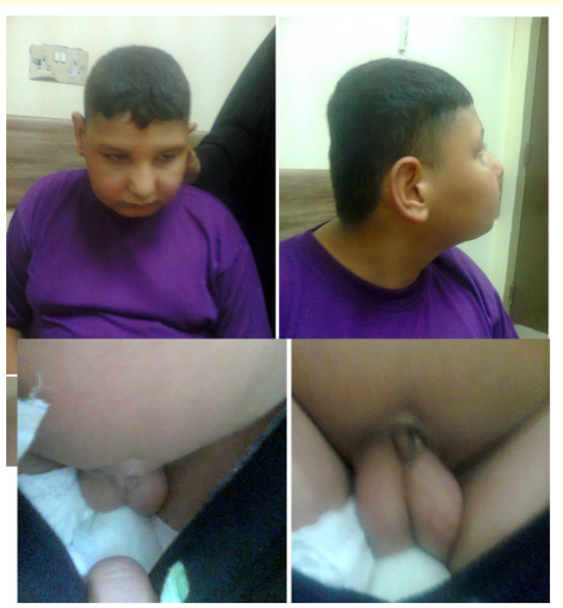

Figure 2: *A patient with Prader Willi syndrome with characteristic facial features and hypogonadism.*

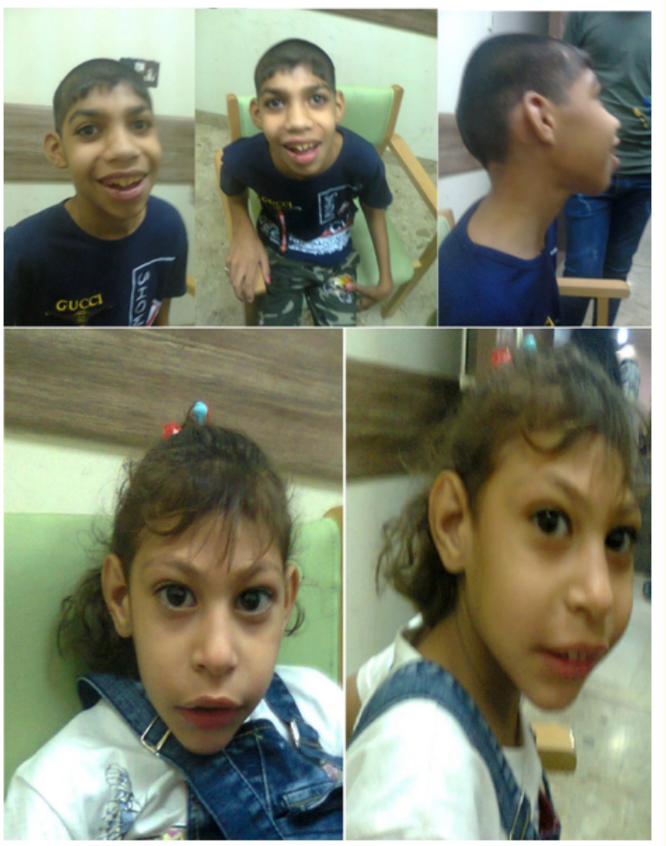

Figure 3: *The boy and girl with microcephaly.*

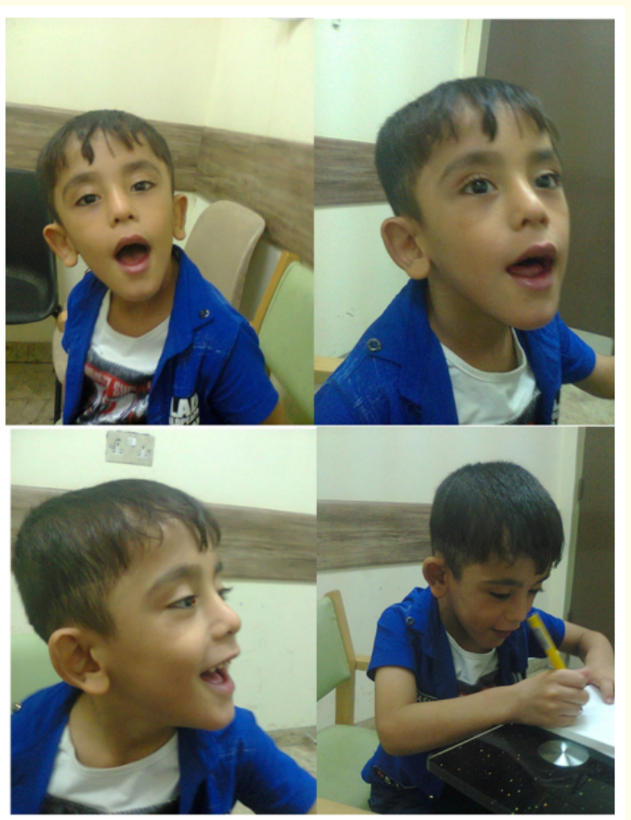

Figure 4A: *A boy with Fragile X-syndrome.*

Figure 4B: *A boy with Fragile X-syndrome.*

Most of the patients especially patients with idiopathic mental retardation were treated based on our previously published experiences [5,8,9] with individualized courses of medical therapies with aim of improving the quality of their life by improving adaptive skills including bowel control and spoon feeding, improving cognition and understanding, improving their fine motor skills and with the ultimate aim of making them more educable. However, it was not possible to record the treatment courses of all patients.

J.T, a seven year old boy with idiopathic mental retardation was first seen during the year 2019 (Weight 24.6 Kg). He had mild non-specific dysmorphic features including low set ears and nasal deviation. At the clinic, he was irritable, anxious and crying (Figure 5A) and didn't cooperate with examination. He had poor speech development and was spilling when eating with spoon and was unable to copy a good circle despite he was receiving specialized education at a specialized school for handicapped children. He was considered to have uneducable idiopathic mental retardation. Table 2 shows the treatment courses which aimed at improving his behavior.

Figure 5A: *At the clinic, he was irritable, anxious and crying, and didn't cooperate with examination as he was not responding to any requests.*

First course
1-Intramuscular cerebrolysin 5 ml every other day, 10 doses. 2-Oral trifluoperazine 1 mg tablet at night. 3-Oral citicoline 3 ml in the morning.
Second course
1-Intramuscular cerebrolysin 5 ml every third day, 10 doses. 2-Oral trifluoperazine 1 mg tablet at night. 3-Oral citicoline 3 ml in the morning.
Third course
1-Intramuscular piracetam 3 ml every third day, 10 doses. 2-Oral trifluoperazine 1 mg tablet at night. 3-Oral citicoline 3 ml in the morning.
Fourth course
1-Intramuscular piracetam 5 ml every third day, 10 doses. 2-Oral trifluoperazine 1 mg tablet at night. 3-Oral citicoline 3 ml in the morning.
Fifth course
1-Intramuscular piracetam 5 ml every third day, 10 doses. 2-Oral citicoline 3 ml in the morning.

Table 2: *Treatment courses received by J.T, a seven year old boy with idiopathic mental retardation and minor non-specific dysmorphic features.*

After the first course of treatment, he was more calm and cooperative, and showed improved speech and improvement in his ability of copying forms (Figure 5B). He was more responding to requests and he couldn't stand on one foot when he asked. After the fourth course of treatment he had normal behavior and was perfectly educable and he could copy a triangle and was able to stand one foot (Figure 5C). After the fifth course of treatment he started drawing, and learning writing and reading, and his specialized school recommended moving him to ordinary school like a normal child.

Figure 5B: *After the first course of treatment, the boy was more calm and cooperative, showed improved speech and improvement in his ability of copying forms.*

Figure 5C: *After the fourth course of treatment, the boy had normal behavior and was perfectly educable and he could copy a triangle and was able to stand one foot.*

A.A, A, a 16-year old boy with idiopathic mental retardation and was first seen on the 22nd of April, because of poor language development that prevented him from joining school. He could copy a good circle during the second attempt and a poor square, but he couldn't copy a triangle. His parent had already taught him to write his name (Figure 6A).

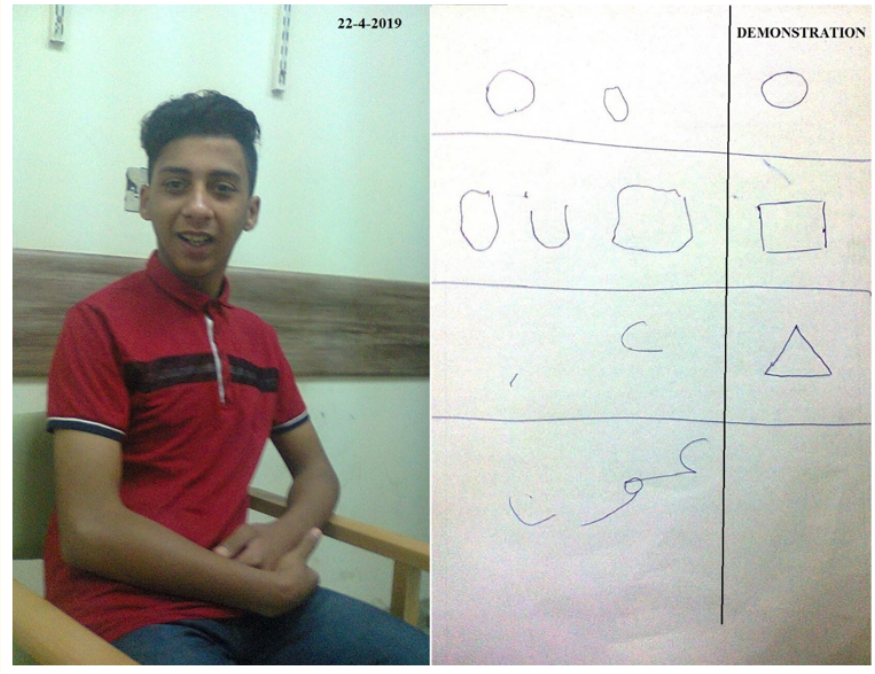

Figure 6A: *At the age of 16, the boy could copy a good circle during the second attempt, and a poor square, but he couldn't copy a triangle. His parent had already taught him to write his name.*

He received intramuscular cerebrolysin injection daily for ten days 10 followed by intramuscular citicoline 4 ml (500 mg) in the morning every other day, 15 doses over one month. After treatment, he showed obvious improvement in speech and was able to copy a triangle, but he couldn't copy a diamond (Figure 6B).

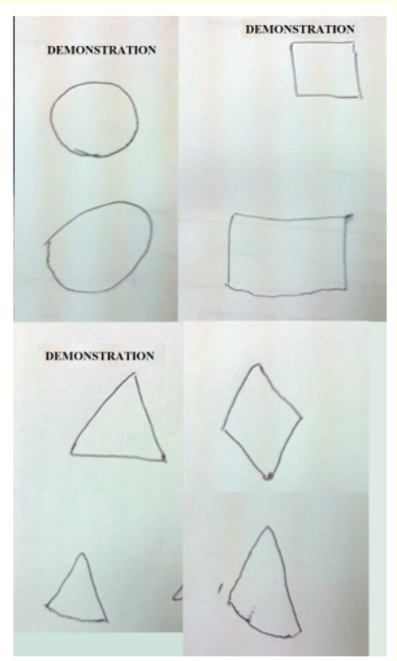

Figure 6B: *After treatment, the boy was able to copy a triangle, but he couldn't copy a diamond.*

D.I was an eight-year old girl with idiopathic mental retardation that prevented her from joining school. She was seen during the year 2019 because of over-activity and poor speech development. She could copy a circle, a poor square and a poor triangle (Figure 7A). She was treated for two months with intramuscular cerebrolysin 5 ml every third day in the morning (20 doses), oral prochlorperazine 5 mg in the afternoon, and oral trifluoperazine 1 mg at night. After treatment, she experienced marked reduction in over-activity and improvement in cognition and fine motor skills manifested by improved ability in copying forms, and she was able to draw a house (Figure 7B).

Figure 7A: *Before treatment the girl could copy a circle, a poor square, and a poor triangle.*

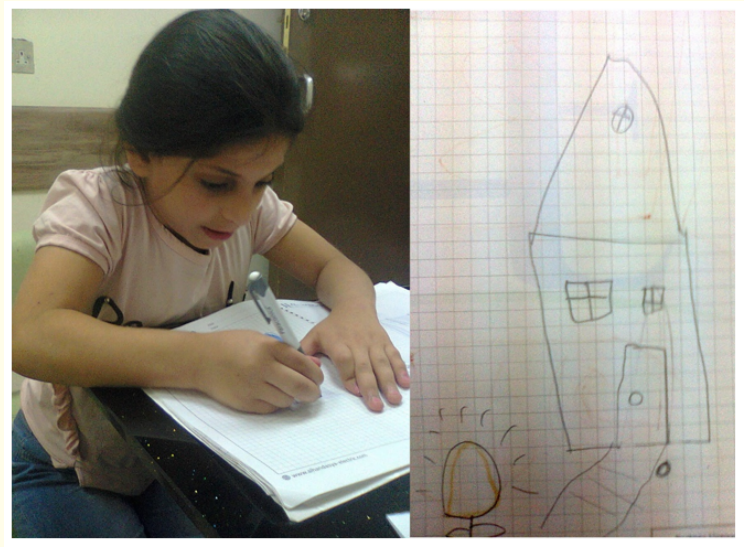

Figure 7B: *After treatment, she experienced improvement in cognition and fine motor skills manifested by improved ability in copying forms, and she was able to draw a house.*

H.S was a five and half years old boy with idiopathic mental retardation, low set ears poor speech development, marked over-activity and did not understand simple commands. His weight was 20 Kg. He was unable to copy a square. He received four treatment courses (Table 3).

	**First course:** Intramuscular citicoline 4 ml (500 mg) every third day in the morning (20 doses over 2 months), and oral trifluoperazine 1 mg at night. **Second course (One month):** Oral trifluoperazine 1 mg at night, oral prochlorperazine 5 mg in the afternoon, and oral citicoline 3 ml (300 mg) in the morning. **Third course:** Intramuscular piracetam 1g every third day in the morning (10 doses over one month, oral trifluoperazine 1 mg tablet in the morning, oral prochlorperazine 5 mg tablet in the afternoon and risperidone 1 mg at night.

Table 3: *Treatment courses received by H.S a five and half years old boy with idiopathic mental retardation associated with low set ears, poor speech development, marked over-activity, and was unable to understand simple commands.*

After treatment, the boy experienced marked improvement with improved speech, reduction of over-activity, improvement in cognition and fine motor skills manifested by improved ability in copying forms and became capable of understanding many requests and commands.

Discussion

We have previously described the causes of mental and developmental retardation in a sample of 36 patients. Eighteen patients (50%) had idiopathic mental retardation including 11 males and 7 females, seven patients (19%) had Down syndrome including 5 males and 2 females, two male patients had Beckwith Wiedemann syndrome, one of them had an affected brother, three males had inborn errors of metabolism, each one had phenylketonuria, homocystinuria and Lesch Nyhan syndrome. The patient with Lesch Nyhan syndrome had an older brother who died from the same condition. Six patients each one had Prader-Labhart-Willi syndrome, Sanjad Sakati Richardson Kirk syndrome, Coffin Siris syndrome, kernicterus, Bartter syndrome, pediatric Huntington disease [5].

We have also previously described the use of a new combination of multifactorial interventions consisting of the use of intramuscular cerebrolysin, intramuscular citicoline, oral pyritinol, and intramuscular piracetam in the treatment of moderately severe idiopathic mental retardation which is considered a heterogeneous condition.Treatment was successful in advancing the mental function of the boy with who was uneducable, but became perfectly educable after treatment [8].

In this study intramuscular cerebrolysin courses were used in of the three well-documented treated cases. Cerebrolysin is a safe peptidergic liquid mixture of free amino acids with a multimodal mechanism of action and has the ability to stimulate nerve cells and to induce neurogenesis which is a process of development of new nerve cells [32].

Cerebrolysin has recently been safely used in the treatment of a variety of childhood neurological and psychiatric disorders including brain atrophy [33], cerebral palsy [34-36], kernicterus [37], agenesis of the corpus callosum [19], pediatric juvenile spinal muscular atrophy [38], Charcot Marie Tooth disease [39], myelomeningocele [40], autism and Rett syndrome [1,2,7].

Intramuscular piracetam was used in two patients. Piracetam (2-oxo-1-pyrrolidine acetamide) is a cyclical derivative of GABA (gamma-aminobutyric acid). It was first synthesized during the 1950s by Corneliu E. Giurgea. There are reports of its use for epilepsy in the 1950s. Piracetam can beneficially influence impaired brain function by improving neuronal and cognitive functions without acting as a sedative or stimulant, increasing blood flow and oxygen consumption in the brain, and improving the function of the neurotransmitters and brain neurotransmission. The modes of action of piracetam has been attributed to differential effects on subtypes of glutamate receptors without GABAergic actions Piracetam has no significant side effect nor has acute toxicity at the doses used in human studies. The LD_{50} is 5.6 g/kg in rats and 20 g/kg in mice, indicating extremely low acute toxicity [19,33-36].

Oral or intramuscular citicoline were used in three patients. Citicoline, the generic name of cytidine 5-diphosphocholine (CDP-choline, cytidine diphosphate choline) when used as an exogenous sodium salt. Cytidine diphosphate choline is a mononucleotide made of ribose, pyrophosphate, cytosine and choline. It is a water-soluble naturally occurring substance that is generally grouped with the B vitamins. It is also considered a form of the essential nutrient choline [41,42]. Citicoline has been recently used with benefit in treatment of childhood neuro-psychiatric disorders including, pervasive developmental disorders including Rett syndrome [1,2,7], brain atrophy [33], kernicterus [37] and cerebral palsy [34-36].

In this study it was possible to demonstrate that the use of a new combination of multifactorial interventions consisting of the use of neuroleptics, intramuscular cerebrolysin, oral and intramuscular citicoline, oral pyritinol, and intramuscular piracetam in four patients was associated with benefit effects on overactivity, cognition and learning.

Conclusion

In this study, the most common causes of mental and developmental retardation were idiopathic mental retardation accounting for 51%, Down syndrome accounting for (8.75%), and Cornelia De Lang syndrome accounting for about 6.25%. The use of innovative multifactorial therapies was helpful in the management of idiopathic mental retardation.

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