P-ISSN: 2664-3685
E-ISSN: 2664-3693
www.paediatricjournal.com
IJPG 2024; 7(1): 13-19
Received: 20-11-2023
Accepted: 30-12-2023

Dr. Basma Jasims Obaid
Children Welfare Teaching Hospital/Baghdad, Iraq

Dr. Sarab Shakir Abbas
Consultant Pediatric Neurologist, Children Welfare Teaching Hospital, Medical City Campus, Baghdad, Iraq

Corresponding Author:
Dr. Basma Jasims Obaid
Children Welfare Teaching Hospital/Baghdad, Iraq

Karyotype and molecular cytogenetic analysis among sample of Iraqi children with idiopathic intellectual disability

Banan Shakir Nasif and Hula R Shareef

DOI: https://doi.org/10.33545/26643685.2024.v7.i1a.216

Abstract
Background: Most children with uncertain etiology have moderate ID, which accounts for 48.8% of all intellectual impairments. Genetic testing allows early etiologic diagnosis, medical comorbidity monitoring, and genetic counselling for families.
Aim of the study: To study the clinical features of Intellectual disabilities, determine the yield of karyotyping in children with idiopathic intellectual disability.
Patients and Methods: A retrospective and prospective observational study were conducted on seventy-two Pediatric patients with intellectual disabilities who visited child welfare teaching hospital outpatient clinic for Pediatric neurological diseases. The data records were collected from the beginning of January 2018 to the end of July 2022, children aged 5 up to 14 years who were diagnosed clinically to have intellectual disability were included. Raven's IQ test, Brain MRI were performed in all patients with intellectual disability. GTG banding karyotype, florescence in situ hybridization and PCR were the materials used.
Results: The male-to-female ratio was ≈ (4:1). Speech difficulty and Behavioral abnormalities were significantly higher among males (P=0.042), (P=0.017) respectively. The majority of children were with normal MRI 45 (62.5%), while the highest proportion of abnormal MRI findings was brain atrophy reported in 16 (22.2%) of cases. Epilepsy was among only 22 (30.6%).
Conclusion: In this study, Individuals with intellectual disabilities including speech delays and/or learning disabilities, with or without behavior problems, are more likely to have chromosome abnormalities, in form of deletion, duplication, and fragile X, and particularly del (22) (22q 11.2)], [del (5) (p15.1- p 15.2)..Most of the cases with duplication had mild levels of intellectual disability and positive history of parental consanguinity.

Keywords: Karyotype, molecular, cytogenetic analysis, Iraqi children, idiopathic intellectual disability

Introduction

Intellectual Disability (ID) is a developmental disability evident during infancy or early childhood, often diagnosed more accurately after the age of 5 when developmental skill assessments become reliable. The American Association on Intellectual and Developmental Disability (AAIDD) defines ID through three criteria: an Intelligence Quotient (IQ) below 70-75, significant difficulties in adapting to daily life activities, and observable limitations in cognitive and functioning skills [1]. This multi-faceted approach underscores that IQ alone does not define ID. The term "Intellectual Disability" is preferred over "mental retardation" due to the latter's stigmatizing nature and its historical misuse, which led to the enactment of Rosa's Law in the U.S. in 2010, mandating the replacement of the term in federal policies [2]. However, the terminology varies globally, with "learning disability" commonly used in Europe. Idiopathic Intellectual Disability (IID) represents unexplained cases of ID, accounting for almost half of all instances, where genetic and clinical examinations do not reveal a cause [3]. Learning disabilities, distinct from ID, encompass a broad range of disorders affecting specific cognitive functions such as reading, writing, and numerical understanding, often linked to central nervous system dysfunction [4]. Developmental dyslexia is a prominent learning disability, affecting a significant portion of individuals with learning challenges, characterized by unexpected reading difficulties in those who otherwise have the necessary intelligence, motivation, and educational opportunities [5]. Academic underachievement and speech disorders, including articulation or phonological disorders, dysarthria, childhood apraxia of speech, and stuttering, are other areas of concern, impacting

educational progress and social integration [6]. Behavioral disorders encompass a wide range of issues, from aggression to self-injury and non-compliance, presenting significant challenges in learning and socialization, requiring substantial management efforts [7]. The prevalence of ID varies globally, with developing countries showing rates between 10 to 15 per 1000 children, mostly mild cases, whereas 1 to 3% of the Western population is estimated to have ID, more commonly diagnosed between the ages of 10 to 14 and more prevalent in males [8]. The categorization of ID into mild, moderate, severe, and profound levels helps in tailoring intervention strategies based on individual needs [9]. Etiologically, ID can result from genetic abnormalities, environmental exposures, or a combination of both, with conditions like Down syndrome, Fragile X syndrome, and fetal alcohol syndrome being among the common causes [10]. Advances in genetic testing, including karyotyping, fluorescence in situ hybridization (FISH), and chromosomal microarray (CMA), have enhanced the ability to diagnose and understand the genetic underpinnings of ID and developmental delays [11]. Psychological assessments for children with ID focus on a holistic evaluation of cognitive abilities, adaptive skills, and emotional well-being, rather than relying solely on IQ scores [12]. Early diagnosis of ID is crucial for setting realistic goals, alleviating parental anxiety, and fostering community acceptance of affected children. Cytogenetic and molecular testing play critical roles in diagnosing chromosomal abnormalities, contributing to the comprehensive management and understanding of ID and associated developmental disorders [13].

Aims of the study to study the clinical features of Intellectual disabilities in children and to determine the yield of karyotyping in children with idiopathic ID.

Method

A comprehensive observational study was conducted on seventy-two pediatric patients with intellectual disability (ID) attending the CWTH outpatient clinic for pediatric neurological diseases from January 2018 to July 2022. The study targeted children aged between 5 and 14 years, diagnosed with ID, excluding those with conditions like hypothyroidism, Down syndrome, birth asphyxia, previous meningitis, inherited or acquired neurological/metabolic diseases, autism, history of head trauma, profound ID, deafness, or poorly documented data. Data were collected through a structured questionnaire following an IQ test (using Raven's IQ test conducted at the National Autism Center/CWTH), with participants requiring a score less than 70% to proceed. Those meeting inclusion criteria underwent further karyotype and cytogenetic analysis. The questionnaire covered demographics (age, gender), characteristics of ID (speech difficulty, behavioral abnormality, academic underachievement), associated features (mild non-specific dysmorphic features, brain atrophy on MRI, epilepsy, consanguinity, family history), severity of ID, and genetic analysis results. Additional assessments included brain MRI for all patients, EEG for those with abnormal body movements, and selected cases received further tests such as thyroid function tests (TFT), liver function tests (LFT), MSMS, brain CT scans, echocardiograms. Genetic analyses were performed at Al-Baylassan Laboratory for Advanced Pathological and Genetic Analysis, employing GTG banding karyotype for microdeletion/micro duplication, FISH for micro duplications detection, and PCR for fragile X syndrome. This study received ethical approval from the Arab Council of Health Specializations, the Iraq Ministry of Health, and Dr. Hula Raoof, ensuring complete confidentiality and use of data solely for research purposes, with personal information anonymized using serial identification numbers. Statistical analysis was performed using Microsoft Excel 2019 and SPSS version 24. Data were presented as mean and standard deviation for parametric data, and numbers and percentages for categorical data. The Chi-square test and Fisher exact test were utilized for homogeneity testing, with a p-value < 0.05 indicating statistical significance. This rigorous approach ensured a thorough investigation into the demographic characteristics, ID attributes, associated conditions, and genetic underpinnings of ID among the studied pediatric population, contributing valuable insights into its prevalence, characteristics, and associated genetic factors in this group.

Results

The study included 72 paediatric patients aged 8 ± 2 years, ranging from 5 to 14 years old. Most were 7, 8, and 9 years old. The male-to-female ratio was 4:1. The majority had speech problems 60 (83.3%). 40 (55.6%) had behavioural problems. 56 (77.8%) underperformed academically. 52 (72.2%) had modest non-specific dysmorphic characteristics. Normal MRI results were seen in 45 (62.5%) of children, whereas brain atrophy was found in 16 (22.2%). Only 22 (30.6%) had epilepsy. 49 parents were consanguineous (68.1%). There was no family history of intellectual impairment in 26 (36.1%). In 54 (75.0%), intellectual disability was mild. According to table VI.

Table 1: Demographic characteristics of study sample (n=72)

Variables			N.	%
Sex	Male		53	73.6
	Female		19	26.4
Speech difficulty	Yes		60	83.3
	No		12	16.7
Behavioral abnormality	Yes		40	55.6
	No		32	44.4
Academic underachievement	Yes		56	77.8
	No		16	22.2
Mild non-specific Dysmorphic features	Yes		52	72.2
	No		20	27.8
MRI	Normal		45	62.5
	Brain atrophy		16	22.2
	Thinning of cc		6	8.3
	WM changes		5	6.9
Epilepsy	Yes		22	30.6
	No		50	69.4
Consanguinity	Yes		49	68.1
	No		23	31.9
Family history	Yes		26	36.1
	No		46	63.9
Level of intellectual disability	Mild		54	75.0
	Moderate		15	20.8
	Severe		3	4.2
Age in years	Mean ± SD	Minimum	Maximum	
	8 ± 2	5	14	

Table 2 shows that the majority (11 cases, 10 cases, and 8 cases) were with chromosomal abnormalities [dup (22) (22q 11.2)], [del (5) (p15.1- p 15.2)], and [Fragile X syndrome]. Other less frequent karyotypes were all listed in detail.

Table 2: Frequency of chromosomal abnormalities in 72 pediatric patients referred for investigation due to intellectual disability

Karyotypes	N.	%
46XYdup (22) (22q 11.2)	7	9.7
46XX dup (22) (22q 11.2)	4	5.5
46XY del (5) (p15.1- p 15.2)	8	11.1
46XX del (5) (p15.1- p 15.2)	2	2.7
Fragile X syndrome	8	6.9
46XY Normal karyotype	5	2.7
46XX Normal karyotype	2	6.9
46XY del (22) (22q 11.2)	5	0.0
46XX del (22) (22q 11.2)	0	4.1
46XY dup (X) (p 11.2 p11.3)	3	2.7
46XX dup (X) (p 11.2 p11.3)	2	4.1
46XY Inv (9) (p12 p13)	4	9.7
46XX Inv (9) (p12 p13)	0	5.6
46, XY,del (16) (16 p 11.2)	4	5.6
46,XY,del (15q 11-q13)	3	4.2
46XX dup (X) (q 28)	3	4.2
46,XY,del (16) (16 p13)	2	2.8
46,XY, dup (10) (q22.3-23.2)	1	1.4
46,XY,del (7) (q11.23 q11.23)	1	1.4
46,XX, del of chromosome 9 and X	1	1.4
46,XX,del (7) (q 32.1)	1	1.4
46,XY,del (7) (p 15.3)	1	1.4
46,XXdup (9)	1	1.4
46,XY, del (13) (q 13.3)	1	1.4
46,XX, del (6) (q 12 q 13)	1	1.4
46, XY,del (6) (x) (2 p 21.3) (q 22-q 24)	1	1.4
46,XY,del (X) (q 13.2 q 26.1)	1	1.4

Speech difficulty was significantly higher among male 47 (78.3%) (P=0.042). Behavioral abnormalities were significantly (P=0.017) higher among males 25 (62.5%). Other clinical presentation including academic underachievement, mild non-specific dysmorphic features, epilepsy, and level of intellectual disability were without significant differences [P=0.886, 0.104, 0.640, and 0.334 respectively], as showed in table 3.

Table 3: Distribution of pediatric patients' clinical presentation in relation to their Sex (n=72).

Variables		Total	Sex				P- value
			Male		Female		
			N.	%	N.	%	
Speech difficulty	Yes	60	47	78.3	13	21.7	0.042
	No	12	6	50.0	6	50.0	
Behavioral abnormality	Yes	40	25	62.5	15	37.5	0.017
	No	32	28	87.5	4	12.5	
Academic underachievement	Yes	56	41	73.2	15	26.8	0.886
	No	16	12	75.0	4	25.0	
Dysmorphic features	Yes	52	41	78.8	11	21.2	0.104
	No	20	12	60.0	8	40.0	
Epilepsy	Yes	22	17	77.3	5	22.7	0.640
	No	50	36	72.0	14	28.0	
Family history	Yes	26	21	80.8	5	19.2	0.300
	No	46	32	69.6	14	30.4	
Level of intellectual disability	Mild	54	42	77.8	12	22.2	0.334 *
	Moderate	15	9	60.0	6	40.0	
	Severe	3	2	66.7	1	33.3	

Chi-square test was used and significant at $p<0.05$.
* Fisher exact test was used and significant at $p<0.05$.

Most cases with mild non-specific dysmorphic features 37 (71.2%) were with positive parental consanguinity, and this difference was statistically not significant (P=0.363), epilepsy, family history, and level of intellectual disability were also failed to find a significant association with parental consanguinity [P= 0.112, 0.279, 0.492, and 0.394 respectively]. As clarified in table 4.

Table 4: Distribution of pediatric patients' clinical presentation in relation to parental consanguinity (n=72)

Variables		Total	Parental consanguinity				P- value
			Yes		No		
			N.	%	N.	%	
Dysmorphic features	Yes	52	37	71.2	15	28.8	0.363
	No	20	12	60.0	8	40.0	
Epilepsy	Yes	22	13	59.1	9	40.9	0.279
	No	50	36	72.0	14	28.0	
Family history	Yes	26	19	73.1	7	26.9	0.492
	No	46	30	65.2	16	34.8	
Level of intellectual disability	Mild	54	37	68.5	17	31.5	0.394
	Moderate	15	9	60.0	6	40.0	
	Severe	3	3	100.0	0	0.0	

Chi-square test was used and significant at $p<0.05$.

* Fisher exact test was used and significant at $p<0.05$.

Eleven cases were with [dup (22) (22q 11.2)], seven of them were with mild level of intellectual disability, 2 with moderate and 2 with severe level of intellectual disability. Also 5 of the cases with Normal karyotype from the total 7 cases, were with mild level of intellectual disability. From the total 10 cases with karyotype [del (5) (p15.1- p 15.2)], 8 were with mild intellectual disability and 2 were with moderate intellectual disability. All karyotypes distribution with the level of intellectual disability were illustrated in table 5.

Table 5: Distribution of frequency of level of intellectual disability in relation to the chromosomal analysis (n=72)

Karyotypes	Total	Mild	Moderate	Severe
		N.	N.	N.
dup (22) (22q 11.2)	11	7	2	2
Normal karyotype	7	5	2	0
del (7) (q 32.1)	1	1	0	0
del of chromosome 9 and X	1	1	0	0
del (6) (x) (2 p 21.3) (q 22-q 24)	1	0	1	0
dup (X) (p 11.2 p11.3)	5	5	0	0
del (5) (p15.1- p 15.2)	10	8	2	0
dup (9)	1	0	1	0
del (6) (q 12 q 13)	1	1	0	0
Inv (9) (p12 p13)	4	3	1	0
dup (X) (q 28)	3	2	1	0
dup (10) (q22.3-23.2)	1	1	0	0
del (7) (q11.23 q11.23)	1	1	0	0
Fragile X syndrome	8	6	2	0
del (22) (22q 11.2)	5	4	1	0
del (7) (p 15.3)	1	1	0	0
del (15q 11-q13)	3	3	0	0
del (13) (q 13.3)	1	1	0	0
del (16) (16 p13)	2	1	1	0
del (16) (16 p 11.2)	4	3	1	0
del (X) (q 13.2 q 26.1)	1	0	0	1

In table 6, 7 cases (63.6%) with karyotype [dup (22) (22q 11.2)] were with parental consanguinity. Also, 6 cases (60.0%) with karyotype [del (5) (p15.1- p 15.2)] were with positive history of parental consanguinity. Each karyotype in correlation to the consanguinity were clarified in table 6. In table 7, cases with brain atrophy were reported in cases with karyotype [dup (22) (22q 11.2)], [Normal karyotype], [del of chromosome 9 and X], [dup (X) (p 11.2 p11.3)], [del (5) (p15.1- p 15.2)], [Inv (9) (p12 p13)], [dup (X) (q28)], [dup (10) (q22.3-23.2)], [Fragile X syndrome], and[del (16) (16 p 11.2)]. Thinning of CC was reported in the case with karyotype [dup (22) (22q 11.2)], [del (5) (p15.1- p 15.2)], [Fragile X syndrome], [del (7) (p 15.3)], [del (15q 11-q13)]. A cases with karyotype [dup (22) (22q 11.2)], Normal karyotype, [del (7) (Q 32.1)], [Fragile X syndrome], del [(6) (x) (2 p 21.3) (q 22-q 24)], and [del (5) (p15.1- p 15.2)] were the only cases reported WM changes in MRI. All cases karyotypes with their MRI findings were illustrated in table 7.

Table 6: Distribution of Parental consanguinity in relation to the chromosomal analysis (n=72)

Karyotypes	Parental consanguinity			
	Yes		No	
	N.	%	N.	%
dup (22) (22q 11.2)	7	63.6	4	36.4
Normal karyotype	5	71.4	2	28.6
del (7) (q 32.1)	1	100.0	0	0.0
del of chromosome 9 and X	1	100.0	0	0.0
del (6) (x) (2 p 21.3) (q 22-q 24)	1	100.0	0	0.0
dup (X) (p 11.2 p11.3)	4	80.0	1	20.0
del (5) (p15.1- p 15.2)	6	60.0	4	40.0
dup (9)	1	100.0	0	0.0
del (6) (q 12 q 13)	1	100.0	0	0.0
Inv (9) (p12 p13)	3	75.0	1	25.0
dup (X) (q 28)	3	100.0	0	0.0
dup (10) (q22.3-23.2)	0	0.0	1	100.0
del (7) (q11.23 q11.23)	0	0.0	1	100.0
Fragile X syndrome	5	62.5	3	37.5
del (22) (22q 11.2)	3	60.0	2	40.0
del (7) (p 15.3)	1	100.0	0	0.0
del (15q 11-q13)	3	100.0	0	0.0
del (13) (q 13.3)	1	100.0	0	0.0
del (16) (16 p13)	0	0.0	2	100.0
del (16) (16 p 11.2)	2	50.0	2	50.0
del (X) (q 13.2 q 26.1)	1	100.0	0	0.0

Table 7: MRI findings in relation to the chromosomal analysis (n=72)

Karyotypes MRI	Normal	Atrophy	Thinning of posterior Aspect of cc	WM changes
dup (22) (22q 11.2)	7	2	1	1
Normal karyotype	4	2	0	1
del (7) (q 32.1)	0	0	0	1
del of chromosome 9 and X	0	1	0	0
del (6) (x) (2 p 21.3) (q 22-q 24)	0	0	0	1
dup (X) (p 11.2 p11.3)	3	2	0	0
del (5) (p15.1- p 15.2)	5	2	2	1
dup (9)	1	0	0	0
del (6) (q 12 q 13)	1	0	0	0
Inv (9) (p12 p13)	1	3	0	0
dup (X) (q 28)	2	1	0	0
dup (10) (q22.3-23.2)	0	1	0	0
del (7) (q11.23 q11.23)	1	0	0	0
Fragile X syndrome	6	1	1	0
del (22) (22q 11.2)	5	0	0	0
del (7) (p 15.3)	0	0	1	0
del (15q 11-q13)	2	0	1	0
del (13) (q 13.3)	1	0	0	0
del (16) (16 p13)	2	0	0	0
del (16) (16 p 11.2)	3	1	0	0
del (X) (q 13.2 q 26.1)	1	0	0	0

Discussion

This study evaluated the efficacy of karyotype analysis in diagnosing intellectual disability (ID) in Iraqi children, using cytogenetic techniques such as GTG and FISH. The study involved 72 pediatric patients, predominantly males (4:1 ratio), with an age range of 5 to 14 years, reflecting similar demographics to studies from Rwanda and India that also investigated children with ID and developmental delays [14, 15]. Key findings indicated that the majority of children exhibited speech difficulties (83.3%), behavioral abnormalities (55.6%), academic underachievement (77.8%), and dysmorphic features (72.2%), with 75% classified as having a mild level of ID. These characteristics align with findings from Uwineza *et al*., where most children had moderate ID, and an Australian study highlighting a higher risk of ID in children of mothers with ID [14, 16]. The study also noted a high prevalence of consanguinity (68.1%), which correlates with findings from Lakhan *et al*. in India, suggesting a link between consanguineous marriages and ID, epilepsy, and mental illness within families [17]. The majority of children had normal MRI results (62.5%), but abnormalities such as brain atrophy and thinning of the posterior aspect of the cerebral cortex were noted, similar to European research by Soto *et al*., which found a significant presence of cerebral abnormalities in children with mental retardation [18]. Only 30.6% of the children had epilepsy, contrasting with Jussila *et al*.'s findings, which showed a lower incidence of significant MRI findings in children with mild ID [19]. The study suggests cautious consideration of routine MRI for children with mild ID due to the need for sedation and the limited etiological insight it provides without specific

neurological deficits [20]. Chromosomal abnormalities, including duplications, deletions, and Fragile X syndrome, were prevalent, underlining the significance of genomic examinations in diagnosing growth, developmental, and congenital anomalies [21, 22]. The study highlighted the association of dysmorphic features, epilepsy, family history, and ID level with positive parental consanguinity, though a significant association was not established, likely due to the small sample size [23, 24]. The research found that duplications were mostly associated with mild ID and consanguinity, similar to findings of deletions and brain atrophy [25]. This supports the notion that chromosomal abnormalities, including subtelomeric region abnormalities and CNV burden, play a crucial role in the etiology of ID, autism, and epilepsy [26, 27]. Studies like Zhu *et al*. and Yao *et al*. also demonstrate the potential of array CGH and FISH in revealing clinically relevant genomic variations and the importance of prenatal diagnosis in managing pregnancies affected by chromosomal abnormalities [28, 29].

Conclusion

Based on the findings of this research, there is a higher probability of chromosome abnormalities, including deletion, duplication, and fragile X, among individuals who have speech delays, cognitive disabilities, and/or behavioural issues [dup (22) (22q 11.2)], [del (5) (p15.1-p 15.2)].A positive history of parental consanguinity and moderate degrees of intellectual disability characterised the majority of cases involving duplication.

Conflict of Interest

Not available

Financial Support

Not available

References:

1. Schalock RL, Luckasson RA, Shogren KA, *et al*. The renaming of mental retardation: understanding the change to the term intellectual disability. Intellect Dev Disabil. 2007;45(2):116-124.
2. Bruce K. Shapiro and Meghan E. O'Neill-Nelson textbook of pediatrics, 21 edition; c2020. volume1/chapter 53/ developmental delay and intellectual disability
3. Koch I, Slovik M, Zhang Y, Liu B, Rennie M, Konz E, *et al*. *USP27X* variants underlying X-linked intellectual disability disrupt protein function via distinct mechanisms. Life Sci Alliance. 2024 Jan 5;7(3):e202302258. doi: 10.26508/lsa.202302258. PMID: 38182161; PMCID: PMC10770416.
4. Lasalvia A, Penta E, Sartorius N, Henderson S. Should the label "schizophrenia" be abandoned? Schizophr Res. 2015 Mar;162(1-3):276-284. doi: 10.1016/j.schres.2015.01.031. Epub 2015 Jan 31. PMID: 25649288.
5. Témoin C. Dépistage et prise en charge des troubles de l'apprentissage chez l'adolescent [Adolescent learning disability: are screening and management helpful?]. Soins Pediatr Pueric. 2021 May-Jun;42(320):31-33. French. doi: 10.1016/j.spp.2021.03.008. Epub 2021 Mar 26. PMID: 34099235.
6. Committee on the Evaluation of the Supplemental Security Income (SSI) Disability Program for Children with Speech Disorders and Language Disorders; Board on the Health of Select Populations; Board on Children, Youth, and Families; Institute of Medicine; Division of Behavioral and Social Sciences and Education; National Academies of Sciences, Engineering, and Medicine. Speech and Language Disorders in Children: Implications for the Social Security Administration's Supplemental Security Income Program. Rosenbaum S, Simon P, editors. Washington (DC): National Academies Press (US); 2016 Apr 6. PMID: 27123507.
7. Ogundele MO. Behavioural and emotional disorders in childhood: A brief overview for paediatricians. World J Clin Pediatr; c2018 Feb
8. Maulik PK, Mascarenhas MN, Mathers CD, Dua T, Saxena S. Prevalence of intellectual disability: a meta-analysis of population-based studies. Res Dev Disabil. 2011 Mar-Apr;32(2):419-436.
9. Mercadante MT, Evans-Lacko S, Paula CS. Perspectives of intellectual disability in Latin American countries: epidemiology, policy, and services for children and adults. Current Opinion in Psychiatry. 2009;22(5):469-474.
10. Lee K, Cascella M, Marwaha R. Intellectual Disability. [Updated 2022 Feb 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; c2022.
11. Shevell MI. Diagnostic approach to developmental delay. In: Maria B, editor. Current management in child neurology. Hamilton, Ontario: BC Decker; c2005. p. 246-250.
12. Karen J. Marcdante, MD, Robert M. Kliegman, MD - Nelson essentials of pediatrics 7th edition ,chapter 10 ,evaluation of the child with special needs p.29
13. Caspersson T, Zech L, Modest EJ. Fluorescent labeling of chromosomal DNA: superiority of quinacrine mustard to quinacrine. Science. 1970;170:762.
14. Uwineza A, Hitayezu J, Jamar M, *et al*. Cytogenetic Studies of Rwandan Pediatric Patients Presenting with Global Developmental Delay, Intellectual Disability and/or Multiple Congenital Anomalies. J Trop Pediatr. 2016 Feb;62(1):38-45.
15. Sharma S, Raina SK, Bhardwaj AK, *et al*. Socio demography of mental retardation: A community-based study from a goitre zone in rural sub-Himalayan India. J Neurosci Rural Pract. 2015 Apr-Jun;6(2):165-169.
16. Leonard H, Petterson B, De Klerk N, *et al*. Association of sociodemographic characteristics of children with intellectual disability in Western Australia. Soc Sci Med. 2015 Apr;60(7):1499-1513.
17. Lakhan R, Bipeta R, Yerramilli SSRR, *et al*. A Family Study of Consanguinity in Children with Intellectual Disabilities in Barwani, India. J Neurosci Rural Pract. 2017 Oct-Dec;8(4):551-555.
18. Soto-Ares G, Joyes B, Lemaître MP, *et al*. MRI in children with mental retardation. Pediatr Radiol. 2003 May;33(5):334-345.
19. Jussila MP, Olsén P, Niinimäki J, *et al*. Is Brain MRI Needed in Diagnostic Evaluation of Mild Intellectual Disability? Neuropediatrics. 2021 Feb;52(1):27-33.
20. Battaglia A, Doccini V, Bernardini L, *et al*. Confirmation of chromosomal microarray as a first-tier clinical diagnostic test for individuals with developmental delay, intellectual disability, autism spectrum disorders and dysmorphic features. Eur J Paediatr Neurol. 2013 Nov;17(6):589-599.

21. D'Arrigo S, Gavazzi F, Alfei E, *et al*.: The diagnostic yield of array comparative genomic hybridization is high regardless of severity of intellectual disability/developmental delay in children. J Child Neurol. 2016;31:691-699.
22. Tos T, Karaman A, Aksoy A, Tukun A. Structural chromosomal abnormalities in patients with mental retardation and/or multiple congenital anomalies: a new series of 24 patients. Genet Couns. 2012;23(2):289-296.
23. Iqbal Z, van Bokhoven H. Identifying genes responsible for intellectual disability in consanguineous families. Hum Hered. 2014;77(1-4):150-160.
doi: 10.1159/000360539. Epub 2014 Jul 29.
24. Hao D, Li Y, Chen L, Wang X, Wang M, Yu Y. Inherited unbalanced translocation (4p16.3p15.32 duplication/8p23.3p23.2deletion) in the four generation pedigree with intellectual disability/developmental delay. Mol Cytogenet. 2021 Jul 8;14(1):35.
25. Vickers RR, Gibson JS. A Review of the Genomic Analysis of Children Presenting with Developmental Delay/Intellectual Disability and Associated Dysmorphic Features. Cureus. 2019;11(1):e3873.
26. Iourov IY, Vorsanova SG, Kurinnaia OS. *et al*. Molecular karyotyping by array CGH in a Russian cohort of children with intellectual disability, autism, epilepsy and congenital anomalies. Mol Cytogenet, 2012, 5(46).
27. Gug C, Stoicanescu D, Mozos I, *et al*. De novo 8p21.3→ p23.3 Duplication With t(4;8)(q35;p21.3) Translocation Associated With Mental Retardation, Autism Spectrum Disorder, and Congenital Heart Defects: Case Report With Literature Review. Front Pediatr. 2020 Jul 8;8:375.
28. Zhu H, Wang A, Zhang H, Ji C, Zhan X. [Genotype and phenotype study of two patients with 22q11.2 deletion syndrome]. Zhonghua Yi Xue Yi Chuan Xue Za Zhi. 2014 Oct;31(5):623-627. Chinese.
29. Yao YY, Zhang CC, Bi H, Zhu F. Prenatal diagnosis of de novo isochromosome 4p with an unbalanced t(4;9) translocation in a fetus with congenital anomalies: A case report and literature review. Taiwan J Obstet Gynecol. 2022 Jan;61(1):157-162.

How to Cite This Article
Nasif BS, Shareef HR. Karyotype and molecular cytogenetic analysis among sample of Iraqi children with idiopathic intellectual disability. International Journal of Paediatrics and Geriatrics. 2024;7(1):13-19.