INTELECTUAL DISABILITY

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ABSTRACT

Intellectual Disability (ID) is a neuro-developmental disorder that results in incom-plete or (arrested) expansion of a brain. Depending upon the severity of the disease, ID could be moderate ID, severe ID, and most severe called profound ID. ID affects about two to three percent of overall population. It has been estimated that half of all cases with are due to environmental factors and the other half are due to genetic factors. ID cases may have intellectual disability only without other asso-ciated abnormalities, a condition called as Non-syndromic Intellectual Disability (NSID) or with other associated abnormalities, a condition called as Syndromic In-tellectual disability (SID). Autosomal recessive disorders are common in isolated populations, because of high rate of consanguinity. Recessive genetic disorders are common in Pakistan where consanguineous marriages are frequently ar-ranged because the cast system is deeply rooted. Understanding of molecular and genetic causes may allow for the decision making to prevent ID. Mutation screening of these genes is required which will lead to development of prena-tal diagnostic tests in Pakistan.

Key words: Intellectual Disability, Neuro-developmental disorder, Autosomal recessive

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INTRODUCTION

Intellectual disability (ID) can be defined as a disor-der that results in incomplete or (arrested) expansion of a brain. Its main characteristics are impaired abil-ities expressed throughout growing phases subsidizing whole stages of brainpower like cognition, speech, neu-ronal functions and societal skills. Symptoms will start showing before the age of 18[1,2]. ID disorder affecting about two to three percent of overall population. Sev-enty five to ninety percent of the affected population has mild ID. Non-syndromic ID or idiopathic ID disorders are counting for thirty to fifty percent of cases. And about one fourth of cases are produced by hereditary sicknesses[3]. According to 2013 genetic report ID cases of unknown origin affect about ninety five million indi-vidual's world widely[4]. ID is the most common neuro-de-velopmental disease of children, affecting overall 1-3% of the population[5]. Prevalence of ID among 3-9 year old children in developing countries including Pakistan has been reported to be 9/1000 and the prevalence rate of intellectual disability under the age of 10 years in Paki-stan is 36‰[6]. The distribution of ID cases in population, depending upon the severity of intellectual disability, is mild ID (about 85%), moderate ID (about 10%), severe ID (about 4%), and most severe called profound ID (about 2%)[7].

SYMPTOMS

Most of the signs and symptoms of ID patients are behavioral. Patients with ID can be learning, crawling, siting, or walking slower development than the normal children, or maybe they will learn to speak slowly as compared with normal children. Intellectually disabled patients may have all or some of the following charac-teristics[8]. They will have slow development of their oral language with the deficiency in memorizing capacity, and having problems in learning social rules of living. They face trouble with problematic matters resolving abilities and having postponements in the growth of adaptive performances such as their own care abilities. Peoples with ID disorder are more slowly in learning as compare with normal children.

TYPES

On divisional bases with associated abnormities, in-telligent disability can be divided into two groups. When ID is either the only isolated feature without other as-

sociated consistent handicaps, it is called non-syndrom-ic intellectual disability (NSID) or when combined with other physical and/or behavioral abnormalities referred to as syndromic intellectual disability[9].

CAUSES

Anything can affects with normal brain growth and ID can result. Nonetheless, a precise cause for ID can only be identified about one third of the cases. The well-known causes of ID are the Genetic circumstances. These contain abnormalities such as Down's syndrome, Fragile X syndrome. Some risk factors which are thought to cause intellectual disability include infections which are present at birth or occur after birth, many envi-ronmental factors, and some metabolic conditions such as hyperbilirubinemia, malnutrition and pre-eclampsia. Toxic conditions are also responsible for causing intel-lectual disability such as intrauterine exposure to alco-hol, cocaine, amphetamines and other drugs. Similarly head trauma before and after birth may cause ID. Like-wise other cases are unexplained which is the largest category for occurrences of intellectual disability[10]. In some cases problems may occur during child birth if a newborn baby is in condition of lake of oxygen or born tremendously untimely means the baby birth occurred before the normal period of time. Some infections such as meningitis, measles or whooping cough, can lead to ID disorder. Contacts to toxic materials for example lead, and severely to ignore someone or abuse may also cause ID. But in two-thirds of all peoples who having ID, the cause is not known[11,12]. It has been estimated that half of all cases with are due to environmental factors (toxins, infections, trauma or perinatal anoxia) and the other half are due to genetic factors (chromosomal, Mendelian genetic disorders). Its impact upon the in-dividual, family, community and nation as a whole can be immense. Majority of the cases are affected from an early age[13]. Recent evidence has recommended that ID may be triggered by the blockage of the inter cellular chemical mechanisms taking place inside human ner-vous system like formation and maturation of neuron, synaptic elasticity, synaptic channels cycling, and gene appearance, also regulation of genes profiling and some more processes of genes processing[14].

DIAGNOSIS

The presence of large family pedigrees with ARNSID can be important tool in genetic linkage analysis to find out causative genes and may thus be helpful in under-standing biology of ID.

For the diagnoses of ID disorder patient is measured intellectually disabled if there is shortfalls in both IQ level and adaptable performances[15].

On the bases of 5th edition of the "Diagnostic and Statistical Manual of Mental Disorders" (DSM-IV), there are three important points for the diagnoses of ID dis-order which are as insufficiencies in overall intellectual capabilities, noteworthy confines in one or more spaces of adaptable performance crosswise numerous surround-ings which has been clearly verified by the adaptable performance counting scale, that are communication, own help services, interpersonal characteristics, and in-dication that the boundaries became seeming in child-hood period or at the age of adolescence[16]. ID disorder is properly diagnosed by the evaluation of IQ level and adaptable performance. And with the third component of starting time of disease in childhood period is using to differentiate ID from other disorders for example de-mentia such as in patients of Alzheimer's disease or be-cause of brain traumatic injuries. For the first IQ testing scale was made by Stanford-Binet in English language, this test was applied in France on school children. Lewis Terman adapted Binet's examination and promoted it as a test quantifying "general intelligence." It was the first generally used intellectual quiz to account scores in "intelligence quotient" form ("mental age" divid-ed by chronological age, multiplied by 100)[17]. Now a days the IQ level is checking by scoring in "deviation IQ" form, with an activity level by a test examiner, two standard deviations less than the median score for the test-taker's age category demarcated as IQ 70. And this valve is the land mark for the diagnosis of ID disorder, this testing method is using for categorization of ID pa-tients. But now present diagnosis of ID is not established on IQ scores separately, but also take into attention a person's adaptable abilities level, the diagnosis of ID is not only decided by the IQ level but also by the count-ing of behavioral characteristics and as well as by the keen observation of the patient, clinical examinations, understanding and communication like skills which are necessary for daily life[18].

GENETIC BASIS

The majority of ID cases have intellectual disability only without other associated abnormalities, a condition called as non-syndromic Intellectual disability (NSID) which is one of the most serious neurodevelopmental disorders[19]. The genetic etiology of NSID has been found only in 10% of cases, with just 19 X-linked (XLID) and six autosomal genes till date[20]. XL ID has been extensively

studied previously, because of the high ratio in male as compare to female, however, it is likely that there are autosomal forms of ID because of heterogeneity are more common than X-linked ID, as only ~4% of genes reside on the X chromosome. The type of autosomal pattern of recessive heritage is counting that may involve in approximately one fourth of all persons with non-syndromic ID. In spite of this, less is known about the genetic ori-gin of non-syndromic autosomal-recessive ID (ARNSID). Thirty loci containing six identified genes were stated to be taking part in autosomal recessive non-syndromic ID (ARNSID)[21]. By using linkage analysis and homozygosi-ty mapping techniques in huge consanguineous families shadowed by re-sequencing of involved genes, which include PRSS12 known as Protease, Serine12 or called Neurotrypsin having MIM no 606709[22]. SCRBN known as Cereblon having MIM no 609262[23]. CC2D1A known as Coiled-coil with C2 group containing protein 1A having MIM no 610055[24]. GRIK2 known as Glutamate recep-tor, ionotropic, kainite 2 having MIM no 138244, TUSC3 known as Tumor suppressor candidate 3 having MIM no 601385, TRAPPC9 known as Trafficking protein particle complex subunit 9 having MIM no 611966[25]. But with the facilities of new techniques of generation sequencing known as exome sequencing method has developed the detection of speedily increasing in counting of AR-NSID contributing genes. According to new research up to date 32 novel genes causing AR-NSID disorder have been described by Najmabadi et al[26].

CONSANGUINITY IN PAKISTAN

Autosomal recessive disorders are common in isolated populations, because of high rate of consanguinity. The latest developments in the field of molecular biology and cytogenetic study has helped a lot in the identification of new genes in various genetic disorders especially autosomal recessive ID. Recessive genetic disorders are common in Pakistan where consanguineous marriages are frequently arranged because the cast system is deeply rooted[27].Countries having higher rate of consanguinity shows a significant burden of autoso-mal recessive disorders notably NS-ARID. The reported rate of consanguinity in Pakistan is 62.7%, out of which 84% marriages are between first cousins[28].

Understanding of molecular and genetic causes may allow for the decision making to prevent ID. Mutation screening of these genes will lead to development of prenatal diagnostic tests. The benefit to the community includes predictive testing and genetic counseling. Most of these studies in Pakistan have been conducted in the last decade. Although, a few genetic centers have been established in the recent past, however, few systematic and well planned surveys have been published so far.

REFERENCES

1. Organization WH. Geneva: World Health Organization; 1992. International Classification of Diseases, 10th Revision. 1994;1.
2. Leonard R, Alison L. Critical incident stress debriefing and its effects on coping strategies and anger in a sample of Australian police officers involved in shooting incidents. Work & Stress. 1999;13(2):144-61.
3. Hussain R, Bittles A. The prevalence and demographic characteristics of consanguineous marriages in Pakistan. Journal of biosocial science. 1998;30(02):261-75.
4. Global Burden of Disease Study 2013, Collaborators (5 June 2015). “Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013.”. Lancet (London, England).PMID 26063472.
5. Chelly J, Khelfaoui M, Francis F, Chérif B, Bienvenu T. Genetics and pathophysiology of mental retardation. Euro-pean Journal of Human Genetics. 2006;14(6):701-13.
6. Roeleveld N, Zielhuis GA. The prevalence of mental retardation: a critical review of recent literature. Developmental Medicine & Child Neurology. 1997;39(2):125-32.
7. Maulik PK, Harbour CK. Epidemiology of intellectual disability. International encyclopaedia of rehabilitation (online) Retrieved January. 2010;25:2012.
8. Daily DK, Ardinger HH, Holmes GE (February 2000).”Identification and evaluation of mental retardation”. Am Fam Physician 61 (4): 1059–67, 1070. PMID 10706158.
9. Siderius LE, Hamel BC, van Bokhoven H et al. (2000). “X-linked mental retardation associated with cleft lip/palate maps to Xp11.3-q21.3”. Am. J. Med. Genet. 85 (3): 216- 220. doi:10.1002/(SICI)1096-8628(19990730)85:3<216::AID-AJMG6>3.0.CO;2-X.PMID 10398231.
10. Laumonnier F, Holbert S, Ronce N et al. (2005). “Mutations in PHF8 are associated with X linked mental retardation

and cleft lip/cleft palate". J. Med. Genet. 42 (10): 780–

11. Wines, Michael (2006-12-28). "Malnutrition Is Cheating Its Survivors, and Africa's Future". The New York Times. Re-trieved 2009-07-21.

12. Sundaram SK, Sivaswamy L, Makki MI, Behen ME, Chugani H (2008). "Absence of arcuate fasciculus in children with global developmental delay of unknown etiology: a dif-fusion tensor imaging study". J Pediatr 152 (2): 250–5. doi:10.1016/j.jpeds.2007.06.037. PMID 18206698.

13. Leonard H, Wen X. The epidemiology of mental retarda-tion: challenges and opportunities in the new millenni-um. Mental retardation and developmental disabilities research reviews. 2002;8(3):117-34.

14. Zlotogora J. The molecular basis of autosomal recessive diseases among the Arabs and Druze in Israel. Human ge-netics. 2010;128(5):473-9.

15. Molinari F, Rio M, Meskenaite V, Encha-Razavi F, Augé J, Bacq D, et al. Truncating neurotrypsin mutation in autoso-mal recessive nonsyndromic mental retardation. Science. 2002;298(5599):1779-81.

16. Higgins JJ, Pucilowska J, Lombardi RQ, Rooney JP. A mutation in a novel ATP-dependent Lon protease gene in a kindred with mild mental retardation. Neurology. 2004;63(10):1927-31.

17. Basel-Vanagaite L, Attia R, Yahav M, Ferland RJ, Anteki L, Walsh CA, et al. The CC2D1A, a member of a new gene family with C2 domains, is involved in autosomal recessive non-syndromic mental retardation. Journal of medical ge-netics. 2006;43(3):203-10.

18. Laumonnier F, Holbert S, Ronce N, Faravelli F, Lenzner S, Schwartz C, et al. Mutations in PHF8 are associated with X linked mental retardation and cleft lip/cleft palate. Jour-nal of medical genetics. 2005;42(10):780-6.

19. Hamosh A, Scott AF, Amberger JS, Bocchini CA, McKusick VA. Online Mendelian Inheritance in Man (OMIM), a knowl-edgebase of human genes and genetic disorders. Nucleic acids research. 2005;33(suppl 1):D514-D7.

20. Barkovich AJ, Najmabadi H, Ayub M, Vincent JB. Asif Mir, Liana Kaufman, 2, 16 Abdul Noor, 2 Mahdi M. Motazacker, 3 Talal Jamil, Matloob Azam, 4 Kimia Kahrizi, 5 Muham-mad Arshad Rafiq, 2 Rosanna Weksberg, 6 Tanveer Nasr, 7, 8 Farooq Naeem, 9, 10 Andreas Tzschach, 3 Andreas W. Kuss, 3 Gisele E. Ishak, 11 Dan Doherty, 12 H. Hilg-er Ropers, 3. The American Journal of Human Genetics. 2009;85:909-15.

21. Najmabadi H, Hu H, Garshasbi M, Zemojtel T, Abedini SS, Chen W, et al. Deep sequencing reveals 50 novel genes for recessive cognitive disorders. Nature. 2011;478(7367).

22. Lawyer, Liz (2010-11-26). "Rosa's Law to remove stigma-tized language from law books". Ithaca, New York: The Ithaca Journal. Retrieved 2010-12-04. The resolution ... urges a change from the old term to "developmental dis-ability.

23. Cooney G, Jahoda A, Gumley A, Knott F (June 2006). "Young people with intellectual disabilities attending mainstream and segregated schooling: perceived stig-ma, social comparison and future aspirations". J Intel-lect Disabil Res 50 (Pt 6): 432–44.doi:10.1111/j.1365-2788.2006.00789.x. PMID 16672037.

24. Centers for Disease Control and Prevention (CDC) (Janu-ary 2004). "Economic costs associated with mental re-tardation, cerebral palsy, hearing loss, and vision impair-ment--United States, 2003". MMWR Morb. Mortal. Wkly. Rep. 53 (3): 57–9. PMID 14749614.

25. Krahn GL, Fox MH. (2013). "Health disparities of adults with intellectual disabilities: what do we know? What do we do?". Journal of Applied Research in Intellectual Dis-ability27 (5): 431–446. doi:10.1111/jar.12067.

26. Haider SI, Ansari Z, Vaughan L, Matters H, Emerson E. (2013). "Health and wellbeing of Victorian adults with intellectual disability compared to the general Victorian population".Research in Developmental Disabilities 34 (11): 4034–4042.doi:10.1016/j.ridd.2013.08.017. PMID 24036484.

27. Najmabadi H, Hu H, Garshasbi M, Zemojtel T, Abedini SS, Chen W, et al. Deep sequencing reveals 50 novel genes for recessive cognitive disorders. Nature. 2011;478(7367).

28. Hussain R, Bittles A. The prevalence and demographic characteristics of consanguineous marriages in Pakistan. Journal of biosocial science. 1998;30(02):261-75.