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Multidimensional speech and language investigation in Noonan Syndrome at a glance: Twin Study

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Abstract: *Noonan syndrome (NS) is a relatively common genetic condition characterized by physical features of short stature, congenital health problem, distinctive facial features, broad or webbed neck and other comorbid characteristics such as feeding, hearing loss, intellectual disability, eye conditions. Due to the syndrome's highly variable expressivity, many mildly affected individuals may go undiagnosed into adulthood or until they have more prominently affected features. Deficit in visual processing, memory, attention, motor functioning and executive functioning in Noonan syndrome can result in an impact on speech, language and cognition skills. The aim of the present study was to understand the physical features, co-morbid conditions and relate them with the existing speech, language, cognition characteristics. A pair of identical twins underwent informal and structured speech, language investigation. The results highlighted deficits in speech, language and cognitive skills in both the twins that eventually required multidisciplinary approach.*

Key Words: *Noonan syndrome, CELF, Dr. Speech.*

1. INTRODUCTION:

Noonan syndrome (NS) is a relatively common genetic condition characterized by physical features of short stature, congenital health problem, distinctive facial features, broad or webbed neck (both children and adults may have excess neck skin also called webbing) and other co-morbid characteristics such as feeding, hearing loss, eye conditions and intellectual disability (Zenker,2021 & Roberts,2022). In 1963, a paediatric cardiologist named Jacqueline Noonan described a series of patients with unusual faces and multiple malformations, including congenital heart disease which was later categorized as Noonan syndrome.Presently nine genes have been documented to underlie this disorder with normal karyotype and changing phenotype with age (Tartaglia, 2011).The most common genetic mutation is found in the protein tyrosine phosphatase non-receptor, type 11 genes (PTPN 11), which accounts for about half of all the cases (Krausz,2013). PTPN11 mutation accounts for 64.7% of cases with clinical features of Noonan syndrome in India (Narayanan, 2017).The incidence of Noonan Syndrome is estimated to be between 1:1000 and 1:2500 live births (Robert et al, 2013) and affects males and females equally (Sharma,2021).

Due to the syndrome's highly variable expressivity, many mildly affected individuals may go undiagnosed into adulthood or until they have more prominently affected features (Carcavilla et al., 2020). Approximately 25% of individuals with Noonan syndrome have intellectual deficit (Roelofs et al, 2016). The unusual facial features lead to structural defects in mouth due to which 72% of individuals with Noonan syndrome have speech articulatory errors, more than 50% of infants have feeding problems (Romano et al, 2010) and voice is reported to be characteristically hoarse or hyper-nasal (Tartaglia et. al, 2011). Cognitive skills in Noonan syndrome vary from high functioning to mild mental retardation (Noonan & Ehmke, 1963; Pierpont, 2015).Alfieri et al, (2011) reported deficit in visual processing, memory, language functioning, pragmatic, communication, attention, motor functioning and executive functioning in Noonan syndrome which can have a significant impact on speech, language and cognition skills.

Noonan syndrome is present with many medical and co-morbid factors, which are highly variable. The syndrome is one of the specific diagnostic categories of developmental disabilities, which affects communication skills. There are experimental researches and single case studies highlighting the speech and language characteristics in NS however, there is a scarcity of research present among twins of Noonan syndrome from a speech language pathologist perspective. Hence, there is a need to highlight the multidimensional speech and language investigation in Noonan syndrome.

2. MATERIAL :

The present study was carried out in two phases. The first phase included language investigation using informal and standardized tests of Linguistic Profile Test (LPT), Pragmatic Profile of Everyday Communication skills in children (Dewart and Summers) and Clinical Evaluation of Language Fundamentals, CELF-5 (Wig, Semel and Secord). Phase II included objective and subjective investigation of speech parameters. This included Paediatric Voice Handicapped Index (pVHI), GRBAS, Dr Speech, Photo Articulation Test in Hindi (PAT-H) speech intelligibility rating scale (AYJNIHH 7-point rating scale) and oral peripheral examination.

3. METHOD :

A pair of identical twins, Twin A and Twin B, aged 13 years came to the speech and language department with the complaint of deficit in communication and social interaction skills as per the peer group. Medical history revealed that Twin A and Twin B had a history of pre-mature birth and feeble birth cry. History of neonatal jaundice was reported in Twin A, whereas Twin B had a hypercalcaemic seizure at the age of 1.6 month. Parental perception revealed a delay in motor, social and cognitive developmental milestone in both the twins. Communication mode for Twin A was predominantly in simple sentences and occasionally in complex sentence whereas Twin B communicated only through simple sentences. Paediatric examination confirmed the clinical features of Noonan syndrome. Psychological test (VSMS, BKT) results indicated a mild impairment in socio-adaptive functioning and moderate impairment in intellectual functioning in both Twin A and Twin B. Both the twins were subjected to speech and language evaluations (Phase I and Phase II).

4. RESULTS :

The present study highlighted the multidimensional speech and language investigation in a pair of identical twins of Noonan Syndrome. Linguistic profile test revealed receptive language age of 5-6 years (receptive semantic and syntax score 73.4%) whereas expressive language age (expressive semantic and syntax score 70%) suggested age range of 4 - 5 years in Twin A. However, Twin B indicated receptive language age of 4 - 5years, (semantic and syntax score 73.4% in receptive language) and expressive language age of 3 - 4 years (expressive scores of semantic and syntax 70%). Twin A and Twin B had comprehensive deficit in semantic anomaly, homonymy, plurals, comparatives, and participial construction skills however; Twin B exhibited additional deficit in synonyms and clinical case marker. LPT results revealed low scores in both syntactic and semantic skills which indicated deficient language skills in both the subjects. The results of Clinical Evaluation of Language Fundamentals, (CELF-5) for Twin A and Twin B indicated a scoring of 75 and 71 respectively in core language score, receptive language index or expressive language index suggestive of moderate severity of language disorder. Both the twins demonstrated better language scores in the categories of semantic feature class, relative phrase, negation and sentence comprehension. However, understanding of spoken paragraph was less affected in Twin A rather than Twin B. Additionally Twin B had difficulty in compound structure skills.

Table 1:Pragmatic Profile scores of Twin A and Twin B

Sections	Twin-A	Twin-B
Section 1 – Rituals and conversational skill	63/72	58/72
Section-2 – Ask for, gives and responds to information	53/80	47/80
Section-3 – Nonverbal communication skills	44/48	42/48

The low scores obtained in Section 1 and 2 (Table 1) depicted that both the twins had difficulty in following rituals, conversational skills and understanding of humours and jokes. The result of section-3 (nonverbal communication skills) indicated better score as followed by Section -2(Ask for, gives and responds to information) and Section -1 (rituals and conversational skills).

The Pragmatics Profile of Everyday Communication Skills in Children consists of two structured interviews. The results of both twin A and twin B suggested that in "communicative function" they were insufficient to identify events/characters and had poor ability to narrate story/event. In "response to communication" both the twins comprehended all the indirect requests literally and replied yes/no appropriately but did not carry out or attempted to clarify the request. In "interaction and conversation" both the twins had a minimal participation and did not exhibit any conversational repair skills. "Contextual variation" was present in the twins and was observed when the situations and persons were different. In addition, the Twin-B showed poor metalinguistic awareness and ignorance to sarcasm. The overall findings of pragmatic test in the twins revealed deficits in pragmatic abilities.

The results of speech investigations were categorized in Phase II. Oral peripheral examination suggested of no facial asymmetry, however cupid like labial structure was observed in the twins. Lingual structural integrity was intact but the functional integrity was affected in Twin A and Twin B. Microganathia, Class II dis-occlusion with high arched palate was seen in both the subjects.

Perceptual scores of Paediatric Voice Handicapped Index (pVHI) revealed mild voice handicapness in Twin A and moderate voice handicapness in Twin B.

Table 2: Perceptual scores of GRBAS rating scale

Domain	Twin-A score	Impression	Twin-B score	Impression
Grade	**2**	Moderate	**3**	Severe
Roughness	**1**	Mild	**2**	Moderate
Breathiness	**1**	Mild	**2**	Moderate
Asthenic	**0**	Normal	**0**	Normal
Strained	**1**	Mild	**1**	Mild

The above Table 2 illustrated the total score and severity of GRBAS perceptual rating scale which supported the findings of pVHI. Twin-A had a mild hoarse voice quality whereas Twin-B had a moderate hoarse voice quality.

Acoustic analysis of voice was done using Dr Speech program and the findings revealed error score in jitter, shimmer; fundamental frequency and noise measures (Table 3) which suggested of mild hoarse voice quality in twin A and had moderate hoarse voice quality with predominantly breathy component in twin B. The results of the instrumental analysis (Dr Speech) were supported by the GRBAS perceptual rating scale (Table 2)

Table3: Acoustic analysis of voice

Parameters	**Twin A**	**Twin B**
Habitual F0(Hz)	234.46	194.61
Jitter%	0.24	0.83
Shimmer%	3.36	7.47
F0 Tremor(Hz)	6.00	10.20
Mean F0(Hz)	233.95	193.71
SD F0(Hz)	116	2.88
Max F0(Hz)	237.10	202.29
Min F0(Hz)	230.89	187.66
NNE (dB)	-13.81	-3.35
HNR (dB)	30.86	9.56
SNR (dB)	19.98	9.67
AMP Tremor (dB)	2.54	3.12

Photo Articulation Test in Hindi (PAT-H) results exhibited substitution errors in bilabial, dental, alveolar, palatal and velar sounds at all the position of word level and sentence level. Omission of blends were present in speech sample of both the twins however distortion errors were only noted in Twin B. Speech was intelligible with careful listening although some words were unintelligible. There was no nasal emission during continuous speech perceived in both the participants.

5. DISCUSSION:

The present twin study aimed to understand the physical features, co-morbid conditions and relate them with the existing speech, language characteristics. Noonan syndrome has a significant impact on the communication profile in individuals. NS exist with highly expressivity variables in genetics, clinical features along with co morbid conditions (Carcavilla et al., 2020). The profile of language skills in both the twins indicated deficits in language. The findings of the present study were in line to the study by Lazzaro.et. al, (2020) which also found a weakness in language profile and established a link to grammar production and non-verbal intelligence. Detailed speech and language investigation on pair of identical twins highlighted the deficient speech and language skills that eventually required a multidisciplinary approach. Recent researches explore genotype-phenotype correlations and also highlighted the cognitive and behavioural profile in NS. Speech and language profile in this disorder have received little attention, and this field remains a challenge with regard to the neuropsychological characterization of this disorder. Limitation of the current study is the limited sample size and therefore there is a need to get more precise data to assess significant difference in speech and language domain. Future directions of the study should focus on early identification and intervention program for the individuals with Noonan syndrome. Adequate awareness about the syndrome well planned strategies, and counselling of the parents will help in making a better prognosis and quality of life for individuals with the syndrome.

6. CONCLUSION:

Noonan syndrome is a genetic disorder that causes abnormal development of multiple parts of the body and developmental delay. As Noonan syndrome is a lifelong condition, the individuals with NS are differently affected and therefore their life expectancy depends on its severity. Detailed evaluation provides information about developmental domains which eventually helps in developing appropriate intervention strategies to enhance speech, language and cognitive skills in individuals with Noonan syndrome.

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