Retrospective study on the incidences of Williams-Beuren Microdeletion Syndrome

Pankaj Gadhia[1]* and Salil Vaniawala[1]

[1] Molecular Cytogenetic Laboratory, S. N. Gene Laboratory Private Limited, President Plaza A, Ring Road, Surat, Gujarat, India

Correspondence Author: Pankaj Gadhia

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Abstract

Objectives: To study the prevalence of Williams–Beuren syndrome (WBS) microdeletion among patients referred for genetic testing from January 2021 to August 2025.

Methods: Peripheral blood samples were processed and Interphase FISH was performed using a commercially available probe mapping to the elastin gene/7q11.23 regions. A total of 30 interphase nuclei were scored per sample; microdeletion was reported when the single orange signal with two green signals observed.

Results: A total of 26 samples were referred during the study period. Sex distribution was 13 (50%) males and 13 (50%) females. Among male referrals, 9 of 13 (69%) were confirmed to have the 7q11.23 microdeletions by FISH. Among female only 4 of 13 were positive.

Conclusion: In this retrospective study, a high proportion of male referrals were confirmed (9/13, 69%) positive, while the confirmation rate among females was 4/13, (31%). These results highlight that targeted FISH remains a useful diagnostic tool for suspected WBS.

Keywords: Retrospective, Williams Beuren syndrome, Microdeletion, Fish technique

Introduction

Williams-Beuren Syndrome (WBS) is rare multisystem disorder occurring in 1 per 7500-10000 live births [1]. Chromosomal microdeletion syndromes are a clinically important group of genetic diseases, where small part of a chromosome which contain group of genes are lost. They typically evident with congenital anomalies, intellectual disability, developmental delay, and behavioural variations. Of these, Williams-Beuren Syndrome (WBS), also called Williams syndrome is one of the better defined, both clinically and at the molecular level. WBS results from a heterozygous deletion of 1.5 to 1.8 Mb of chromosome 7q11.23, containing about 26 to 28 genes, one of which is the ELN (elastin) gene, responsible for cardiovascular and connective tissue integrity. Lack of ELN, hemizygous in origin, is responsible for the primary vascular manifestations, most notably supravalvular aortic stenosis (SVAS), characteristic. Clinically, WBS patients diagnose with facial gestalt, cardiovascular issues, intellectual disability, behavioural pattern of increased sociability, and early hypercalcemia. Growth retardation, endocrine and renal abnormalities, and hypersensitivity to sound are some of the frequent features [2]. WBS can be diagnosed on clinical presentation, but it requires a genetic confirmation. Methods like fluorescence in situ hybridization (FISH), and chromosomal microarray analysis (CMA) are all practiced. Generally, about 98–99% of patients with the clinical diagnosed for WBS have a deletion at 7q11.23, this genetic tests have very high diagnostic value.

There is very limited epidemiological information from India, primarily presented in terms of small-case-series or case reports. For instance, two cases were documented in a Western Indian study with the incidence estimate of 1 in 20,000 to 50,000 live births [3]. The results indicate that WBS are possibly under-diagnosed in Indian clinical practice, most probably because of fewer access to genetic testing and low clinician examination. Such an information gap creates the necessity for more extensive systematic research that will be able to determine true prevalence and diagnostic yield of WBS in various populations. Retrospective clinical and laboratory record reviews offer a simple method to increase the knowledge about the frequency of WBS, especially in resource-scarce or neglected regions.

This retrospective analysis was therefore conducted to extrapolate the Williams-Beuren microdeletion syndrome prevalence in a cohort of patients referred for genetic testing at a tertiary referral laboratory. By comparing report findings of genetic testing (FISH) and clinical information, we aim to determine the incidence of WBS in the population, define

referral patterns, and compare the findings with reported studies. These results are meant to guide clinical perception, maximize diagnostic procedures for WBS in India.

Materials and Methods

Blood samples were collected from clinically confirmed cases of Williams-Beuren Syndrome (WBS) after obtaining informed consent. Peripheral blood cultures were established, and fluorescence in situ hybridization (FISH) was performed on interphase cells using the LSI WS (Elastin gene) probe (Vysis, USA). Prepared slides were examined under a Zeiss fluorescence microscope, and the images were captured and processed for analysis.

Results

A retrospective study was carried out between January 2021 and August 2025 to determine the incidences of Williams–Beuren syndrome (WBS). During this period, a total of 26 samples were referred to our laboratory. Of these, 13 (50%) were males and 13 (50%) were females, representing different age groups (Table 1). Among the male cases, 9 (69%) were confirmed as WBS, whereas only 4 (31%) of the female cases tested positive for WBS. The remaining 9 cases were negative. Figure 1a: Interphase FISH analysis showing two green signals and two orange signals, indicating the absence of microdeletion. While Figure 1b: FISH displaying two green signals corresponding to chromosome 7 and a single orange signal, consistent with a microdeletion in the elastin gene.

Table 1: Sex and age wise distribution of Williams-Beuren Syndrome (WBS)

No.	Sex	Age ranges	Total cases (%)	FISH + ve (%)	FISH – ve (%)
1	Male	5 months to 15 years	13 (50)	09 (69)	04(31)
2	Female	2 months to 11 years	13 (50)	04 (31)	09 (69)
Total			26	13	13

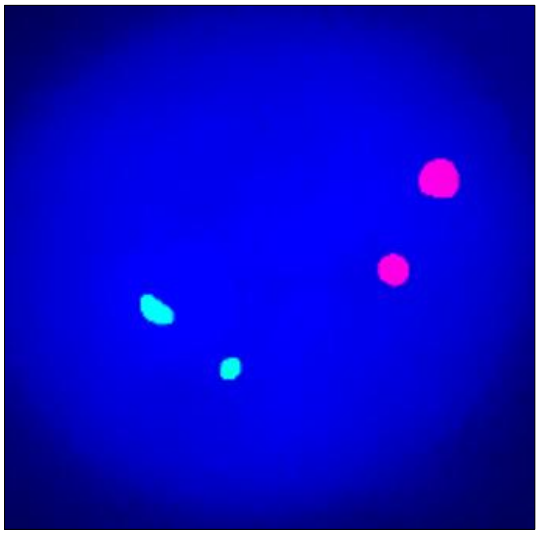

Fig 1(a): Interphase FISH highlighting the two green and two orange spots indicating no microdeletion

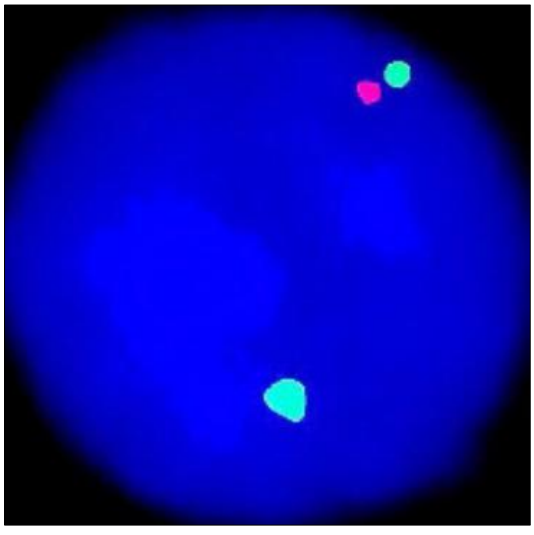

Fig 1(b): Presence of both chromosome 7 (green) copies and a single orange spot indicating microdeletion of elastin gene

Discussion

Williams-Beuren syndrome (WBS) is a rare genetic disorder (1 in 7,500 – 20,000) characterised by a microdeletion at 7q11.23 with about 28 genes including elastin gene. Our objective was to study the role of genetics in diagnosis of WBS. In this current retrospective effort from January 2021 to August 2025, we examined 26 clinically suspected Williams–Beuren syndrome (WBS) cases referred to our laboratory. Microdeletion of the 7q11.23 was established in a high percentage of cases by cytogenetic and molecular investigation, thus confirming the diagnostic value of fluorescence in situ hybridization (FISH). Our results are significant with reference to incidences of WBS in the population referred to and the clinical insight of genetic diagnosis in suspected cases.

The case distribution gave the overall representation of the two sexes, which is consistent with the commonly accepted hypothesis that WBS is non-sex-biased. In positive cases, detection was greater in males than in females. The same gender-neutral occurrence has been found in earlier research, although minor discrepancy in rate of detection has been noted sometimes based on the population being examined [4-5]. Such discrepancies might be due to the referring practice, clinical know-how, or inadequate numbers of samples.

Compared to other studies in the field and abroad, our rate of prevalence among referred samples compares to international rates in reports where WBS incidence has been reported as approximately 1 in 7,500 to 1 in 20,000 live births[6]. Our study needs to be referenced not as a population prevalence estimate since research was limited to a clinically suspected population that was referred for cytogenetics. But our case illustrates the merit of specific genetic testing in children who present with typical facial characteristics, cardiovascular malformation, developmental delay, and behavioural profiles consistent with WBS.

Early diagnosis of WBS is useful to clinicians due to its correlation with a spectrum of congenital and developmental comorbidities. Supravalvular aortic stenosis (SVAS) and other cardiovascular malformations are among the most severe of the medical complications and require early monitoring and surgeries [7-8]. In addition, individuals with WBS typically present with certain neurocognitive and behavioural phenotypes such as robust verbal skill within intellectual disability, hyper sociability, and increased anxiety. Identification of these characteristics and, using molecular cytogenetics, confirmation of diagnosis not only facilitates proper clinical management but also gives families genetic counselling and long-term planning.

Some of the pitfalls in the diagnostic process for WBS are also emphasized by our studies. The condition tends to be misdiagnosed or underdiagnosed because there is variable expressivity of phenotypic characteristics. There is minimal cause for concern when in infancy slight expressions occur such as feeding problems or failure to thrive. In addition, where molecular diagnostic laboratories are not readily accessible, WBS can go undetected. These factors might explain the relatively low number of referred cases within our population since the investigation was carried out over a period of more than four years.

Conclusion

In this study adds to the expanding literature on the incidences of WBS and highlights the important of cytogenetic testing in establishing a diagnosis. Despite the limitations of our results with regard to sample size and referral basis, they reinforce the necessity of increasing diagnostic facilities and sensitizing clinicians in settings where resources are not readily available. Detection and intervention at an early stage remain the cornerstone of a fulfilling life and long-term outcomes for individuals with Williams–Beuren syndrome.

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