



Original Research Article

Profile of Friedreich's ataxia in a tertiary neurology institute: a study from eastern India

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ABSTRACT

Introduction: Friedreich Ataxia (FA) is an autosomal recessive inherited form of ataxia. Clinical presentation includes cerebellar and sensory ataxia, associated with pyramidal signs, an absence of tendon reflexes in the legs, deep sensory loss, and foot deformity.

Aims and Scope: To know the hospital-based incidence, epidemiological profile of FA. To know the commonest mode of presentation. To watch for the complications. To observe its radiological features along with electrophysiological properties.

Settings and Design: Prospective clinical study in the department of neurology of S.C.B Medical College, Cuttack, Odisha, India. The study was done for 2 complete years.

Material and Methods: All patients who presented with clinical symptoms of FA with positive for allelic mutation were included in the study. The patients were evaluated in detail by neuroimaging and other tests. Brain and spinal cord MRI were done in all the patients followed by nerve conduction. Ethical approval was obtained from institutional ethical committee.

Statistical analysis used: SPSS version 21.0

Results: Total numbers of patients were 12. Male to female ratio was 2:1. Most common presentation was unsteadiness of gait and other cerebellar signs. 25% patients (3/12) had ejection fraction reduced. Optic nerve atrophy was found in approximately 25% of individuals. Atrophy of the cervical spinal cord and cerebellum were observed in 58% (7/12) cases in MRI.

Conclusions: FA is one of the commonest recessive ataxias of young people. It presents progressive ataxia and large fibre neuropathy with multisystem involvement. Usually it has very bad prognosis with cardiac complications.

Key Messages: FA is one of the common cause of genetic ataxia. It is a multisystem disease with involvement of both central nervous system and peripheral nervous system. The knowledge of FA is necessary for early diagnosis and genetic counselling.

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1. Introduction

Friedreich ataxia (FRDA) is an autosomal recessive inherited form of ataxia. Clinical presentation includes cerebellar and sensory ataxia, associated with pyramidal signs, an absence of tendon reflexes in the legs, deep sensory loss, and foot deformity. Approximately two thirds of individuals with FRDA have cardiomyopathy, up to 30% have diabetes mellitus, and approximately 25%

have an "atypical" presentation with later onset or retained tendon reflexes.¹ The prevalence of FRDA is 2:100,000-4:100,000. The carrier frequency is 1:60-1:1001. Typical Friedreich ataxia is observed in about 75% of affected individuals and atypical presentations are observed in about 25%. Individuals with typical Friedreich ataxia (FRDA) develop progressive ataxia with onset from early childhood through to early adulthood, starting with poor balance when walking, followed by slurred speech and upper limb ataxia.² FA is a slowly progressive disorder. Usually, the onset of symptoms is during adolescence (mean 15.5 years, SD 8

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years).³ Patients usually become wheelchair bound after a mean disease duration of 11–15 years (range 3 to 44 years).⁴

The core syndrome is an early onset, slowly progressive ataxia associated with areflexia. Ataxia is due to involvement of peripheral sensory nerves as well as spinal degeneration along with cerebellar and sometimes also vestibular dysfunction. Patients develop appendicular and truncal ataxia. Dysarthria is present in 70%.⁵ Loss of deep tendon reflexes due to degeneration of dorsal root ganglia along with peripheral neuropathy is an early and definitive feature of FA. Plantar responses are extensor in 70 to 90%. Muscular weakness and wasting more seen in the lower limbs - can complicate advanced. Proprioceptive deficits with abnormal position and vibration sense are present in all FA subjects. Nerve conduction studies reveal signs of an axonal sensory neuropathy with reduced or absent nerve action potentials typically first present in the sural nerve. Cortical potentials of somatosensory evoked potentials are delayed or absent.⁶ Cardiac involvement mainly affects young patients below the age of 40 years.⁷ The prevalence for diabetes among FA patients varies between 8 to 49% depending on the definition of diabetes. Scoliosis is considered typical for FA. Its prevalence varies between 33 and 100% depending on the individual study.³ Foot deformities (pes cavus, club foot, pes planus) significantly interfere with mobility in 55 to 90% of patients.⁴ MRI usually shows spinal cord atrophy. Cerebellar shrinkage is less common. Volume loss of the medulla oblongata and cortical atrophy may be seen in advanced cases.

The objectives of this study were to know the hospital-based incidence, epidemiological profile of FA. To know the commonest mode of presentation. To watch for the complications. To observe its radiological features along with electrophysiological properties.

2. Materials and Methods

Prospective clinical study in the department of neurology of S.C.B Medical College, Cuttack, Odisha, India. The study was done for 2 complete years. All patients who presented with clinical symptoms of FA with positive for allelic mutation (strongly positive >66 GAA Repeats- PCR amplification), were included in the study. All the history of presentation and epidemiological parameters were tabulated in a pre-structured format. The patients were evaluated in detail by neuroimaging and other tests. Brain and spinal cord MRI were done in all the patients. The MRI Scanner was 1.5 T in strength and reporting was done by experienced radiologists. Nerve conduction studies were done and was analysed. Statistical analysis was done by SPSS version 21.0. Ethical approval was obtained from institutional ethical committee.

3. Results

1. Total numbers of patients n=12
2. Male: female – 2:1
3. All were positive with high numbers of GAA triplet repeat (>66 alleles).
4. Mean age of presentation was 12.5 years.
5. Most common presentation was unsteadiness of gait and other cerebellar signs, seen in all patients.
6. Scoliosis was present in 58% (7/12) cases. Pes Cavus was found in all the patients.
7. Sensory abnormality was seen in nerve conduction velocity test in all patients.
8. 25% patients (3/12) had ejection fraction reduced.
9. Electrocardiography (ECG) is abnormal in 58% (7/12) cases, with T wave inversion, left axis deviation, most common anomaly.
10. Optic nerve atrophy found in approximately 25% of individuals with reduced visual acuity was found in 17% patients.
11. Decreased cognitive skills in form of attention deficit was seen in 17% (2/12) cases.

Atrophy of the cervical spinal cord and cerebellum were observed in 58% (7/12) cases in MRI. In rest of the cases MRI was normal. (table-1)

Table 1: (observation variations)

Characteristics	
Total numbers of patients	12
Male: female	2:1
Mean age	12.5
Most common presentation	Gait abnormality and cerebellar signs
Cardiological complication (diminished ejection fraction)	3/1
Optic nerve involvement	4/12
Cognitive decline	2/12
Cerebellar atrophy in MRI	7/12

4. Discussion

FA is a very rare disease. The prevalence of FRDA is 2:100,000-4:100,000. The carrier frequency is 1:60-1:100. In present study total numbers of population, diagnosed as FA were.⁸ All the patients were having high numbers of GAA repeat. In an Indian study cohort with expansion at the FRDA locus found in 6% indicating that the prevalence of this disease in the Indian population is likely to be low. We also coincide in the fact.^{3,9} One study reveals the importance of GAA expansion. Larger GAA expansions correlated with earlier age at onset and shorter times to loss of ambulation. The size of the GAA expansions was associated with the frequency of cardiomyopathy and loss of reflexes in the upper limbs. Gait abnormality and ataxia was

the most common presentation. In every previous literature reveal similar picture. Rare cases present later age group. In approximately 15% of individuals with FA, onset is later than age 25 years. In individuals with LOFA (late onset FA), the age of onset is 26–39 years; and, in VLOFA (very late onset FA), onset is after age 40 years. In our study only one patient was diagnosed in 3rd decade. Scoliosis is considered typical for FA. Its prevalence varies between 33 and 100% in several studies.^{3,4} In the present study 58% had scoliosis. It's similar to various previous studies. Nerve conduction studies reveal signs of an axonal sensory neuropathy with reduced or absent nerve action potentials typically first present in the sural nerve. In the present study similar results were obtained.¹⁰ According to some studies 20% of patients have an abnormal ejection fraction decreasing with age.^{10,11} In our study its slightly higher. It can be explained by delayed presentation to hospital. Vision is impaired in about one fifth of patients with optic atrophy in about one third. FA can cause complete blindness in late stages.¹² In present study 25% patients were suffering from optic nerve atrophy. Spinal atrophy is most common presentation. Cerebellar shrinkage is less common. Volume loss of the medulla oblongata may be seen in later condition.^{8,13,14} Similar trend was observed in our cohort.

5. Conclusion

FA is one of the commonest recessive ataxias of young people. It presents progressive ataxia and large fibre neuropathy with multisystem involvement. Usually it has very bad prognosis with cardiac complications. Cardiomyopathy is most lethal complication. The longer the triplet sequence, the more lethal complications are. Detailed epidemiological study is not available in south eastern Asia. Genetic studies are needed in south eastern Asia to analyse the pattern of disease and its geographical variation from western countries.

6. Conflict of interest

None

7. Source of funding

None

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