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ORIGINAL ARTICLE

# Subacute Sclerosing Panencephalitis: Clinical and Demographic Characteristics

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## ABSTRACT

**Objective:** To determine the clinical and demographic characteristics of children diagnosed with Subacute sclerosing panencephalitis (SSPE).

**Study Design:** Case series.

**Place and Duration of Study:** The Aga Khan University Hospital, Karachi, from January 2000 to June 2012.

**Methodology:** A retrospective analysis was done, regarding medical charts of 43 children under the age of 16 years with a discharge diagnosis of SSPE. Demographic and clinical characteristics were recorded. Results were expressed as percentages.

**Results:** Most of the 43 patients were male (72%). The average age at presentation was 8.7 years with average duration of symptoms being 100.6 days. History of measles was present in 17 patients (39.5%). All children had seizures at presentation and 65% had cognitive impairment. Most patients required poly therapy for control of seizures. Sodium valproate was the most commonly used anti-epileptic agent; Isoprinosine was tried in 22 (51%) patients. CSF for anti-measles antibodies was positive in approximately 86% of the 40 (93%) children. EEG showed burst suppression pattern in 36 (83.7%) cases. Forty-two patients (97.6%) were discharged home in a vegetative state.

**Conclusion:** SSPE is progressive neurodegenerative disorder. It can be prevented by timely immunization against measles. Measles antibody in the CSF is diagnostic for SSPE and is helpful in early diagnosis. Most patients experience a gradual but progressive decline in motor and cognitive functions.

**Key Words:** *Subacute sclerosing panencephalitis. Children. Seizures. Measles antibody. Motor and cognitive function decline.*

## INTRODUCTION

Sub-acute sclerosing panencephalitis (SSPE) is a progressive, grey matter neurodegenerative disorder caused by a mutant measles virus.[1] It is a potentially preventable illness provided a proper measles immunization schedule is followed. The worldwide prevalence is < 1 to 20/million population,[2] however, figures are substantially higher in the developing countries owing predominantly to inadequate vaccination coverage.[3,4]

SSPE usually presents few years after the natural measles infection with seizures and behavior changes as the initial presentation of the disease. However, over the years, measles virus has undergone modification resulting in variable severity of presentation; vision loss has been reported as the initial symptom in the patient population by Dyken.[5] SSPE causes a slow, progressive decline in cognitive function but, fulminant course is not uncommon.[1,4,6,7] Treatment of SSPE is mainly supportive and usually lifelong. Specific therapy with immune modulators has been tried but is still controversial.

Atypical presentation may be seen and can be a challenge to diagnosis. In a developing country like Pakistan, it is important to understand and comprehend the clinical presentation and course of the disease, so that effective preventive strategies can be planned. Hence, an observational analysis of SSPE cases was carried out to get an insight at the disease in the population so that relevant data could be collected and utilized in formulating national guidelines and/or treatment plans to combat this lethal disease.

The objective of the study was to determine the clinical and demographic characteristics of children diagnosed with subacute sclerosing panencephalitis (SSPE).

## METHODOLOGY

Children under 16 years of age discharged from pediatric unit of AKUH with a diagnosis of SSPE from January 2000 to June 2012 were included in the study. Any patient who did not fulfill the diagnostic criteria of SSPE was excluded from study.

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The study was approved by the Ethical Review Committee (ERC) of the Aga Khan University Hospital (ERC Number 2038-Ped-ERC-11). This was a retrospective chart review. Data on 43 children under 16 years of age diagnosed with SSPE admitted in the Pediatric Neurology ward of Aga Khan University Hospital (AKUH) was retrieved using ICD 10 discharge codes. Medical charts of all children were reviewed for demographics, related biochemistry and clinical variables, therapeutic and diagnostic interventions, and outcomes at discharge. SSPE case was defined as any patient who had typical clinical, radiographic and electroencephalographic (EEG) findings suggestive of SSPE along with anti-measles antibodies and/or oligoclonal bands in cerebrospinal fluid (CSF).[8] Data was analyzed using Statistical Package for Social Sciences (SPSS) version 20 and results were expressed as percentages.

## RESULTS

A total of 52 charts were reviewed, but only 43 patients fulfilled the inclusion criteria. There was a male predominance (n=31) as compared to females (n=12). Mean age at presentation was 8.7 years with a range of 1.8 - 14 years. Average duration of symptoms was 100.6 days. Minimum duration of symptoms was one week; maximum duration being 2 years. Thirteen children (30.2%) were vaccinated against measles and 19 (44.2%) were unimmunized.

Vaccination status for 11 (25.6%) children was not known. Seventeen (39.5%) patients had a past history of measles whereas there was no history of measles in 14 (32.6%) children. Past history of measles was not known in 12 (27.9%) patients (Figure 1). Regarding clinical presentation, seizures were present in all children diagnosed with SSPE. Myoclonic seizures were the most common seizures observed. They were seen in 32 (74.4%) patients. Nine (21%) children presented with generalized tonic clonic and 2 (4.6%) with generalized tonic seizures. Two (4.7%) patients presented with a history of frequent falls. Behavior changes were reported in 23 (53.5%) children at presentation. Twenty patients (46.5%) exhibited extrapyramidal symptoms including

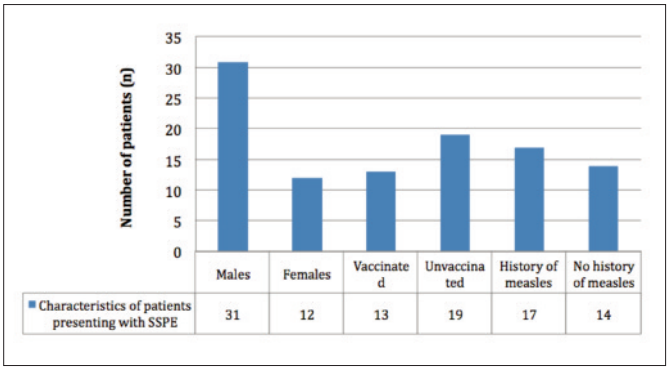


**Figure 1:** Characteristics of patients diagnosed with SSPE at the Pediatric Unit of the Aga Khan University Hospital between 2000-2012.

dystonia and choreoathetosis. As the disease progressed, 23 (53.5%) of these patients developed cognitive and motor impairment as well.

All children underwent an eye examination. Only one child had optic atrophy. Sodium valproate was the most common anti-epileptic used. It was used in 37 (86%) of these patients in combination with other antiepileptic agents. Patients showed better response with poly-therapy, a maximum of four agents was used at a time.

Isoprinosine, a specific immune modulator, was used in 22 (51.1%) patients; Isoprinosine with interferon beta was tried in 2 (4.7%) patients. Nineteen (44.2%) patients did not receive any specific medication for SSPE. Mean hospital stay for our children was 7.25 days. A lumbar puncture was done in 40 (93%) patients. CSF was positive for anti-measles antibodies in 37 (86%) patients; oligoclonal bands alone were positive in 3 (7%) patients; oligoclonal bands and anti-measles antibodies were positive in 9 (20.9%) patients. EEG was done in all patients. It showed burst suppression characteristic of SSPE in 36 (83.7%) cases. Four (9.3%) patients showed multifocal spike and wave discharges whereas EEG in 3 (7%) children demonstrated diffuse encephalopathy.

Neuroimaging (MRI brain with contrast) was done in 23 (76.7%) patients. Five (21.7%) scans were suggestive of frontal lobe changes; other MRI findings included cerebral atrophy in 1 (4.3%) patient, white matter and basal ganglia change in 2 (8.7%) patients.

MRI was normal in 15 (65.3) patients. Imaging was not possible in the remaining 20 patients due to financial constraints. All patients were discharged from the ward. Forty two (97.7%) were in vegetative state and 1 (2.3%) was in a state of deep coma.

## DISCUSSION

This data revealed a male predilection which is in accordance with the previous reports on SSPE.[9,10] Mean age at presentation was 8.7 years. SSPE was seen at a younger age in these children as compared to what has been reported in the literature previously.[11] Few studies have published an older age at presentation of 9 - 11 years.[12] Kondo *et al*. reported an elevated occurrence of SSPE in Karachi children and attributed it to measles infection in early age.[3] Seven (41%) patients had measles in early infancy affirming the same trend.
The duration of symptoms observed in this study population was also variable; 7 days being the shortest period of illness reported before diagnosis demonstrating the fulminant course of the disease. However, majority of these patients had an average course of illness of 100.6 days. Bojinova *et al*. have observed similar variation regarding duration of symptoms.[11]

Vaccine is the most important tool in the prevention of this disorder. The trends in SSPE incidence correlate with the improved immunization coverage across the

globe.[13] The current higher trends observed locally reflect the pitfalls in the measles immunization coverage at the national level. Tariq *et al*. have discussed the Pakistan perspective of sub acute sclerosing panencephalitis and commented on the lack of commitment to universal immunization observed nationwide.[14]

It is usual but not mandatory to have a past measles infection, as patients can have subclinical measles or poor host response to measles infection resulting in subtle manifestations. Literature review supports a past history of measles in only 50% of cases diagnosed with SSPE.[15,16] There was no clear history of measles in 28% children.

Regarding the clinical course, it is not uncommon to have cognitive decline or behavior changes before the onset of seizures. Interestingly, patients in this study had overlapping symptoms; many had cognitive/behavioral changes with seizures at presentation. Dyken has also observed similar trends in his study group.[5] Malik *et al*. have reported cognitive and behavioral impairment in children aged 2-16 years presenting with SSPE.[23]

Myoclonic seizures (74.4%) are the most common seizures seen in SSPE, which were also the most common seizure type seen in our patient group. Akram *et al*. have also reported myoclonic seizures as the most frequently observed seizures in children presenting with SSPE, followed by generalized tonic clonic seizures affecting 16% of children in their study group.[17]

Generalized tonic and generalized tonic clonic seizures have also been observed and documented by Milewska *et al*.[18] The late onset symptoms like choreoathetosis; hypertonia, were seen in these patients. These have been supported by certain studies in literature.[11] Eye changes have been reported in literature. Only one child in this study had optic atrophy.[19]

SSPE patients are resistant to anti-epileptic agents for control of seizures, as are most patients with neurodegenerative diseases. Generally symptomatic control is achieved by poly-therapy. Among these patients, a minimum of 1 and maximum of 4 agents were used. Sodium valproate was the most commonly used drug (86%). Leviteracetam was used in one case (4.7%).

The role of sodium valproate for the control of myoclonic seizures is well established.[20] Although specific therapy is not strongly recommended, some schools of thought support the use of Isoprinosine early in the course of illness.[21] The combined use of Isoprinosine and interferon has shown clinical improvement and prolonged survival in some patients, though these agents need to be continued even after apparent remission.

Raised CSF measles antibody titers are considered diagnostic for subacute sclerosing panencephalitis.[22] In this study, approximately 86% of the children tested positive for anti-measles antibody in the CSF. Approximately 84% children showed burst suppression pattern of SSPE. Malik *et al*. have reported that 6.2% Pakistani children presenting for a first EEG have a burst suppression pattern suggestive of SSPE. Correlation of clinical findings and a past history of measles infection with the abnormal EEG warrants measles antibody testing in such children in order to arrive at a definitive diagnosis.[23] Akram *et al*. described 50 patients with SSPE who were diagnosed on the basis of EEG and CSF findings.[17]

MRI brain with contrast is another imaging modality that is being used towards diagnosing SSPE, though neuro-imaging is not diagnostic. It was done in 23 of these patients. Abnormal scans suggestive of SSPE were reported in 8 patients. Remaining MRIs were normal. MRI findings are slow to evolve and MRI brain can be usually normal in SSPE if done early in the course of disease.[24] This is in accordance with the normal MRI observed in majority of these patients. On the contrary, Kumar and colleagues from India have reported cerebral atrophy and white matter changes in most of the MRIs done in children diagnosed with SSPE.[25] This difference could be in part due to the clinical stage of the SSPE during which an MRI was done. MRI done during stages 3 and 4 are more likely to be abnormal as MRI changes depend significantly on the duration of the disease.[7]

All 43 patients were discharged alive from the hospital. Forty two (97.7%) children were in vegetative state which is in accordance with the natural disease course of SSPE that establishes SSPE as a disease of morbidity and not immediate mortality.

## CONCLUSION

In this study, patients with SSPE has measles with presence of anti-measles anti-bodies in CSF is more sensitive for diagnosing SSPE than typical EEG and MRI findings. Multiple anti-epileptics were generally required for control of symptoms in these patients, however, seizures became refractory to anti-epileptic treatment as the disease progresses. Most patients go through a phase of progressive disability before succumbing to this fatal neurodegenerative disorder. Considering the rising number of SSPE patients, the need for global immunization could not be stressed more. Routine, timely and large scale measles vaccination remains the key for eliminating this lethal disease.

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