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Continued persistence of increased Subacute Sclerosing Pan Encephalitis cases in India, 2010-2012

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ABSTRACT

AIMS & OBJECTIVES: **Sub-acute sclerosing pan-encephalitis (SSPE) is a neurological disorder caused due to persisting mutated measles virus. It involves loss of cerebral function, paralysis, dementia and deterioration of motor functions. There has been lack of reports on SSPE from India. Thus, the present study is an attempt to know the epidemiology of SSPE in measles patients from India.**

MATERIALS & METHODS: **360 serum-cerebrospinal fluid(CSF) pairs received from patients clinically suspected of SSPE, were referred to National Centre for Disease Control(NCDC) from Delhi, Haryana and Uttar Pradesh and were tested for the presence of Immunoglobulin G (IgG) antibodies against measles, between January 2010 – April 2012. Demographic details were analysed using Microsoft Excel and Epi Info 7.0.9.34 software.**

RESULTS: **Out of 360 serum-CSF pairs, 226 (i.e. 62.78%) gave positive results for IgG antibody against measles. The sex ratio of female v/s male was 1: 2.73 (2010), 1: 3.77 (2011) and 1: 3.83 (2012). The age of onset of SSPE was between 0-12 years, comprising 65.48%. The next predominant age group was 13-24 years comprising of 31.41%, followed by the age group, 25-37 years. Majority of the positive samples were obtained from All India Institute of Medical Sciences (AIIMS), Delhi (56/226-24.77%) and the maximum cases as well as the maximum positives were obtained during October- January.**

CONCLUSION: **The risk of acquiring SSPE is mainly in the age group of 0-12 years. A gap in the measles vaccine is evident from the data and needs to be filled up. We also need to look into the measles vaccine regimen of our country and see what best suits, in order to minimize the SSPE squeal.**

Keywords: Measles, Subacute Sclerosing Panencephalitis (SSPE)

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INTRODUCTION

Sub-acute sclerosing pan-encephalitis (SSPE), is a rare, chronic progressive encephalitis that affects primarily children and young adults, caused by a persistent infection of immune resistant measles virus (which can be a result of a mutation of the virus itself).The disorder is characterized by loss of cerebral function, paralysis, dementia and deterioration of cerebral and motor function. It occurs during childhood and early adolescence. [1] The frequency of SSPE is about 7 cases for each one million cases of natural measles. In Turkey, annual incidence rate was 1.65/million young population and 0.87/million total population between 1975 & 1987.[2] From 1989 through 1991, a resurgence of measles occurred in the United States with 6.5-11 cases of SSPE/100,000 reported cases of measles.[3]The disease is rare in developed countries,

attributed to widespread immunization with measles vaccine which reduced the number of cases to a great extent.[4] In developing countries like India, the annual incidence of SSPE was calculated to be 2.14 cases/million population or 4.3 cases/million children below 20 years, which is mainly due to the problem of malnutrition and deficiency of Vitamin A. [5]

Measles is an acute highly infectious disease of childhood caused by a specific virus of family Paramyxoviridiae, genus *Morbillivirus*. Complications with measles range from mild and less serious diarrhoea to pneumonia, otitis media, corneal ulceration and rarely a long term persistent infection, SSPE. The mutations in the measles virus that result in SSPE, are known to affect the genes namely matrix (M), hemagglutinin (HA), nucleocapsid (N) and fusion, with the matrix gene reporting most of the mutations.

The mortality of measles varies greatly in different parts of the world. It is 100 to 400 times more likely to cause death in a preschool child of a developing country than it is in the US and Europe. In developing countries, case fatality rates range from 2 to 15 percent as compared to less than 0.2 per 10,000 notified cases in developed countries. Before the vaccine became available in the 1960s, measles killed between 7 and 8 million children a year and caused an estimated 135 million cases a year worldwide. Today, it still kills about 1 million children of the estimated 30 million who get measles. Thus measles is still a leading killer among vaccine-preventable diseases of childhood, taking its toll mainly among malnourished children whose natural defences have been weakened by other infections, and who live in crowded urban localities.

The main cause for such high number of cases is insufficient vaccine coverage in these areas (6).

There has been lack of reports on SSPE from India. Thus, the present study is an attempt to look into the prevalence of SSPE in measles patients from India.

MATERIALS & METHODS

Sample Collection

A total of 360 serum-CSF pairs received from patients clinically suspected of SSPE were referred to the Virology Laboratory of National Centre for Disease Control (NCDC) from different hospitals of Delhi, Haryana and Uttar Pradesh, between January 2010 to April 2012; for the purpose of IgG antibody detection against measles.

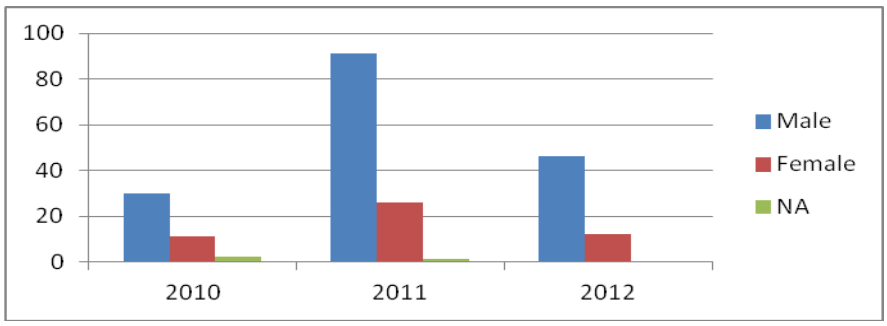
Detection through ELISA Detection of IgG antibodies against measles in serum and CSF was carried out using commercial kit by the manufacturer's protocol.

Data Analysis

Data was analysed using the Epi Info Version 7.0.9.34 software and Microsoft Excel.

RESULTS

Data was analysed from samples obtained from January 2010 to April 2012.Out of 360 serum-CSF pairs referred to NCDC, 226 (i.e. 62.78%) were positive for IgG antibody against measles. In terms of the number of males and females that were affected there were 98 males and 26 females in 2010, 30 males and 11 females in 2011 and 46 males and 12 females in 2012. The sex ratio of male v/s female was 2.73:1 (2010), 3.77:1 (2011) and 3.83:1 (2012), Fig 1.



[NA (3) refers to the individuals whose data was not available to NCDC]

Figure 1. Bar chart showing the number of males and females positive for SSPE in the study

The age group that mainly represented the SSPE positive patients was 0-12 years, comprising 65.48%. The next predominant age group was 13-24 years, 31.41%, followed by the age group 25-37 years (2.21%), Fig 2.

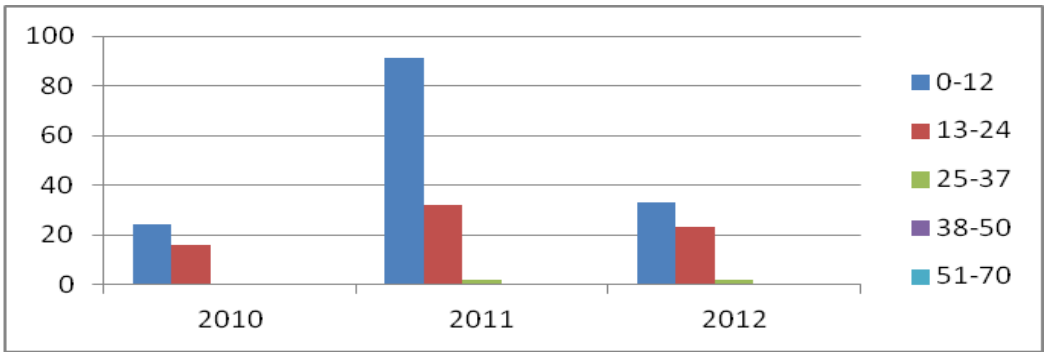
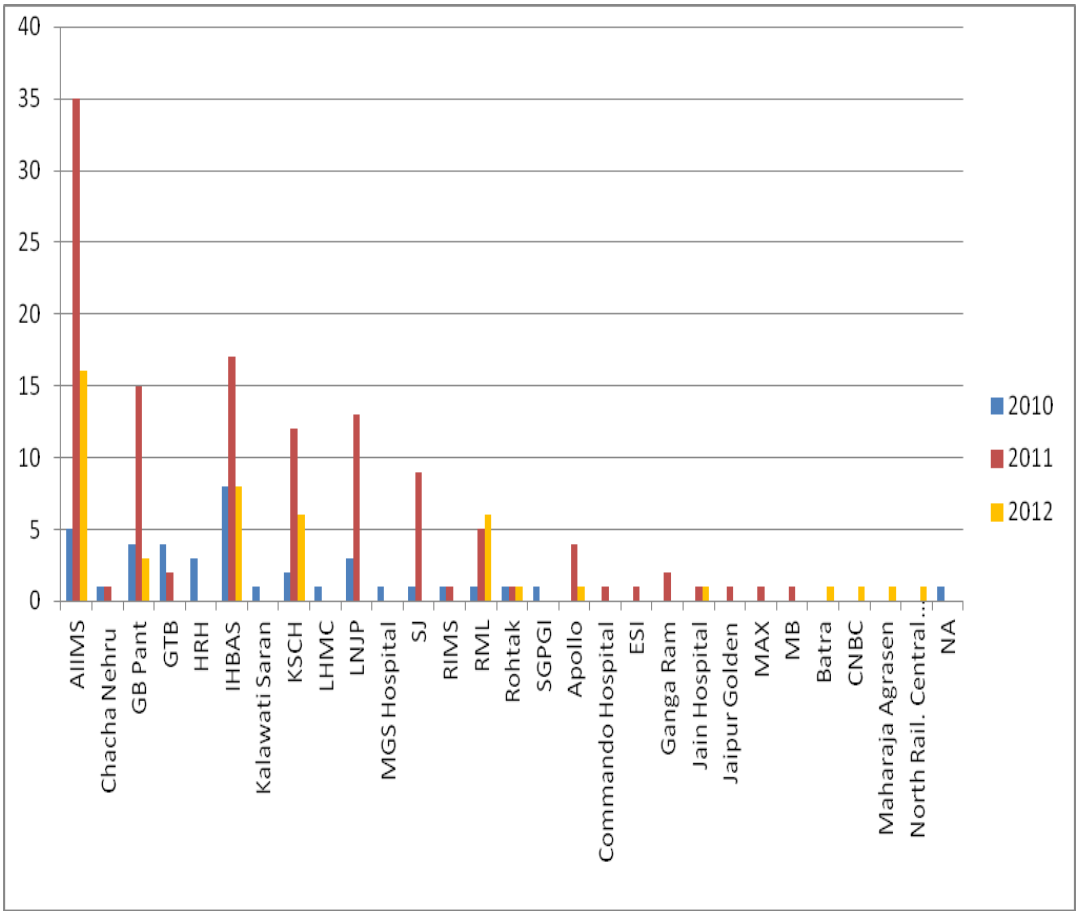


Figure 2: Bar chart showing the age group of individuals that were positive

Majority of the positive samples were obtained from AIIMS (56/226-24.77%). The other hospitals that delivered positive cases include IHBAS (33/226-14.6%), GB Pant (22/226-8.46%), KSCH (20/226-7.69%), LNJP (16/226-7.07%), RML (16/226-7.07%), and SJ (10/226-4.42%). The representation of all hospitals from which positive samples were obtained has been shown in the bar chart in Fig 3.



[NA refers to the individuals whose data was not available to NCDC]

Figure 3. Bar chart showing the number of SSPE positive cases from various hospitals from Delhi, Uttar Pradesh and Haryana during 2010-2012

Samples were obtained from January 2010- April 2012. Month wise data revealed that the maximum cases as well as the maximum positives were obtained during October- January. In 2010, majority of the positive cases occurred in November, December and January (Fig 4).

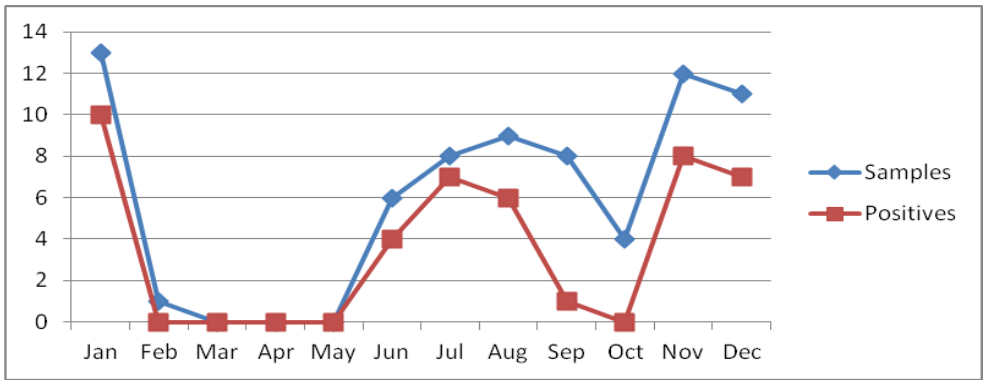


Figure 4: Line Graph showing the number of samples collected and tested positive for SSPE during 2010

During 2011, majority of the cases were obtained during November, followed by October and December (Fig 5).

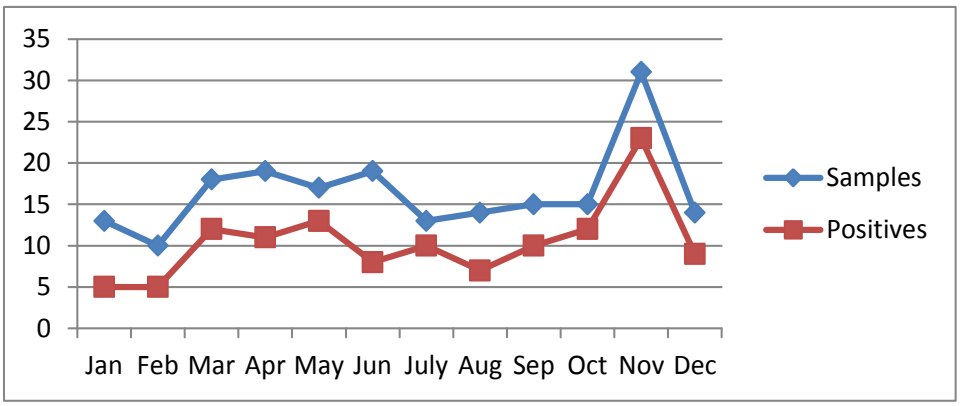


Figure 5: Line Graph showing the number of samples collected and tested positive for SSPE during 2011

For the year 2012, majority of positive cases were obtained in January (Fig 6).

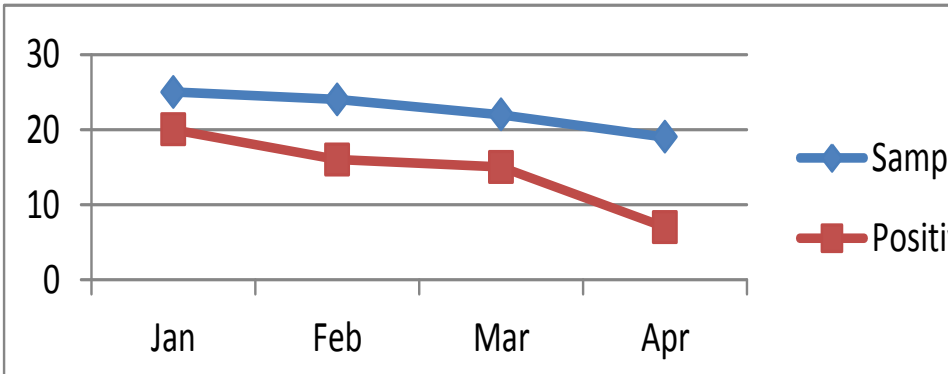


Figure 6: Line Graph showing the number of samples collected and tested positive for SSPE during 2012

DISCUSSION

One of the important diagnostic criteria for SSPE is the presence of measles antibodies in serum and CSF.

As observed from the data, there are higher chances of occurrence of SSPE in males as compared to females. As reported by Khare et al and Mishra et al (7, 8, and 9), the sex ratio of male v/s female was 5.7:1, 6:1 and 3.2:1 in 1990, 1994 and 2005 respectively. Similarly in our study, the sex ratio of male v/s female was 2.73:1 in 2010, 3.77:1 in 2011 and 3.83:1 in 2012.

Total numbers of clinically suspected SSPE cases included in the study were 360, out of which 226 were detected positive for anti-measles IgG antibodies in serum and CSF both. The number of cases positive for IgG antibodies against measles as determined by Khare et al and Mishra et al (7, 8, and 9) was 47 in 1990, 65 in 1994, and 114 out of 205 in 2005. The reason for occurrence of measles in developing countries is insufficient vaccination which may be due to low first dosage, reduced quality, poor cold chain maintenance or delayed supplemental immunization.

Measles is known to occur during winter and early spring season. It occurs in people who have not received any vaccine, or in people who have received only one dose of vaccine and are unable to seroconvert. Nearly 5% children, get a single dose of vaccine and are unable to become immune, therefore, a second dose is required to be given to all the children.

The predominant age group that was found to be affected was 0-12 years, which formed 65.48% of the total cases. The average age of occurrence of SSPE worldwide is 6-13 years.

Tamil Nadu independently introduced measles vaccination in 1980, with special central government permission. Based on the Tamil Nadu experience of the ready acceptance of measles vaccine by the community, in 1985 it was licensed in India and introduced nationally in a phased manner under the 7th five-year Plan, until it reached all districts by 1990. EPI was then renamed UIP. Measles continue to occur partly due to inadequate coverage with one dose and partly due to single-dose vaccine failure. To remedy this, in 2010 the Immunisation Division has begun implementing a second dose of measles vaccine either through immunisation delivery channel or through State-wide campaigns. To cover the immunity gap inevitably created by the 9-month schedule, a second dose of measles vaccine was recommended, universally, by WHO. The Indian Academy of Paediatrics (IAP) recommends a dose of measles-mumps-rubella vaccine (MMR) at 15-18 months of age, fulfilling the need for a second dose of measles vaccine. The Delhi Government has adopted this recommendation for children in Delhi. In the rest of the country, UIP practices the single dose schedule (10, 11).

The principal problem of measles immunization is timing; immunization before the age of 9 months runs the risk of the vaccine being rendered ineffective by the natural antibodies acquired through the mother. Immunization later than 9 months means that a significant proportion of children will contract measles in the interval between wearing off natural protection and the introduction of the vaccine. The most effective compromise is immunization as close to the age of 9 months as possible. The WHO Expanded Programme on Immunization recommends immunization at 9 months age. This age can be lowered to 6 months if there is measles outbreak in the community. For infants immunized between 6 months and 9 months of age, a second dose should be administered as soon as possible after the child reaches the age of 9 months provided that at least 4 weeks have elapsed since the last dose.

In countries where the incidence of measles has declined, the age of immunization is being raised to 15 months in order to avoid the blocking effect of persistent transplacentally acquired antibody.

Studies have shown that in most of the developing countries, nine months is the optimal age for measles immunization. This recommendation has been adopted in India. The choice of 9 months is to balance the tension between the need for early protection and the advantage of delaying it for best vaccine efficacy. The highest seroconversion rate and antibody titre were obtained when measles vaccine was given at or after 12 months of age. Vaccinated at 9 months, 10-15 percent infants will fail to seroconvert, whereas 95 percent would seroconvert if vaccinated at 12 months and 98

percent if vaccinated at 15 months. But experts opine that this should not prevent health workers from administering measles vaccine to 6-8 month old malnourished children who are at high risk of complications from natural measles and who may not return at 9 months of age. If these children do return, they should receive a second dose of measles vaccine as soon as possible after 9 months of age.

In conclusion, the risk of acquiring SSPE is mainly in the age group 0-12 years. A gap in the measles vaccine is evident from the data and the same needs to be covered up. We also need to look into the measles vaccine regimen of our country and see what best suits, in order to minimize the SSPE squeal.

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