Original Article

Time and place distribution ofAcute Encephalitis Syndrome (AES) Japanese Encephalitis (JE) cases in Gorakhpur

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Abstract:

Introduction: 1000 children below the age of 15 years died from encephalitis in the states of UP, Bihar and Assam since 1978. JE vaccinations in 2010 and deep bore wells in 60 districts in India are the two preventive measures in use. Hypothesis generation through a time, place distribution study followed by a risk factor study would help target preventive and curative measures. A spatial temporal analysis of the 2012 encephalitis epidemic in the district of Gorakhpur, having the most cases, is reported.

Material and Method

Government of UP data on 714 cases of AES/JE occurring during 2012 in Gorakhpur district was analysed. Time and place distribution is described. Various hypotheses on mode of transmission besides other important features of the epidemic were generated. Data was used to create video maps of the 2012 AESJE epidemic using Epi-info 7. Onset of symptoms was used on the time axis and longitude-latitude data from residential details was used to describe the place distribution. Videos were interpreted to draw important inferences which may be used in planning a strategy to break the 2013 epidemic

Result:

Thirty (4.20%) of 714 patients fitting case definitions were confirmed cases of Japanese encephalitis. 148 (20%) died. 669 (93.69%) were below 15 years of age. Male to female ratio was 1.45:1. On 9th Aug 2012 the usual 5 cases per day mark was crossed with 10 cases/day reported. On 22th August the peak of 19 cases/day was reached. On 11th September the epidemic started receding at rates slower than the rise showing multiple spurts. The medical college had 1.5 times the cases than anywhere else. On 10th Dec the daily incidence had returned to under 5 levels. District wise place distribution of the 2009, 2011 and 2012 cases shows Gorakhpur as having 714 i.e. twice the number of cases than anywhere else in 2012.

Conclusion:

The epidemic is seasonal and perhaps spreads man to man. Mosquito having a life time range of 5 miles cannot spread the virus 30 kms away to the next case. For every case there are about 500 infected children making the number of <15yrs infected as 357000. Given 44, 36, 275 as 2012 population of Gorakhpur and 40% (17,74,510) below 15 years old, 20% were infected and transmitting. A reporting of more than 4 cases near 7.8.12 heralded a dangerous spurt up to 19/day lasting about a month. The epidemic was mainly contributed by the medical college area where incidence rate was highest during the spurt perhaps because of a high case density produced by centripetal referral. Patients need to be treated near their home.

Key Words: AES (Acute encephalitis syndrome), Epidemic

Introduction

Acute encephalitis syndrome (AES) is defined as the acute onset of fever, headache, vomiting, change in mental status and often with new onset of seizures and focal neurologic signs in a person of any age at any time of year[1]. It is produced by acute inflammation of the brain due to infectious and non-infectious etiologies[2], and is also called acute febrile encephalopathy, viral encephalitis, infectious encephalitis, and brain fever. Acute encephalitis can be associated with severe complications, including impaired consciousness, seizures, disability or death[5]. Japanese Encephalitis (JE) has been considered to be the leading cause of AES in Asia. It is caused by an Arbo virus belonging to the Flavi virus family, carried by *Culex tritaeniorhynchus*

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mosquito which grows in swine and birds, and infects man through the mosquito. Man is the dead end host and cannot transmit the disease. However, this may not be true for other viruses/ agents causing AES. More than 100 different pathogens have been recognized as causative agents of AES including Japanese encephalitis (JE), Herpes simplex, Varicella-zoster, Epstein barr virus, mumps, measles, Enteroviruses, Influenza, Adeno virus, Echo virus, Mycoplasma pneumonia being the most frequent pathogens. Bacterial, fungal, parasitic (like cerebral malaria) and some viral encephalitides (like Herpes simplex, Varicella-zoster) have specific treatment. However, the etiology of AES in 68-75% cases remains unknown and the majority of cases of viral acute encephalitis syndrome (~90%) have no specific treatment[4].

Both AES and JE began in South India. Initially, JE was identified as the etiologic agent in most cases of AES in India[3]. Recently however as a result of massive vaccination campaigns in UP and Bihar, JE caused less than 5% of total AES but the total numbers of AES remained unchanged. Efforts to combat this 34 year old annually occurring epidemic across UP, Bihar and Assam have been development of standard operating procedures (SOPs) to take care of hydration, nutrition, brain edema, covering non-viral agents by Tetracycline and symptomatic support of complications like respiratory arrest. The only preventive measures being used are vector control measures in affected districts and deep bore hand pump to break the faecal-oral route. If unlike JE man is not the end host for AES and transmission is occurring from man to man, an assumption which even if unproved will be an error towards the safe side given the mortality in this deadly epidemic, then an affective preventive strategy based on sound epidemic control principles is the only way at present to break the spread of the epidemic and prevent large number of deaths and resulting disability. This paper is being written in support of such a strategy. The place and time distribution of the epidemic has been fairly consistent over the years. Accurate affected district wise localisation of the place and time by such spatial temporal studies can provide great logistic help in predicting where and when to target research, prevention, detection and management strategies. For determinants, studies comparing places involved and not involved on ecology, meteorological data, entomology of known vectors and infection transmitter (Fever tracking) densities during the epidemic would lead to identification of place and time specific risk factors. Comparing cases and controls would lead to identification of more patient specific risk factors both of which are important. The next step in research should be identification of the virus and developing a diagnostic marker and a vaccine against it. A microbiological/ immunological surveillance over two epidemics would be able to detect any change in the antigenicity or the species of the virus causing the next epidemic as compared to the previous one.

The aetiology and transmission of AES have been studied in various human, animal, entomological and laboratory-based studies. These studies have enhanced the understanding of AES. Outbreaks are usually investigated when a large number of cases are reported over a short period of time or cases occur in several healthcare facilities. Surveillance studies, on the other hand, typically involve a more wide-ranging diagnostic evaluation of consecutive AES cases presenting to a health facility over an extended period of time. The distribution of AES cases according person, place and time is still needs to be studied in details to determine the nature of transmission of causative agents other than JE virus. Disease mapping can be used to pinpoint the areas where outbreaks originate and effectively target high-risk areas for early prevention and control[7].

Video analysis of spatial temporal characteristics of the disease has made it possible to detect the clustering of cases and link the clustering dynamics at geographical locations that carry certain risk factors among agent, host and environment promoting spread of infection and occurrence of incident cases. Therefore, this study reporting Spatial-temporal pattern of the 2012 epidemic in the highest affected district was planned with the objective to ascertain the mode of transmission of AES and provide logistics and technology to those combatting the epidemic in affected areas in India to map the epidemic and target measures of prevention and management cost effectively.

MATERIALAND METHODS

Gorakhpur is a city in the eastern part of the state of Uttar Pradesh in India. 90 km south of Nepal between Lat. 26°132 N and 27°292 N and Long. 83°052 E and 83°562 E. The study is retrospective descriptive in nature in which

all the cases of AES (714) in 2012 in Gorakhpur district of UP were included for video mapping. The cases were reported to Government of UP in prescribed reporting format which was kindly provided by them for analysis. The data supplied by the Government consisted of some demographic, residential, disease related and person related details of cases of AES.

The data made available in Microsoft Excel was used for spatial-temporal video mapping using Epi-info 7 software and the videos studied in detail and interpreted.

RESULTS AND DISCUSSION

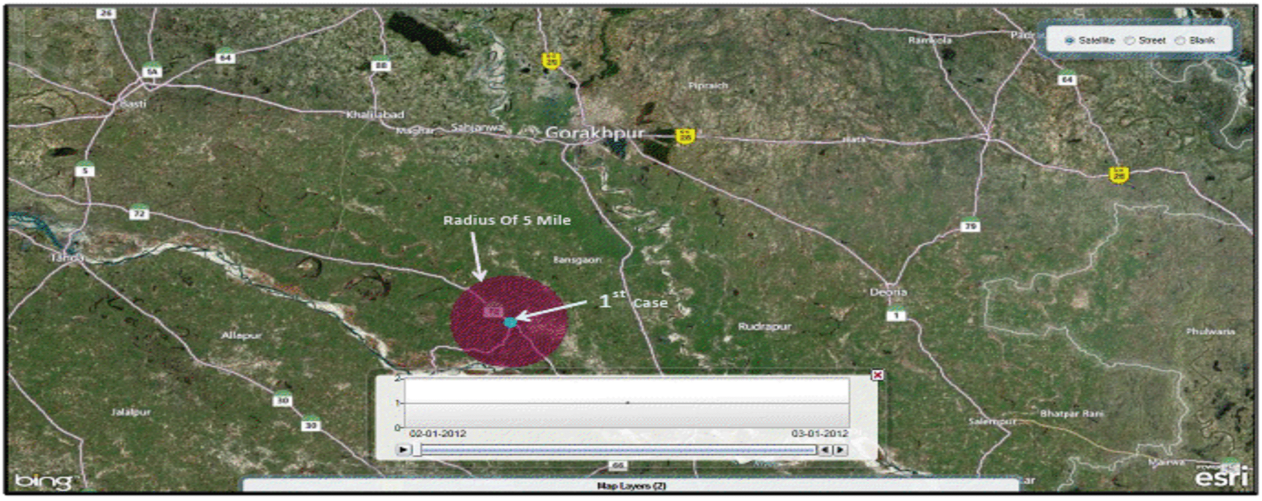
Study Population: Out of total 714 cases of AES/JE reported to Government of UP in 2012 from Gorakhpur District, 30(4.20%) were confirmed cases of Japanese encephalitis. The agent producing the rest 684 (95.80%) cases is not known. The case fatality rate was 20.73 % (148 deaths). In a study from Vietnam by Paireau et al[8] case fatality rate was 25% from 2004–2009.

Out of 714 cases 669 (93.69%) were below 15 years of age. 423 (59.24%) were male and 291(40.76%) were female with a 1.45:1 ratio. In study done by Paireau et al[8] in Vietnam, observed similar pattern (male: female ratio was 1.21:1). The maximum number of cases were in 1-5 years of age group followed by 5-10 years, both in males and females (Table 1), only 5% cases were under one year of age while the study done by Khinchi Y R[9] in 2010, 23% patients were below 1 year of age .The females outnumbered males in the 0-1 year (6.85% & 4.96% respectively) and more than 10 years (20.54% & 17.96% respectively).

Place distribution: In Table 2 we see the district wise place distribution of the 2009, 11 and 12 AES/JE epidemic in Uttar Pradesh showing a fairly consistent place distribution over a period of 4 years. Incident cases of JE have decreased over the years to near 5% but AES numbers have stayed nearly constant.

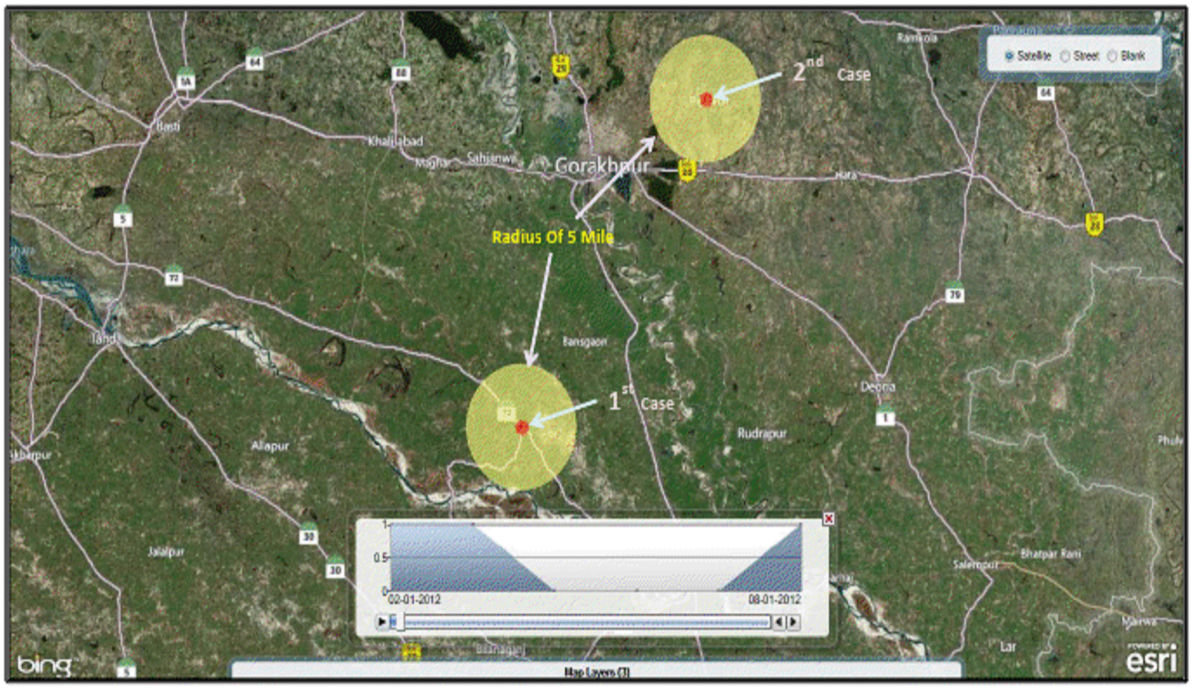
Map 1: Shows that on 3.1.12 first case of AES/JE occurred near Bharwaliya Village of Uruwa Block, South west of Gorakhpur, at SH 72 and SH 81 junction.

Map 2: Shows that on 8th January, just 5 days after the first case, the second and the third case marked 2 and 3 occurred in Pipraich and Bachaiepur village of Pali Block, near Dhanagata Police Station, along NH 64, both more than 50 kilometers from the first case. Circles round the cases shows the 5 miles radius in which the infection carrying Culex mosquito can travel in its entire life. Transmission is therefore by man not, mosquito who that can travel > 50 miles distance in that time. Another explanation is that for every case of AES there are about 500 infected children[10] not presenting as AES. For Gorakhpur to report 714 cases in 2012 there would have been 714 x 500=3,57,000 infected. Since the under 15 population of Gorakhpur in 2012 was 0.40 times the total population, i.e. 0.40 x 44,36,275 = 17,74,510 were susceptible. Therefore 20% of the under 15 years children in Gorakhpur district were infected. So the origin of the cases may have been polycentric depending on infected and transmitting case density.

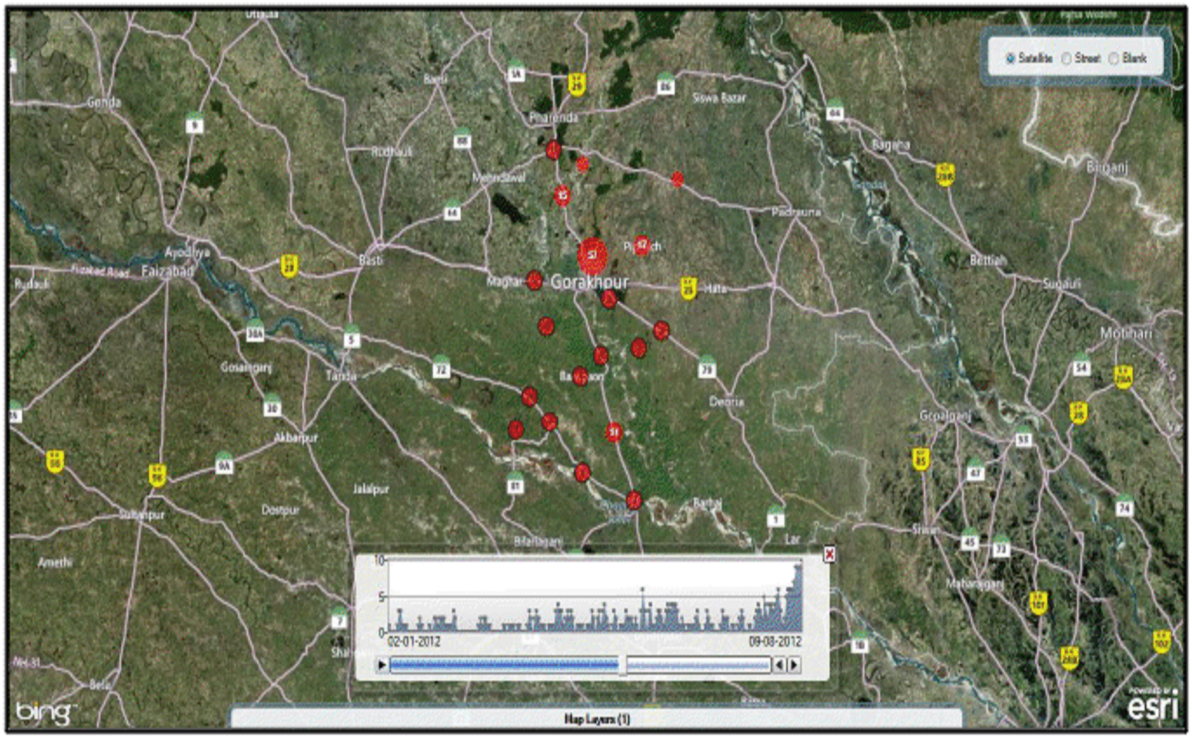


Map 1. Depicting First case of AES/JE in 2012 of Gorakhpur Distt.

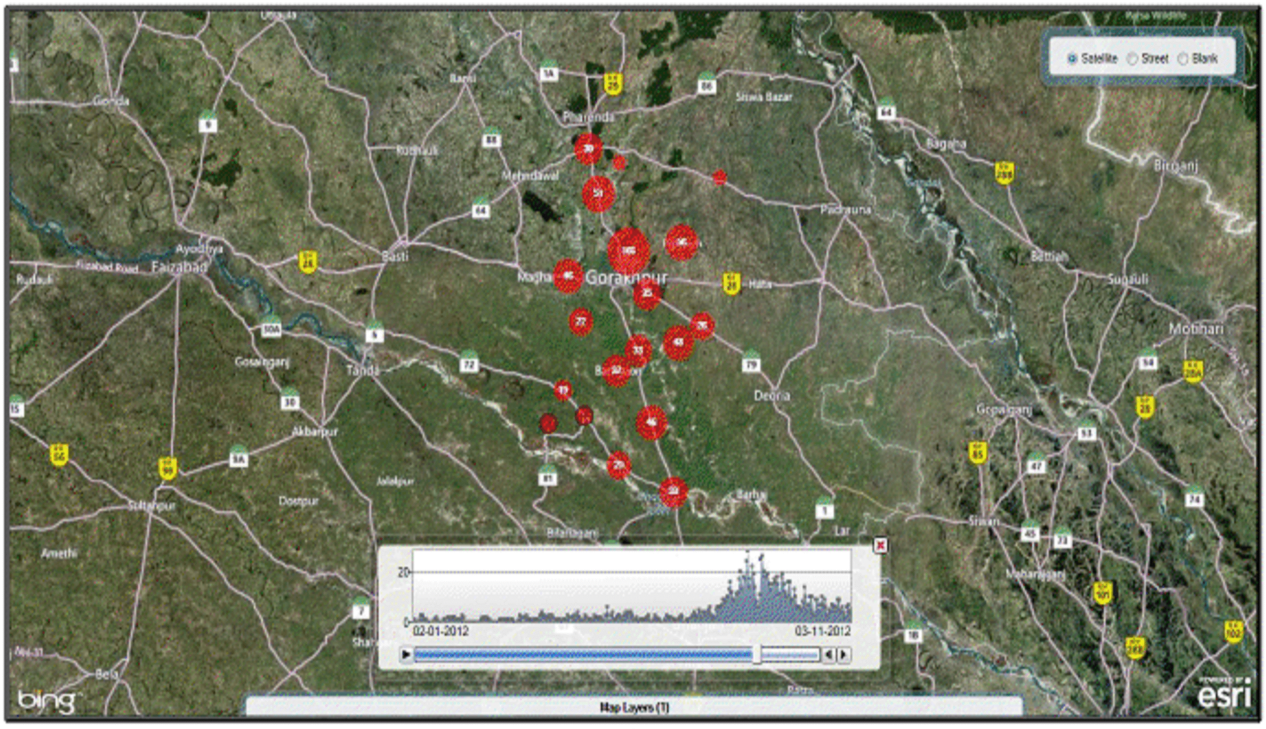
Map 3: Shows the start and ascendance of the epidemic. On 9th August 2012 epidemic start when daily reporting of cases crossed the 4/day critical cut off and rises to 19 on 22.8.12 in just 13 days (Fig. 1). So a higher daily reporting than 4 per day heralds the start of the epidemic. The fastest rate of increase in number of cases during ascendance is in the Medical College area where case



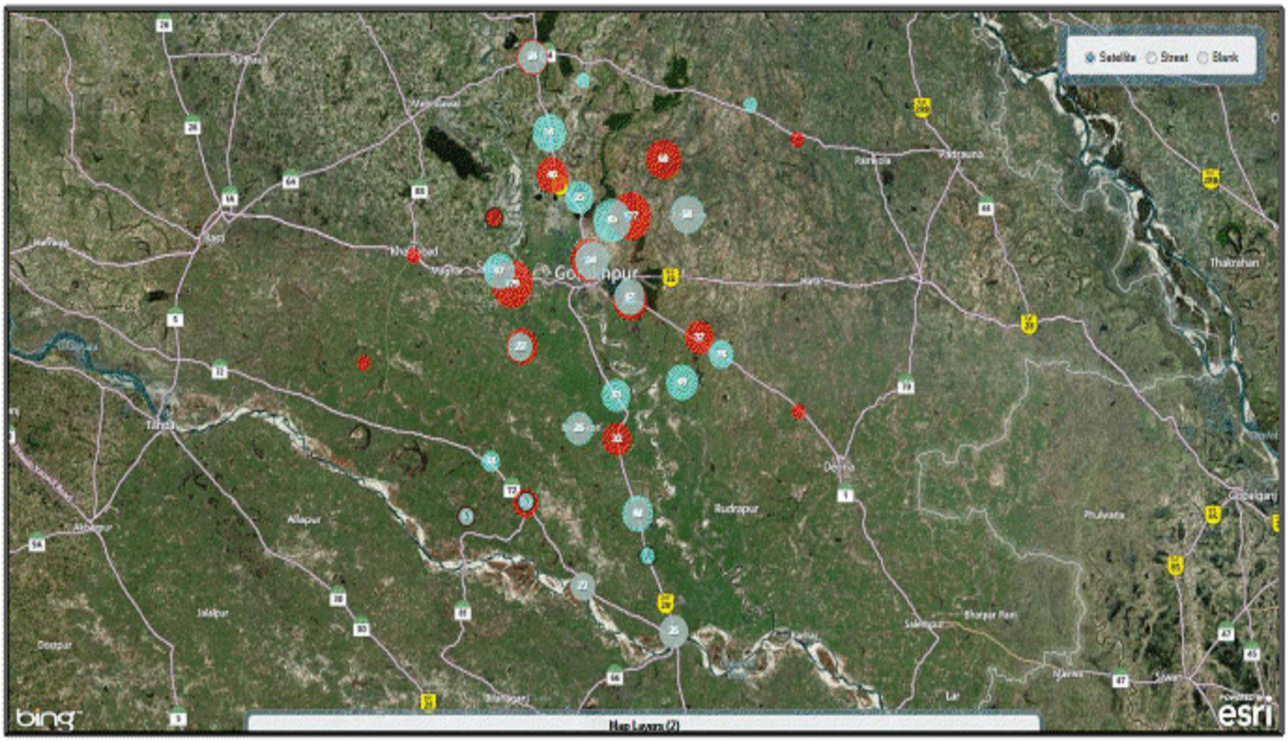
Map 2. Depicting First & Second case of AES/JE in 2012.



Map 3. Depicting the Start of Epidemic.



Map 4. Depicting the End of Epidemic.



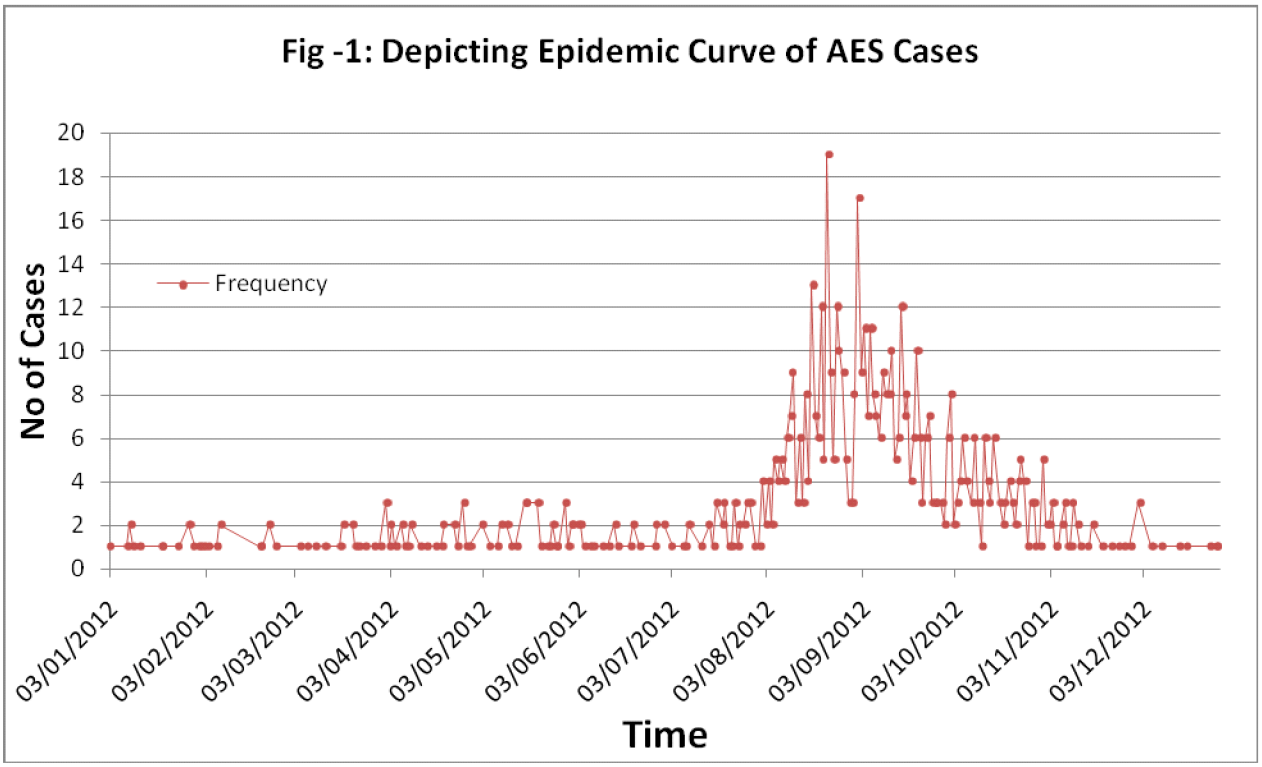
Map 5. Depicting overlap of AES/JE cases of 2011 over 2012.

Table 1: Age –Sex distribution of AES cases in Gorakhpur (N=714)

Age Groups(Years)	Male No. (%)	Female No. (%)	Total No. (%)
0-1	21(4.96)	20(6.85)	41(05.74)
1-5	192(45.38)	122(41.79)	314(43.98)
5-10	132(31.20)	90(30.82)	222(31.09)
10-15	51(13.00)	41(14.04)	92(12.89)
>15	21(4.96)	19(6.50)	45(06.30)
Total	423(100)	291(100)	714(100.00)

Table 2: District wise distribution of AES/JE cases of 2012, 2011 and 2009 in Uttar Pradesh.

Sr.No.	AES/ JE 2012				AES/ JE 2011			AES/ JE 2009		
	District	JE		Total	JE		Total	JE		Total
		No	Yes		No	Yes		No	Yes	
1	Gorakhpur	684	30	714	813	38	851	610	76	686
2	Kushinagar	447	21	468	696	29	725	507	76	583
3	Deoria	353	13	366	488	24	512	283	44	327
4	Maharajganj	224	07	231	320	17	337	293	57	350
5	S K Nagar	180	14	194	172	11	183	120	19	139
6	Siddharth Nagar	119	12	131	122	17	139	101	12	113
7	Basti	78	08	86	90	05	95	60	09	69
8	Mou	19	00	19	11	02	13	06	05	11
9	Gonda	08	00	08	06	01	07	06	01	07
10	Azamgarh	07	00	07	04	06	10	05	01	06
11	Balia	06	00	06	05	04	09	03	00	03
12	Balrampur	06	03	09	12	06	18	09	03	12
13	Gazipur	01	00	01	05	00	05	02	00	02
15	Baharaich	00	10	10	-	-	-	-	-	-
16.	Ambedkar Nagar	-	-	-	01	00	01	-	-	-
17.	Faizabad	-	-	-	-	-	-	01	00	01
	Total (%)	**2132**	**118** (5.23)	**2255**	**2745**	**160** (5.51)	**2905**	**2005**	**303** (13.13)	**2308**



density is likely to be highest due to centripetal referral. Centripetal referral is thus to be prevented by containing the travel of cases to where they occur by providing them necessary treatment near their homes.

Map 4: Shows the descendance which is slower than the ascendance and more peaked. On 3.11.12 the daily incidence has returned <4/day and the epidemic was now an endemic. The descendance may be attributed to the infected population developing rapid immunity against the virus which could not find a susceptible host nearby. However the immunity did not last a year because either it was short lived or the antigenic nature of the virus changed.

Map 5: Shows of place distribution of 2011 epidemic over 2012 epidemic showing remarkable overlap so that it could have been fairly accurately predicted in 2011 where epidemic will occur in 2012.

Conclusion: The epidemic is seasonal and perhaps spreads man to man. Mosquito having a life time range of 5 miles cannot spread the virus 30 kms away to the next case. For every case there are about 500 infected children making the number of <15yrs infected as 357000. Given 44, 36, 275 as 2012 population of Gorakhpur and 40% (17,74,510) below 15 years old, 20% were infected and transmitting. A reporting of more than 4 cases near 7.8.12 heralded a dangerous spurt up to 19/day lasting about a month. The epidemic was mainly contributed by the medical college area where incidence rate was highest during the spurt perhaps because of a high case density produced by centripetal referral. Patients need to be treated near their home.

Recommendations: We suggest that such an analysis be repeated in all 60 involved districts of India to allow accurate targeting of prevention and control measures besides doing virological, entomological and environmental research on risk factors in these areas. Also, an open ended questionnaire maturing to a standardized pilot tested, item analysed close ended questionnaire should be developed during the 2013 epidemic for an adequately powered case control study. A mobile 30 bedded clean air hospitals air dropped and assembled in 3-4 hours at block level near potential sites can be used to provide standard algorithmic treatment to

cases in that area besides providing safe disposal of biomedical wastes and analysis of patients fluids to isolate the virus and develop diagnostic markers and vaccine.

In affected areas of the 2012 epidemic

1. **Fever tracking:** Fever, headache vomiting is probable to be observed and disoriented, convulsing, comatosed is possible to be transported to the Epidemic Hospital. Definite is either by demonstrating the antibody or the virus.

2. **Preventing transmission:** From man to man virus can travel by air, water (orofecal), uncooked food, contact or vector (unknown). Preventing spread can be around the source, at transmitting medium level or around the susceptible target. Around the source measures are containment by preventing travel and proper disposal of biomedical waste. Transmission can be stopped by decontaminating common contact objects like hand grips in buses and trains, tables and chairs being used in public places twice a day using 5% sodium hypochloride solution and vector control. At level of the susceptible target daily Chlorination of the family drinking water, hand washing after defecation and before eating, avoiding uncooked food and covering cooked food before eating has to be practiced.

3. **Decreasing mortality and disability:** Besides early detection and rapid retrieval to clean air mobile virus hospital near the patients home, preventing convulsions and aspiration, maintaining hydration and nutrition, detecting and managing raised intracranial tension, nursing care, management of complications like respiratory arrest and tetracycline cover to combat non viral etiologies may be undertaken.

Acknowledgments

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