Japanese Encephalitis in Nepal (1993-1997)

Epidemiological Analysis and Review of Literature

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Few Words

I am very pleased to get this opportunity to read this document containing epidemiological analysis of five years data on Japanese Encephalitis. This document contains precise descriptions of Japanese encephalitis (JE) for a period of 5 years (1993-1997) based on important epidemiological parameters like time, place and person. This work has all strength to compete with other publications available in terms of its attempt of highlighting the epidemiology of JE in Nepal.

The problem of JE is exacting tremendous burden of morbidity and mortality on the vast population inhabiting outer and inner terai of this country. Major brunt of disease lie on the children of pre-school and school age. The high case fatality rate among the patients of this disease is another relevant issue of concern for the program. Since this disease hits the rural agricultural areas in terai the socioeconomic impact of this disease has on the rural community is discernable. In this context it is crucial that appropriate prevention and control activities be developed through strategic planning. Some of the important strategies in my opinion would be to consider the implementation of vaccination program for children of vulnerable age group and better case management in the hospitals of endemic areas by applying proper and adequate nursing care. Immunization program must consider the issues of efficacy of vaccines in use worldwide and their cost meticulously before its implementation in Nepal. Other strategies like insecticide spraying, environmental management, biological control and personal protective measures also have to be well evaluated in terms of their effectiveness and cost implication before being promoted as means for JE prevention and control in Nepal.

Lastly I would like to congratulate authors and others concerned who have worked so hard for turning the publication of this document into reality. I am confident that this document will also serve as guidelines and reference for whosoever engaged in the field of prevention and control of Japanese Encephalitis here in Nepal and abroad.

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Foreword

It gives me a great pleasure in writing this foreword for the report of "Japanese Encephalitis in Nepal". The report fills a deeply felt void in the medical literature on Japanese Encephalitis (JE). Besides the epidemiological situation of last five years, it also contains guidelines for the care of the normal people and JE sick people. Based on its contents it can be used as a practical manual.

Japanese Encephalitis (JE) a mosquito transmitted Virus disease has been emerging public health problem in Nepal. Severe epidemics have occurred for the last several years with report of increasing morbidity cases and mortality deaths inspite of adopting strong collective effort through our health care delivery system at different levels of services. In addition, the disease has been found mainly affecting children below 15 years of age and those who have improved clinically suffer from varying degrees of brain damage requiring life long care with a considerable amount of national expenditure.

The epidemiology of JE is complex due to a complex transmission cycle of the virus involving a variety of vertebrate and invertebrate hosts. The epidemiological knowledge about the disease plays a key role to develop sound surveillance systems for forecasting epidemics and control strategies. "Japanese Encephalitis in Nepal" is intended to provide an update of epidemiological knowledge of the disease in Nepal, it will certainly help control of JE epidemics in the years to come.

"Japanese Encephalitis in Nepal", this manual will be extremely useful not only for the DHOs, MOs, PHOs , but also for the students and staffs involved in the vector borne diseases. I do hope, it will be helpful as a referral document for the situation and programme planning in general.

I would like to thank to Dr.Mahendra Bahadur Bista and his co-authors for their hard work and dedication to taking a good initiation for bringing out such an excellent study report.

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PREFACE

In a country where health scenario is dominated by infectious diseases, health care personnel have a major responsibility towards the fragile vulnerable group of people mainly small children whose mortality rate in Nepal is very high. It is necessary not only to reduce the mortality rate due to the disease, but also to assure a good quality of health service to affected people through a better health care management.

Epidemiology and Disease Control Division has published "Japanese Encephalitis in Nepal". This is an epidemiological study of five years data of Japanese Encephalitis (JE) recorded in all the endemic areas of the country. As the number of JE cases as well as JE affected areas have been seen in increasing trend for the last several years, we carried out this study to assess the actual situation of JE in the country and to determine its possible cause and risk factors. Efforts also have been made to find out possible solutions towards JE control and prevention.

Besides the findings of the study, required basic information regarding management procedures of JE cases as well as preventive measures are included. The information and findings have been described in a systematic way and compared with the findings of similar studies done abroad. In addition, one of the major topics among preventive measures, JE vaccination, has also been dealt with. Epidemiological and Disease Control Division is currently reviewing the future prospects of JE vaccination to be included as part of the routine immunization programme in the endemic areas.

I hope that "Japanese Encephalitis in Nepal" will prove to be a useful working reference for all involved in the management and control of JE.

The publication of this study report at this stage has become possible with concerted efforts of many individuals within and outside the division.

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First of all I would like to thank Dr. Kokila D. Shrestha and Dr. Manas K. Banerjee of EDCD who guided us in the preparation of the report.

Sincere thanks go to Mr. Shankar B. Joshi, Mr. Sagar Prasai, Mr. Mahendra M. P. Lakaul, Mr. Lat Narayan Shah, Mr. Chandeswor Yadav, Mr. Parsuram Shrestha, Mr. Rajendra K. Raut of EDCD and Mr. Narendra Raj Tandukar of WHO, for their contribution.

I am fortunate to receive assistance from Dr. J. M. Luna, MO/WHO who helped to give shape and form to this report.

I am deeply indebted to many persons including Regional Directors /Medical superintendent/DHO's, Medical Recorders, Statisticians of different Hospitals/PHO's/PHC's and other Health Personnel of JE affected districts. Without their involvement and support this study might never have been born.

Lastly, I also thank Mr. Richesh Vaidya, our secretarial staff for typing the manuscript so painstakingly.

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Biodata of Dr Mahendra Bdr Bista MBBS, MPHM

Dr. Mahendra Bahadur Bista Director, EDCD/DHS has long working experience as director in various divisions of Department of Health Services. Since he joined Ministry of Health in 1973, he worked in different hospital like Trisuli, Dadeldhura in remote areas of Nepal and Biratnagar hospital in Terai as medical superintendent. He also served as director of Mid-west regional directorate health office.

During his tenure he has attended many national and international meetings/workshop. Some of them are HIV/AIDS, Leprosy, EPI, IMCI, Nutrition, ARI, Vitamin A, Malaria, Kala-azar, Epidemiological Surveillance, Emergency Preparedness etc. Similarly, he has attended SAARC Technical Expert Meeting, SAARC Ministerial Conference on Children in New Delhi and in Pakistan on separate occasions. In addition, he was Temporary Advisor to the Regional Director WHO, Second consultation on EPI vaccine supply and Quality, 23 - 24 Sept.,1996 and Third Meeting of South-East Asia Regional Technical Consultative Group (TCG) for Vaccine Preventable Diseases 25th - 28th Sept, 1996, Kathmandu, Nepal.

The author's many scientific works have been published in many national news media and scientific journals.

He was consulted as external examiner in Post-graduate Public Health examination in Institute of Medicine, Tribhuvan University.

He was awarded Prabal Gorkha Dakshin Bahu III and IV class separately by His Majesty's The King. He was also decorated with Sewa Medal and Coronation Medal for his contribution in Public Health arena of Nepal. He received appreciation letter and certificate from Regional Director, Dr. Uton Muchtar Ratei, WHO/SEARO and Prime Minister of Nepal, Rotary International respectively for successfully completing NIDs, 1997/1998

He is a life member of Nepal Medical Association, member of Indian Medical Association and Nepal Public Health Association.

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   III. Early Warning Reporting System ; an approach for the surveillance of communicable diseases in Nepal" , scientific article, under publication in journal of Nepal Health Research Council , 1999.
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Dr. Shanker Bahadur Shrestha, a residence of Lalitpur district, has been involving in general health services under the Ministry of Health for nearly two decades. After schooling at Tripadma Vidyashram Public High School in Lalitpur, he started his higher education at Institute of Medicine, Tribhuvan University to do certificate in General Medicine. With this medical education he worked with Ministry of Health as Health Post Incharge since 1980 in the capacity of General Health Services.

He studied MBBS course under the government service at Tribhuvan University Central Campus and completed the same in 1987 including one year of compulsory internship.

After obtaining MBBS degree he served as chief of District Health Office in Myagdi district and Dolakha district from 1987 to 1990. He also served as a Medical Officer in national hospitals like Bir Hospital, Infectious Disease Hospital for nearly five years.

In 1992, he went to Bangkok, Thailand to do M.S. in Tropical Medicine from Faculty of Tropical Medicine, Mahidol University and he completed the same with major subject on malaria in 1994.

For nearly two years he has been working with Epidemiology and Disease Control Division actively involving with Malaria, Kala-azar and Encephalitis control programmes in particular.

The author has gained experiences through the observational study of health services programmes at international levels and has participated in a number of national and international workshops concerning malaria and other tropical diseases. In addition, he has received training from Japan in maternal and child health with respect to infectious diseases control.

His popular articles and columns on general health have been appearing in many national dailies and periodicals.

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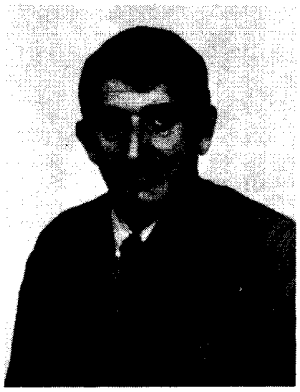

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Background Information:

Background Information:

Country Profile:

Geography:

Nepal is a landlocked country lying between 80°04' and 88°12' east longitude, and 26°22' and 30°27' north latitude. It extends over an area of 147,181 sq. km. In average, its east to west length is about 885 km, and although its north to south width is not uniform, it varies from a maximum of 245 km to a minimum of 145 km. It is nestled at the foothills of the Himalayas sharing its northern border with the Tibetan autonomous region of the People's Republic of China, and its eastern, southern and western borders with India.

Topography:

Topographically, Nepal is divided into three distinct ecological regions namely *mountainous*, *hilly* and *terai*. The mountain region ranges in altitude from 4,877 meters to 8,848 meters above sea level and covers 35 % area of the country. Because of the harsh terrain, transportation and communication facilities in this region are very limited, only 7.3 percent of the population live here. In contrast, the hill region ranges from 610 meters to 4877 meters above sea level and covers 42 percent of area. It is densely populated providing living space for 46% of the total population of the country. Transportation and communication facilities are much more developed here than in the mountain region. Unlike the mountains and hills, the Terai region in the southern part of the country can be regarded as an extension of the relatively flat Gangetic plains. This area which covers 34,019 sq. km is the most fertile part of the country. Paddy is the major crop in this area. While it constitutes only about 23% of the total land area, about 47% of population live here. Because of its flat terrain, transportation and common facilities are more developed in here than in the other two regions of the country. Eco-system of this belt is very favorable for the breeding of *Culex* mosquitoes the proven vectors of Japanese encephalitis in Nepal.

Climate:

The climate shows distinct variations depending upon the nature of terrain. In Terai, the mean maximum and minimum temperatures in winter fluctuates between 50°F (10°C) and 80°F (27°C) and in summer between 75°F (24°C) to 100°F (38°C). In the hilly region, mean temperature declines during winter as low as 37°F (5°C), and it is still much lower at higher altitudes of

the mountainous areas. The rainy season occurs during the Southeast monsoon, with very heavy precipitation in the period from July to mid September, the months reporting highest number of Japanese Encephalitis cases. Rainfall during the other seasons is light or negligible. Annual rainfall is approximately 100 inches (250cms) in the eastern region and is largely confined to the monsoon months, whereas in the western areas it is only 40 inches. The Terai areas receive heavy precipitation, ranging between 75 to 90 inches. The relative humidity varies between 80% and 90% during the monsoon but declines in the other months.

Political system:

The political system is a constitutional monarchy. For administrative purpose, the country has been divided into five developmental regions (Eastern, Central, Western, Mid-Western and Far Western), 14 zones and 75 districts. Districts are divided further into Village Development Committees (VDCs) and Municipalities. There are altogether 3912 VDCs and 58 municipalities including one metropolitan and three sub-metropolitan cities. The total population is about 21 million (CBC, 1996).

Health Infrastructure:

Under the Department of Health Services (DHS) there are five Regional Health Directorates, each located at the headquarter of each of the five development regions of Nepal. In 62 of the 75 districts, there is a District Health Office (DHO) with a district hospital and a district public health office (DPHO) under its umbrella. In 13 districts, which have sub-Regional or Zonal Hospital, the PHO has its independent institutional status. All 205 electoral constituencies in the country are envisaged to have one Primary Health Care Center (PHC); each DHO/PHO has between 9 to 17 health posts (HP), and each VDC, a Sub-health Post (SHP). PHC, HP, and SHP serve as the peripheral level health institutions responsible to deliver health services. Currently the institutions involved in the delivery of health services include 74 hospitals, 117 PHCS/HCS, 754 HPS and 3187 SHPs. A total of 12,682 Trained Birth Attendants (TBAS), 42,427 Female Community Health Volunteers (FCHVs), several thousand mothers' group (MGs), Village Health Workers (VHWs) and Maternal and Child Health Workers (MCHWs) are working in SHPs. (Annual Report 1996/1997). There are central, regional, sub-regional and private hospitals, nursing homes as well as teaching hospitals rendering service to the population. Besides this, there are people, especially in the rural communities, who attend other

components of the health delivery system like traditional healers, ayurved, and homeopathic practitioners.

Historical Background of JE situation:

Japanese Encephalitis (JE) is an arthropod borne viral disease of Public Health importance in the South-East Asia Region. After human immune deficiency virus infection (HIV), JE may be the leading cause of viral encephalitis worldwide (Tsai, T.F., 1994). Merely three decades ago JE was endemic to only a few countries of East Asia like Japan, Korea and China, which later spread to the other countries of SEA region of WHO and parts of Oceania (Okuno, T., 1978). Even though cases and outbreaks resembling JE clinically have been observed since 19th century it was only in 1935 JE viruses were isolated from human cases in Japan (Monath, T.P., 1985). A severe epidemic of JE has been recorded in Japan in 1964 with 6000 cases and case fatality rate (CFR) as high as 60 percent. Similarly, epidemics of JE were reported in many provinces of China in the early 1950s with almost all provinces being affected by now (Yu Yongxin, 1995).

Approximately 50,000 cases and 10,000 deaths are estimated to have occurred every year in the Asian continent (Bunce et.al.,1998; Dominant Com. Dis., WHO, 1997). In the South East Asia Region (SEAR) JE is prevalent in Northern Thailand, as well as in Bihar, Uttar-Pradesh, Tamil Nadu and West Bengal states in India, in the Terai areas of Nepal and in Sri Lanka. Cases have been reported in Bangladesh, Indonesia and Myanmar as well (Dom. Com Dis., WHO, SEARO, 1997). The first indication of JE transmission in SEA region was from Sri Lanka where an outbreak was apparently reported in 1948 (Tsai, T.F., 1994). In India, epidemics of JE were first recognized around Vellor (Sehgal, S.J., 1989). In Nepal an epidemic of JE was first recognized in Rupandehi district of the Western Development Region (WDR) in 1978 (Joshi, D.D., 1986; Bista M.B. et. al., 1992). The disease was then thought to be imported from Gorakhpur and surroundings areas of Uttar Pradesh of India, where JE epidemic occurred (Umenai et. al., 1985; Khatri et. al., 1982; Joshi, D.D., 1983). Then subsequently epidemics occurred in Morang district of eastern Nepal gradually spreading into other districts in successive years.

In recent years the epidemiological pattern and geographical distribution of Japanese encephalitis have changed in Asia. In Taiwan, Japan, South Korea and China clinical cases of JE have decreased dramatically. This has been

possible through the integrated control effort comprising of human vaccination program, water management, immunization of pigs, systematic piggery and community awareness program. On the other hand, the incidence of JE has increased in India, Nepal, Sri Lanka, Thailand, Burma, Bangladesh and Vietnam (Umenai, T. et. al.,1985).

Vectors:

Thirty species of mosquitoes belonging to five genera of *Culex, Anopheles, Aedes, Mansonia* and *Amergeres*, harbor the viruses of JE. The mosquito-borne mode of JE transmission was elucidated with the isolation of JE virus in 1983 and subsequently in other field studies that also established the role of aquatic birds and pigs in the viral enzootic cycle (Tsai, T.F., 1994). Entomological studies carried out during the outbreaks of 1981-1984, have shown *Culicine* mosquitoes namely *Cx tritaneorhyncus*, *Cx gelidus*, *Cx vishnui, Cx. Pseudovishnui* and *Cx fuscocephala*, as suspected vectors of transmitting JE virus both in animals and humans (Pradhan, 1981; Regmi et. al., 1984; Khatri et. al. 1983). Since *Cx tritaneorhynehus* is found in abundance in the rice-field ecosystem of the endemic areas during the transmission season, and because JE virus isolates have been obtained only from a pool of *Cx. Tritaneorhynchus* females this species is suspected to be the principal vector of JE in Nepal (Gubler et. al., 1989; Darsie et. al., 1989).

Culicine mosquitoes breed in irrigated rice fields, shallow marshes, ponds, pools and ditches with fresh or polluted water with grass or aquatic vegetation in partial shade or full sun. Breeding preference of *Cx tritaneorhynehus* and epidemics of JE associated with paddy field ecosystem have been adequately substantiated by different studies (Tyagi, B.K., 1997). Experts believe that rice fields are the probable predominant source of larval breeding in this country because they have demonstrated abundant presence of potential JE vectors in the rice fields (AFRIMS Report, 1985).

Culex mosquitoes prefer to feed outdoors (exophagy) principally on vertebrate hosts other than man. They feed predominantly on cattle (85 - 88%); 4-5% of blood meals were from pigs, and 2-6% from humans (Reuben et. al., 1992). Humans, as mentioned earlier, are the incidental hosts. The important factors governing spillover of the disease to man are the related abundance of the vectors, the availability of amplifying hosts, the

density and absolute number of mosquitoes, adequate man mosquito contact and longevity of vector (JE-Guidelines, WHO, 1996).

Vertebrate Host other than human beings as reservoir (JE-Guidelines WHO, SEARO, 1996; Gubler et. al., 1989)**:**

Pigs are important amplifying host of JE virus. Infected pigs generally do not manifest overt symptoms of illness. Virus of JE proliferates in pigs. The later remain viremic for several days so that the biting mosquitoes become infected. Since pigs become infected as a result of the bite of an infected mosquito and can transmit the virus to many others, they are called amplifiers of virus transmission. In some places, upon 100% of pigs have antibodies to JE.

Bovines do not appear to serve as an amplifying host. The major vectors of JE feed on bovines and there is serological evidence of bovines being infected with the virus. However, viremia is very difficult to be demonstrated. Also, bovines tend to live many years so the number of susceptible animals introduced every year is very few. Thus, bovines may act as mosquito attractants but are not considered as the natural hosts of the virus.

Bats have been shown to develop viremia.

Horses are the only domestic animals so far known which show the signs of encephalitis due to JE virus infection. Since they are not prevalent in large parts of South-East Asia they don't play a significant role in the transmission.

Among birds, herons and egrets may play an important part in the natural history of the JE virus. There is no convincing evidence that migratory birds can transfer the virus from one region to another. Pigeons and sparrows can develop viremia and can infect mosquitoes.

In Nepal infection in pigs and ducks has been proved through serological studies (Joshi, D.D., 1984 & 1994) and *Culicine* mosquitoes have been found to be breeding and growing in close association with wading birds and ducks.

Infectious agent:

JE virus is one of the species of the family *flaviviridae*. It is an enveloped RNA virus and is antigenically related to St. Louis encephalitis (SLE) virus, Rocio virus, West Nile virus and several other flaviviruses (Gubler, 1989). Biological activities like mediation of viral bindings to susceptible cells, hemagglutination, possible participation in endosomal viral function and induction of host-protective immune response are ascribed to the "E" protein of the virus.

Uptil now prevalence of three different strains of JE virus (JEV) have been reported in Nepal (Nep 1/90, B-2524 and B-9548). A study on seroepidemiology of JEV infection carried out by Takashi Kubo et. al. in 1996, found out that the number of JE cases and deaths that occured due to JE in Nepal for the last two decades correlated well with the findings in India. This has been proved also by their antigenic study and is attributive to free and frequent travel of the people of both the countries through the open border.

Clinical spectrum:

Clinical manifestations of JE vary from a mild self-limited febrile illness with headache, aseptic meningitis, to a most severe form of illness with encephalitis (Thongcharoen, P. et.al., 1989; Kumar, R. et.al., 1990). Incubation period ranges between 5 - 15 days. Illness starts with an abrupt onset of high fever and headache. Kalayanarooj, S., has given a very clear and precise description of clinical manifestations and outcome of JE based on Thailand's context (**Annex 1**). Some of the major signs and symptoms are described below:

A. Early symptoms (Prodromal stage)

1. Fever
2. Rigor
3. Headache
4. General malaise
5. Nausea
6. Vomiting

B. Late signs and symptoms (Acute encephalitis stage, usually between the third-fifth day)

1. Altered sensorium (clouding of consciousness, excitement, confusion disorientation, stupor and coma)
2. Convulsions
3. Stiff neck
4. Muscular rigidity
5. Mask like face
6. Abnormal movements (coarse tremor, chorea-athetotic movements, etc.)
7. Dehydration
8. Weight loss

C. Other signs and symptoms (early or late)

1. Increased deep tendon reflexes.
2. Thick, slow speech
3. Aphasia
4. Paresis and/or paralysis

Gastrointestinal symptoms like anorexia, nausea and abdominal pain are common in children. Irritability, vomiting and diarrhea or an acute convulsion may occur in early hours and days in infants and children. Seizures occur in more than 75% of pediatric patients but are less frequently observed in adults (Tsai, JE vaccines; Vaccines, Stanley et. al., 1994).

Although symptoms suggest raised ICP (intracranial pressure), papilledema and other signs of raised ICP are rarely seen, and dexamethasone does not improve outcome. (Hoke, C.H. et. al., 1992). Signs of extra pyramidal involvement including tremor, mask like facing, rigidity and chorea athetoid movements are characteristic of JE.

There have been reports of recurrence of symptoms of JE several months after resolution of acute illness. Reason and significance of recurrence is not clear.

Diagnosis:

In an area endemic to JE, when clinical features of a fever patient resembles with JE infection, a case can be suspected as JE. Virus can hardly be recovered from blood but can be recovered from CSF in about one third of

patients. The most widely used diagnostic method is IgM Capture ELISA. Specific anti-JE IgM, can be detected in CSF or in serum or in both in approximately 75% of patients within first four days of illness, and nearly in all patients after 7 days of onset of symptoms. Moreover, presence of IgM in the CSF indicates local antibody formation associated with brain infection and is not seen in persons with asymptomatic infection with JE virus (Thomas, P. Manath, JE 1988).

Conventional serological procedures like hemagglutination inhibition, complement fixation, IF or neutralization are also in practice until now. Assays for JE viral genomic sequences by polymerase chain reaction (PCR) have been developed, but clinical studies have not been reported. (Tanaka, M., 1993). In many patients who die during the first week after onset of symptoms, the virus may be isolated from the brain, or viral antigen may be demonstrated by immunoflurescence. Virus may be isolated from CSF during the early phase of the acute illness, in such cases fulminating infection is present and prognosis is poor. Isolations from blood are uncommon.

- Diagnosis of JE at National level will be guided by the following case definitions (based on recommendations of the National Workshop on VBDS, 1997):

"Any case having elevated temperature (over 38°C), altered consciousness or unconsciousness, will be considered as POSSIBLE MENINGTIS/ ENCEPHALITIS and be referred for Lumber Puncture".

"If the suspected case has between 5 and 1000 cells (predominantly lymphocytes per mm^3) in the CSF, it will be diagnosed as having PROBABLE VIRAL ENCEPHALITIS".

"If a case of probable viral encephalitis as defined above presents a positive specific anti-JE IgM in the CSF or serum at the time of illness, the case will be considered as a CONFIRMED CASE OF ENCEPHALITIS DUE TO JAPANESE ENCEPHALITIS VIRUS".

Diagnostic Methods

- At HP levels, diagnosis will be made based on the clinical features presented by the patient. If classified as POSSIBLE MENINGITIS/ ENCEPHALITIS, the case needs to be referred to a more specialized treatment facility.

- At PHC, District and Zonal Hospitals, patients meeting the case definition of POSSIBLE MENINGITIS/ENCEPHALITIS, will be subjected to lumbar puncture for CSF. CSF should be examined for cell count, protein, sugar, gram and ZN stains, and culture wherever possible.

- In absence of skilled laboratory technician, lumbar puncture must be carried out to look out for pressure, turbidity and cell count.

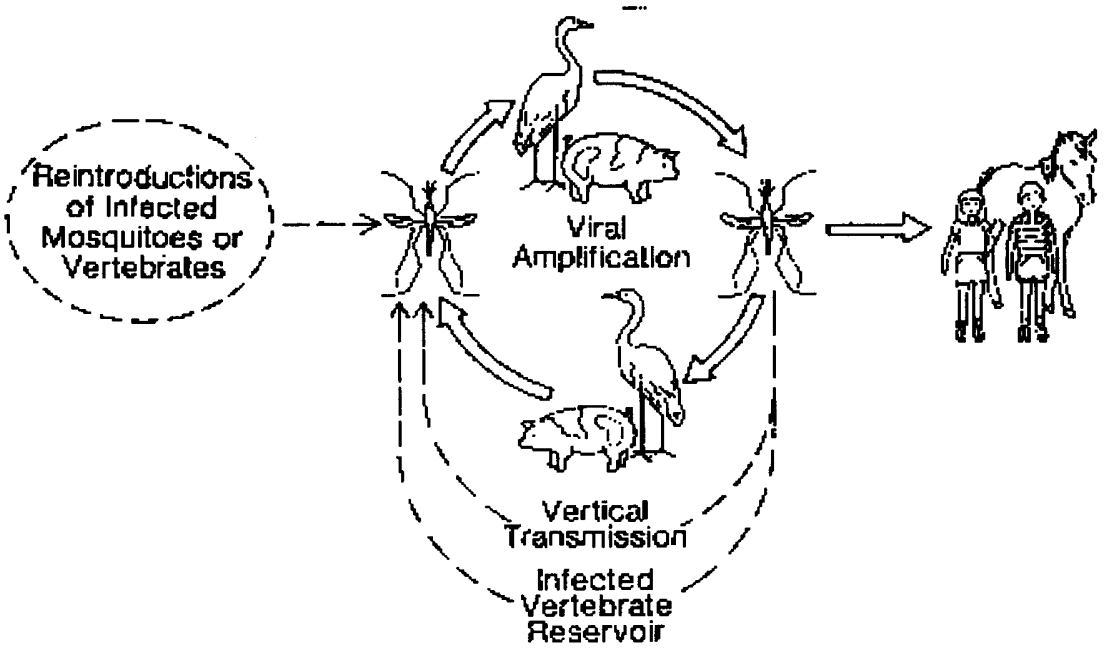
- Serum specimens for specific IgM to be detected, should be collected and referred to the National Public Health Laboratory, Teku, Kathmandu, following the guidelines according to the protocol for the collection, storage and transportation of laboratory specimens (**Annex 2**)

- Japanese encephalitis is an obligatory notificable disease, which needs to be reported within 24 hours after detection, to the Epidemiology and Disease Control Division, Teku (Tel. 262268, 255796, Fax. 262268) or to the Vector Borne Disease Center, Hetauda (Tel. 057-20572 Fax. 057-20484) by the institution chief.

Epidemiology:

It is primarily a zoonotic disease infecting mainly vertebrate animals, e.g. pigs, birds, horses etc. Man is involved in transmission cycle as accidental host and plays no role in perpetuating the virus (Pavri, 1979).

JE is principally a disease of rural agricultural areas, where vector mosquitoes live and grow in close association with the main vertebrate hosts. Pigs, wading birds and ducks have been incriminated as an important vertebrate amplifying hosts for JE virus (see drawing in next page). Humans and horses may become ill in transmission cycle.



(Tsai, T.F., 1994)

In subtropical location of SEA and Indian sub continent JE transmission follows the seasonal occurrence of rain and migratory patterns of avian vertebrate amplifying hosts. Transmission is seasonal, occurring approximately from April-May to September-October.

JE is transmitted to Human beings through the bite of infected mosquitoes. The maintenance and spread of JE virus appears to be mainly through a pig-mosquito-pig cycle (Gould et. al., 1974; Johnes et. al.,1974) and bird-mosquito-bird cycle (Joshi, D.D. et. al., 1998). Domestic pig raising is common in terai communities of Nepal because pigs are accepted as an important source of meat and thus is considered as a profitable venture in this country. This has aggravated the situation in agricultural areas. Man is an accidental and a dead-end host of the transmission cycle. The clinical disease of JE in man occurs in an approximately one on every 20 to 1000 infections with the mean of one case for every 300 infections (Kalyanarooj, S., 1995).

Studies suggest that virus may be transmitted transovarially in vector mosquitoes. This could be one of the possibilities how virus overwinters in temperate locations (Soman, R.S. et.al., 1985).

Water logging required for paddy crops either through irrigation or natural rainfalls, **nutrient support to larvae** of vectors and **appropriate ecological conditions** for the growth of mosquitoes provided by paddy ecosystem favor the increased vector density. The latter in its turn enhances risk of human infection.

JE vectors are zoophilic. Thus, cows and certain other animals are believed to divert vectors mosquitoes by then reducing human risk of infection. Immunization of pigs prevents abortion and still births, and also may reduce viral transmission by limiting or preventing the viremia in these animals (Vaughn, D.W. et..al., 1992).

Rural villages acquire conditions favorable for JE transmission. Thus, exposure and infection occur at an early age. In hyperendemic areas most of the cases are found in 0 - 14 years age group.

Some studies shows house-hold crowding, religion, ethnicity, exposure to domestic animals and lane of air-conditioning and mosquito nets are some of the risk factors associated with acquisition of JE infection (Chaudhari, N. et.al., 1992)

There is variable risk of acquiring JE infection during travel to an endemic country. It depends on the destination and season of travel and activities of the individual.

Risk Factors for Acquiring Japanese Encephalitis During Travel To Asia (Tsai, T.F., 1994)**:**

Risk Factors:

- Travel to endemic developing country
- Travel during transmission season
- Travel to rural areas
- Extended period of travel or residence
- Outdoor activities, especially in twilight period and evenings
- Advanced age and children below 15 years of age
- Pregnancy (risk to developing fetus)

Protective Factors:

- Repellents
- Protective clothing
- Residence in air-conditioned or well-screened areas

Strategies for Prevention and Control (JE-Guidelines, WHO/SEARO, 1996; Gubler et. al., 1989):

The strategy for prevention and control of JE includes these major components, viz., health education, vector control and immunization.

Training and Health Education

It is about developing national guidelines for the prevention and control of JE, and to develop simple information for the local residents on how to avoid exposure to mosquito bites. Community participation should be enhanced to encourage and motivate communities to participate in reducing breeding places of vector mosquitoes by filling of pools, weekly drainage of accumulated water and lowering of water levels in rice fields, etc.

Vector Control Measures

Short-term measures

The large-scale increase in vector densities and migration of mosquitoes suggest that the coverage that can be achieved by ground application space-spraying cannot be expected to achieve a significant impact on the overall mosquito population *per se* in these areas.

In high-risk areas that are relatively small, clearly defined, and where there is clear seasonally of JE activity, prevention of transmission can be achieved through control measures carried out prospectively, timed to coincide with the rise in vector densities so as to maximize the chances of interrupting the transmission cycle. Larviciding is impractical due to widespread breeding habitats.

Adulticiding by residual spraying or space-spraying is another option. Lists of potentially useful insecticides are included in **Annexes 4** and **5**. Aerial

application is the only measures likely to allow large-scale reduction of vector densities. However, the method may well be limited by its cost. The alternatives to aerial application -spraying/fogging/ULV- should be concentrated around peridomestic animal shelters and vegetation in order to achieve the maximum knockdown and residual insecticidal activity.

Applications at 3-7 day intervals should be employed. When available and where feasible aerial-ULV applications of insecticides could be made to cover large affected areas. The spraying operations carried out should be evaluated entomologically to ensure correct application. Applications should be made at dusk and dawn, if possible, to coincide with the periods of maximum activity of vector species.

Long-term measures

Long-term vector control measures should sustain low vector densities. The most reasonable vector control measures are:

(a) Water management in irrigated rice fields which allows periodical drying of fields (intermittent irrigation) to control vector breeding and is carried out in collaboration with agricultural and irrigation authorities. This may reduce breeding habitats.

(b) Use of insecticides to control agricultural pests, which may have an indirect influence in controlling vector populations.

(c) Selection of varieties of rice with minimum water requirements.

(d) Use of larvivorous fish. This experimental technique may be applicable in permanent water bodies. In relation to rice cultivation, the temporary nature of water availability and the vast acreage's of land involved pose problems in the operational aspects of this method. This method requires capability for mass-scale rearing and rapid periodic release of fish by a central/local authority, and/or involvement of individual communities in these activities.

(e) Other environmental manipulations include reduction by drainage, filling and weeding.

Immunization

JE immune plasma or globulin is not available commercially. At present three types of vaccine are in use for immunization against JE. **(Annex 3)**

Materials and Methods:

An epidemiological analysis of five years data on JE cases diagnosed both, on clinical and laboratory diagnosis was carried out. This data was collected by passive surveillance mechanism, be the hospitals rendering services to the JE affected people. Analysis was of retrospective and descriptive nature. The burden of JE in terms of its morbidity and case fatality was assessed. Age, sex, location and hospital specific incidence and case fatality information was furnished with help of two important indicators namely, ***case incidence*** (no. Of cases/100,000 risk area population) and ***case fatality rate*** (no. of deaths/no. of cases diagnosed). Data was analyzed with the help of MS Office using MS Word and MS Excel. MS Excel was also used to make the graphic representation.

Patients clinically diagnosed as encephalitis and admitted to almost all hospitals of the country, constituted the case material for the present study. The available data on age, sex, address, date of onset of illness, date of addmission to the hospital and the outcome of the illness of the encephalitis cases admitted to these hospitals was compiled, tabulated and analyzed for this study. The primary objectives of this study were to find out the morbidity and mortality of JE cases by age and sex, to characterize the outbreaks of JE, to determine seasonal and geographical distribution and the fatality rate by national as well as district wise, so as to make fruitful conclusions to help prevent and control JE in Nepal.

Results:

JE risk area and population:

This five years retrospective study of hospital based data on cases and deaths of JE revealed 24 districts (see **Table 1** and **MAP-1**) from Eastern, Central, Western, Mid-Western and Far-Western development regions of Nepal to be affected from JE. More than 11.5 million people are at constant risk of JE. Region wise risk area population is 4.2, 3.3, 1.8, 1.4 and .84 million for

Central, Eastern, Western, Mid-western and Far-western Regions respectively. Majority of the risk area population lives in Southern Plains bordering with Indian States of UP, Bihar and West Bengal. Bankey, Kailali, Morang, Bardia, Rupandehi, Chitwan, Parsa, Kanchanpur, Jhapa, Sunsari, Dang, Palpa, Dhanusha are the mainly affected districts.

Table 1: District-wise Distribution of JE Cases, Deaths and Case Incidence Rate (1993 – 1997)

Year	93			94			95			96			97		
District	Case	Death	CI	Case	Death	CI	Case	Death	CI	Case	Death	CI	Case	Death	CI
Jhapa	12	6	1.93	78	11	12.34	9	3	1.39	127	29	19.27	122	22	18.13
Morang	50	8	7.1	197	21	27.42	148	19	20.18	214	26	28.58	151	9	19.75
Sunsari	8	1	1.65	36	2	7.29	26	1	5.16	100	14	19.44	84	8	15.99
Saptari	24	6	4.94	14	0	2.82	1	0	0.19	15	2	2.9	14	2	2.65
Siraha	9	1	1.87	10	2	2.03	20	4	3.99	37	13	7.23	8	2	1.53
Udayapur	-	-	-	-	-	-	-	-	-	-	-	-	8	0	3.19
Dhanusha	3	0	0.52	30	10	5.18	45	8	7.61	16	4	2.65	25	5	4.05
Rautahat	-	-	-	-	-	-	-	-	-	-	-	-	1	0	0.21
Bara	-	-	-	-	-	-	2	1	0.44	3	1	0.65	-	-	-
Parsa	55	17	14.16	6	1	1.51	94	24	23.22	66	7	15.96	101	12	23.93
Makwanpur	2	0	0.6	-	-	-	4	0	1.17	-	-	-	-	-	-
Chitwan	35	8	9.47	37	8	9.8	48	10	12.46	43	6	10.93	65	7	16.18
Lalitpur	-	-	-	-	-	-	12	8	4.97	20	5	8.12	-	-	-
Kathmandu	5	4	0.71	16	3	2.22	11	2	1.49	18	3	2.4	27	6	3.32
Nawalparasi	9	4	1.97	9	3	1.93	5	0	1.05	8	2	1.65	32	2	6.47
Rupandehi	21	5	3.85	128	34	23.03	119	22	20.97	134	26	23.13	103	16	17.41
Kapilvastu	3	1	0.77	12	0	3.03	17	1	4.2	8	3	1.93	28	3	6.64
Palpa	-	-	-	23	10	9.14	38	8	14.4	29	5	11.06	29	6	10.83
Dang	4	4	1.08	72	16	19.08	26	7	6.75	11	6	2.79	8	3	1.99
Bankey	71	16	23.84	500	114	164.5	328	79	105.7	369	66	116.4	1110	146	343.1
Bardiya	26	3	8.59	343	88	11.1	47	6	14.89	40	7	12.41	120	12	36.48
Surkhet	-	-	-	-	-	-	-	-	-	-	-	-	9	1	3.51
Kailali	108	24	24.79	275	56	61.82	206	46	45.36	171	32	36.88	812	138	171.5
Kanchanpur	1	0	0.37	50	3	18.21	43	4	15.34	21	2	7.33	96	7	32.85
Total	446	108		1836	383		1246	255		1450	260		2953	407	

MAP 1: Districts with Reported Cases of JE.

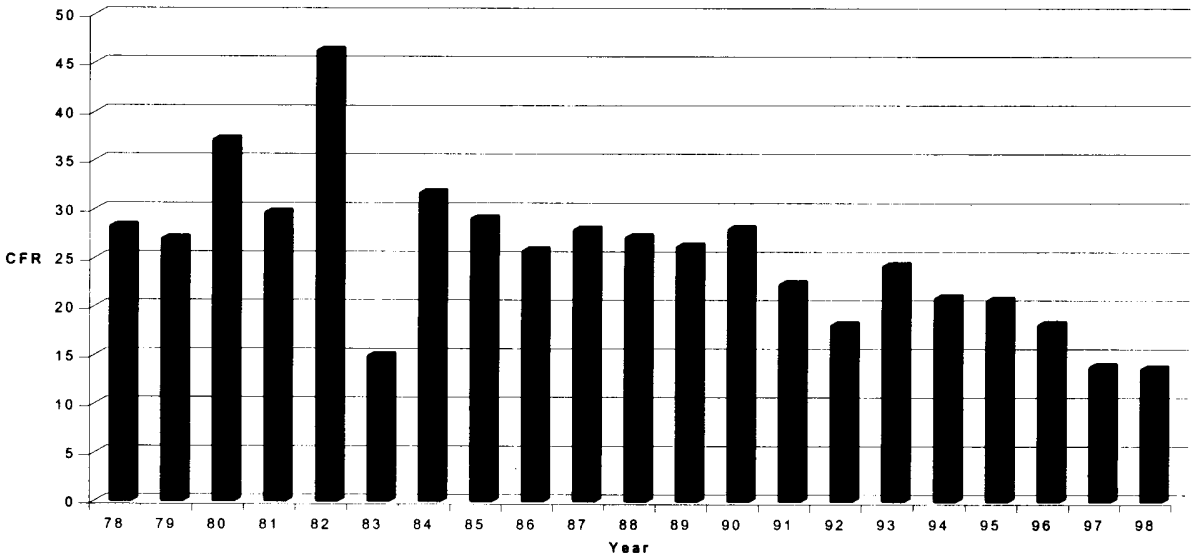
NEPAL, 1993-1997.

Source: EDCD/DHS/NoH

Morbidity and Mortality status:

During 1993-1997 health institutions engaged in the management of JE cases have reported a total of 7931 cases and 1413 deaths with a case fatality rate (CFR) of 17.82%. The highest number of cases were reported in 1997 and the lowest in 1993 (i.e., 2953 and 446 respectively). CFR was highest in 1993 and lowest in 1997 (i.e., 24.2 and 13.78 respectively). There has been more than 40% decrease in CFR from 1993 to 1997. Improved case management skills acquired by the health personnel of hospitals over the years, and early service seeking behavior developed among the residents of endemic areas as a result of health education campaign conducted at local and national levels, may have contributed to the reduction of CFR (**Fig.1**).

Figure 1. JE Case Fatality Rate (CFR) by Year. Nepal, 1978-1998.



The second highest number was reported in the year 1994. In 1995 and 1996 the number of cases was lower than in 1994 which may have happened because of the immunity acquired by significant proportion of population in 1994 which slowly eroded in successive years. Since the ratio of apparent versus in-apparent infection may range from 1:500 to 1:1000 (the average figure being 1:300-ICMR Bulletin, 1980), the vastness of acquisition of immunity acquired by large population of the endemic areas during epidemics may explain sudden decline in number of cases in between.

District wise distribution of cases:

Twenty-four districts from terai region from Jhapa in the east and Kanchanpur in the Far West were affected from JE. Almost 85% of the total cases were reported from 8 districts comprising Kailali (Far-Western Region), Bankey and Bardiya (Mid-western Region), Rupandehi (Western Region), Parsa (Central Region), and Morang, Sunsari and Jhapa districts (from the Eastern Development Region). During 1993-1997, 30% of the total cases were from Bankey and 20% from Kailali; 10% of the cases were reported from Morang district, 7% from Bardiya, 6.4% from Rupandehi, whereas Sunsari, Jhapa and Chitawan reported less than 5% of the total cases each. Rest of the districts reported 1 to 3 percent of the total cases each. Udaypur, Rautahat, Bara and Makwanpur districts reported less than 1 percent of total cases.

Case incidence (CI) during the period 1993-1997 (see **Table 1** above) ranged from 0.19 in Saptari (1995) to 343 in Bankey (1997). CI was always above 100 for Bankey except for the year 1993 when it was 24. Kailali revealed second highest CI (i.e. 171.5 in 1997). In Morang, Rupandehi, Bardiya and Chitwan districts, CI ranged from 7 (1993) to 29 (1996), 4 (1993) to 23 (1994,1996), 9 (1993) to 36 (1997) and 9 (1993) to 16 (1997) respectively. It is interesting to note that CI for JE in 1997 has decreased in comparison to 1996 in all districts of EDR whereas in the CDR, WDR, MWDR and FWDR the trend of CI is distinctly reverse. This shift of caseload from eastern to central and western terai in these two years needs further investigation and research (**Table 2**). Districts generally show increasing trend of CI over the years which may be explained by the improved surveillance efforts including improved referral of the cases to the hospitals. **Map-2** (next page) shows the JE case-incidence by district during 1997.

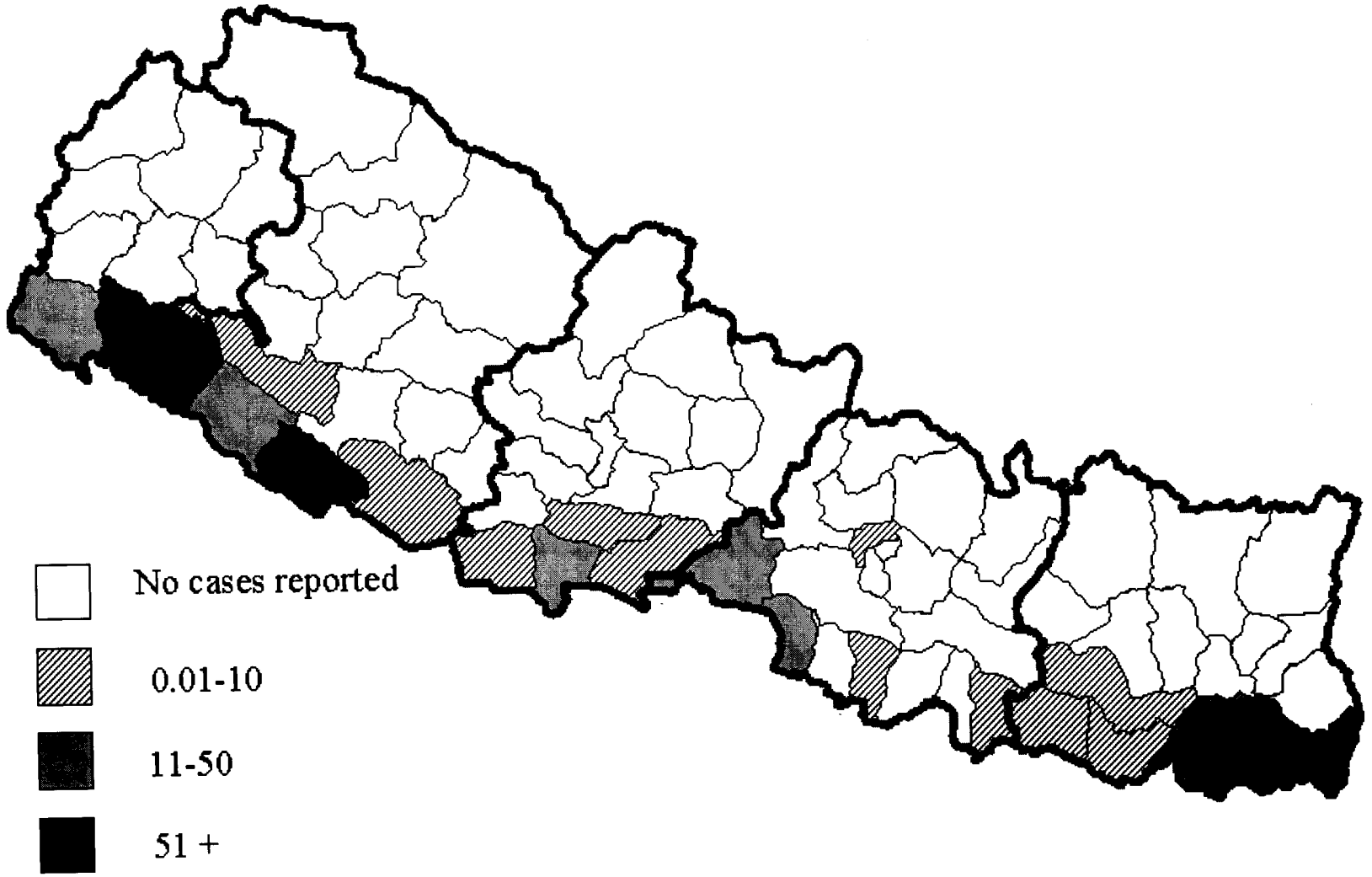
Table: 2 Region-wise Distribution JE Cases, Deaths and Case Incidence Rate (1993 – 1997)

Year	1993			1994			1995			1996			1997		
Region	Case	Death	CI	Case	Death	CI	Case	Death	CI	Case	Death	CI	Case	Death	CI
Eastern	103	22	3.43	335	37	10.93	204	27	6.52	493	84	15.43	387	43	11.86
Central	100	29	2.38	89	22	2.08	216	53	4.94	166	26	3.72	219	30	4.81
Western	33	10	2.02	172	47	40.02	179	33	10.52	179	37	10.3	192	27	10.82
Mid-western	101	23	8.38	915	218	74.36	401	92	31.92	420	79	32.74	1247	162	95.22
Far-western	109	24	15.47	325	59	45.18	246	50	33.5	192	34	25.61	908	145	118.6
Country	446	108	4.15	1836	383	16.74	1246	255	11.13	1450	260	12.68	2953	407	25.3

Hospital wise distribution of cases and deaths:

Bheri Zonal Hospital reported the highest number of cases and deaths during this period (**Fig. 2**), constituting the total cases 2087 and the total deaths 394, with a CFR of 18.9%. This was followed by Seti Zonal Hospital with a total of 786 cases and 169 deaths, CFR being 22%. Koshi Zonal hospital reported 760 cases and 83 deaths with a CFR of 11%. CFR was 21% for Lumbini Zonal Hospital wich reported a total of 494 cases and 102 deaths. Similarly, other major hospitals which provided service to the JE patients in different districts were (in decresing order of case load): Bardiya District Hospital, Lumbini Zonal Hospital, Tikapur PHC, Narayani Zonal Hospital,

MAP-2 **JE: Case Incidence (x 100,000 population). Distribution by District. Nepal, 1997.**



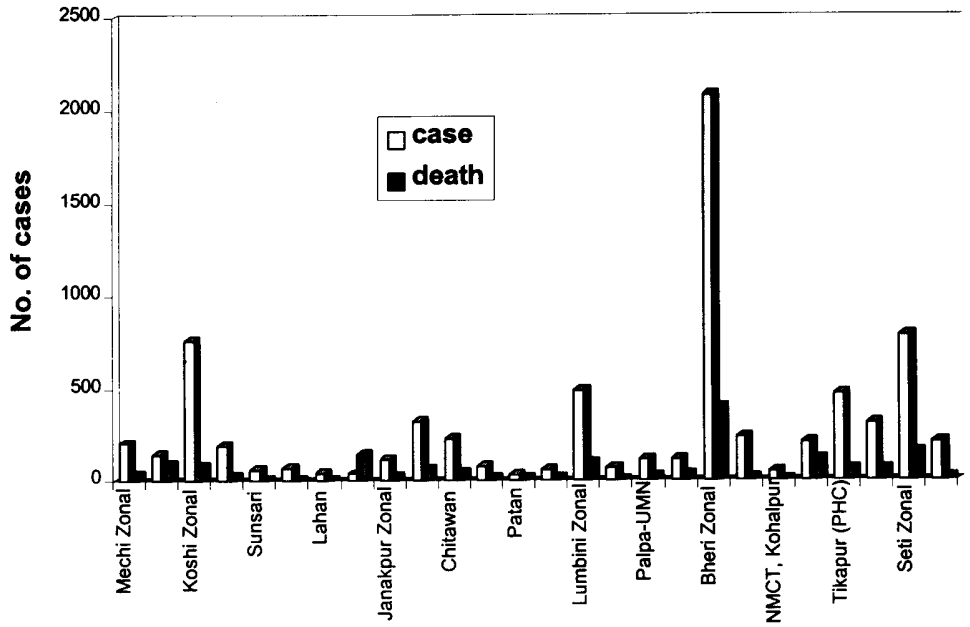
Source: EDCD/DHS, MoH

Bhagni PHC, Nepalgunj Medical College Teaching Hospital, Bharatpur Hospital, Mahakali Zonal Hospital, Mechi Zonal Hospital, BPKIHS Hospital, AMDA Hospital, Dang Hospital, UMN Palpa Hospital and Janakpur Zonal Hospital (**Table 3**, below)

Table 3: Case load, deaths and CFR of Major Hospitals (1993-1997):

Hospitals	Cases	Deaths	CFR (%)
BHERI Zonal	2087	394	19
Seti Zonal	786	169	22
Koshi Zonal	760	83	11
Bardiya	576	116	20
Lumbini Zonal	494	102	21
Tikapur PHC	471	62	13
Birgunj	322	61	20
Bhagni PHC	312	65	21
Nepalgunj Medical College Teaching	289	27	9
Bharatpur, Chitwan	228	39	17
Mahakali Zonal	211	16	8
Bhadrapur	206	32	16
BPKIHS Teaching	189	24	13
AMDA Damak	142	39	27
Dang	121	36	30
UMN Palpa	119	29	24
Janakpur	119	27	23

Fig. 2 Average cases and deaths of JE by Hospitals Nepal, 1993-1997



Region specific distribution of JE cases and deaths:

Region specific analysis of JE cases and deaths revealed that in this period of 5 years, approximately 40% of the cases were reported from hospitals of the MWDR. After MWDR, FWDR, EDR, CDR and WDR have 22, 19, 10 and 9.5 percent of the total reported cases respectively (**Table 4**). The number of cases reported by Region during the period 1993-1997 was 3084, 1780, 1522, 790 and 755 for the Mid-West, Far-West, Eastern, Central and Western Development Regions respectively. Similarly, 574, 312, 213, 160 and 154 deaths were reported for the regions in the same order as mentioned for morbidity above. Except for the year 1993, MWDR always reported the highest number of cases among the different regions. Case incidence (CI) was always higher for the FWDR except in 1994 and 1996.

Table 4: Percentage case-load by region (1993-1997)

	No. of case	No. of death	% Case	% Death	CFR
EDR	1522	213	19	15	14
CDR	790	160	10	11	20
WDR	755	134	9.5	9	20
MWDR	3084	524	39	41	19
FWDR	1780	312	22	22	18
Total	7931	1413	100	98	18

The maximum number of JE deaths during the five years period was reported from the MWDR (i.e. 41%). After MWDR, mortality percentage for JE is as follows: FWDR 22%, EDR 15%, CDR 11% and WDR 9%.

Case fatality rate has been higher in the CDR and WDR (i.e. 20%) followed by MWDR (19%), 18% in the FWDR and 14% in the EDR. Comparing the above numbers with the national CFR average of 17%, the CDR and WDR must put emphasis on quality case management proper nursing care of JE patients by providing adequate training for health personnel.

Based on burden of morbidity in the regions, MWDR, FWDR and EDR need prioritized attention for the implementation of disease prevention and control program.

Age-specific distribution of cases and deaths:

Age specific analysis of JE cases and deaths has revealed that 60% cases belonged to the age group below 15 years. Case fatality rate (CFR) was higher (i.e., 21%) for the 0-4 year age group, followed by 20% for the 15+ age group, 16% for the 5-9 year age group and 15% for the 10-14 year age group.

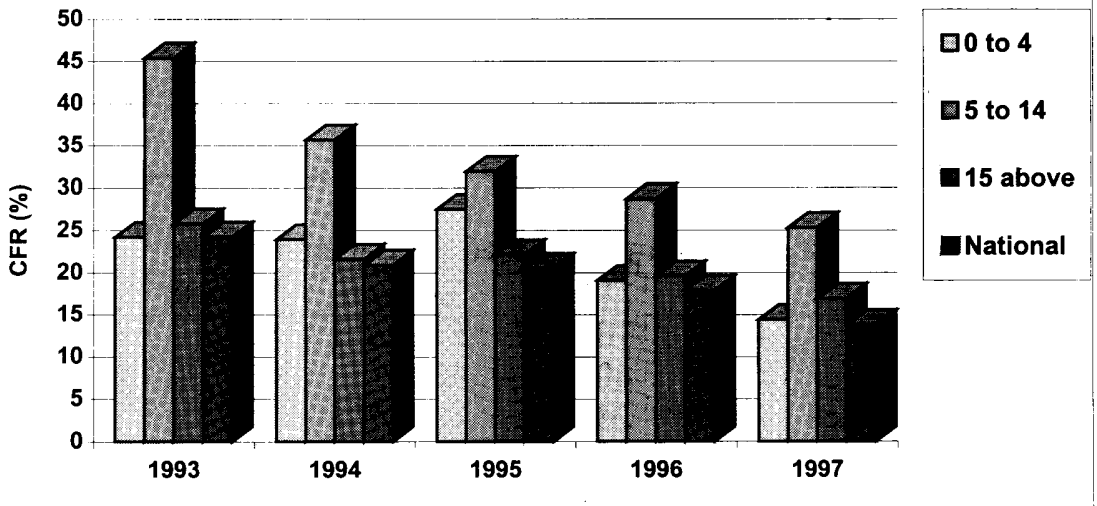
It is interesting to note that age specific CFR over the years shows decreasing trend in the 0-4 year age group (except in 1995 when CFR was 27.46): from 24.17 in 1993 to 14.37 in 1997 which is a 40% decrease in CFR (**Table 5**). The age group 5-9, also shows decreasing trend over the years from 30 in 1993 to 12 in 1997. Same decreasing trend is also observed in the 10-14 years age group (from 19 in 1994 to 13 in 1997); CFR in the year 1993 was 15 for this age agroup. Age group above 15 also showed a decreasing trend: from 26 in 1993 to 17 in 1997.

Table 5: Age specific percentage load of cases and deaths (1993-1997)

Age	Cases	Deaths	% Case	% Death	CFR
0 – 4	1159	239	17	17	21
5 – 9	2154	335	27	24	15.5
10 – 14	1489	230	19	16	15
15 +	2781	555	35	39	20
Age not mentioned	348	55	4	4	16
Total	7931	1414	100	100	10

In the 5-9 year age group, CFR has decreased by 60% from 1993 to 1997. This significant decreasing trend (**Fig. 3**) in CFR in the age groups 0-4 and 5-9 could have been caused by the priority given by hospital management to the patients of these age groups, where improved nursing care may have played an important role.

Fig. 3 Agewise CFR of JE, Nepal, 1993-1997



Sex-specific distribution of cases and deaths:

A total of 4495 male and 3358 female were affected with JE during the period 1993-1997, compraising of 57% male and 43% female, being the male:female ratio of approximately 1.3:1 (**Fig. 4**); 55% of the deaths were reported to be among males. The deaths among males and females were 783 and 606 respectively. Case fatality rate for male was 17% and 18.0% for female (**Table 6**). Until 1994 the case fatality rate for male was compartively higher than that for female, but after that it has showed a reverse trend, with the case fatality rate for female higher than that for male. The higher number of cases and deaths in males can be explained in terms of high outdoor mobility of males and their exposed body parts in comparison to females.

Fig. 4 Cases of JE by sex, Nepal, 1993-1997

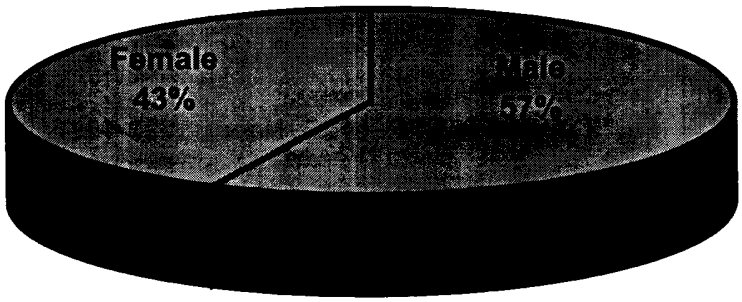


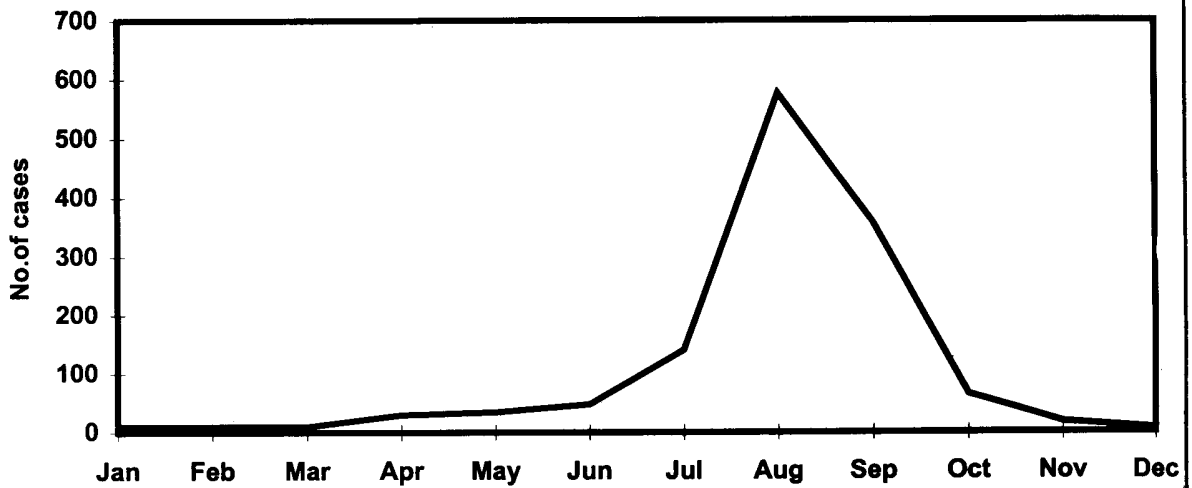
Table 6: Sex specific percentage case load of cases and deaths

Sex	Cases	Deaths	%Case	%Death	CFR
Male	4495	783	57	55	17
Female	3358	606	42	43	18
Sex not mentioned	78	24	1	2	30
Total	7931	1413	100	100	

Month-wise distribution of JE cases:

Every year of the studied period (1993 to 1997), cases started building up in the months of April-May to reach a peak in the months of August and September. From October onwards, cases started to decline, leveling off in the month of November **(Fig. 5)**. Seventy-five percent of the total number of cases were concentrated in the period ranging from June to October. This seasonality in the distribution of JE cases has been adequately substantiated by many studies (Bastola et.al. 1998, Dr. Tyagi WHO REG Forum).

Fig. 5 Average monthwise distribution of JE cases, Nepal 1993-1997



Discussion:

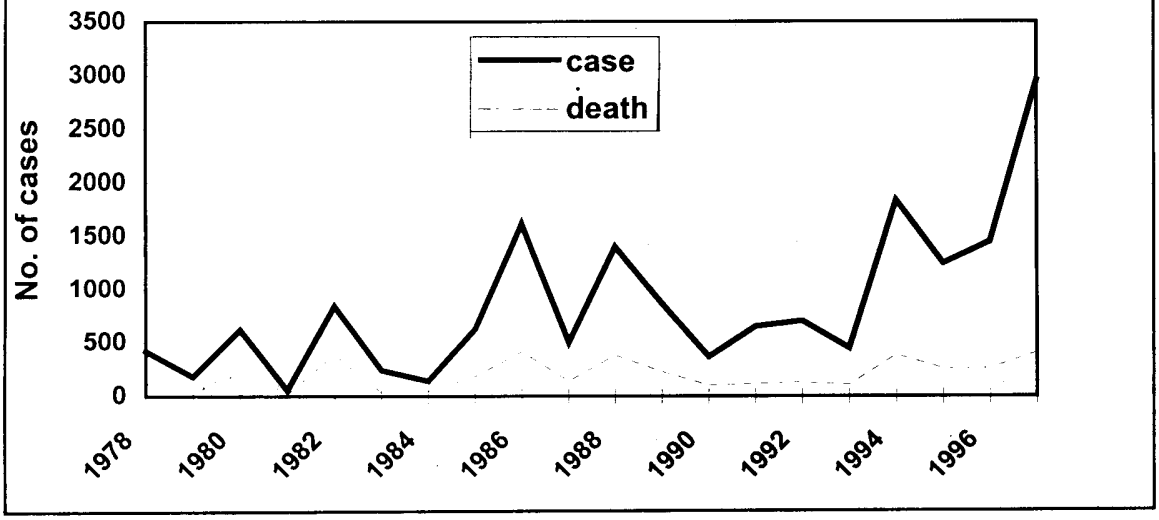
Six hundred thirty eight samples from individuals visiting Tribhuvan University Teaching Hospital were tested for antibodies against Japanese Encephalitis Virus (JEV) using neutralization method, out of which 15.4% (98/638) were found seropositive (Kubo et.al., 1996). In addition to this, in the Country Report presented by the Epidemiology Division/DHS/MoH during the WHO-SEAR/WPR Bi-regional Meeting on Control of Communicable Diseases in Beijing (1997), it mentions that a total of 229 serological and CSF samples of encephalitis cases were examined for JEV antibodies at the Zoonosis/Arbovirus Laboratory of the National Institute of Communicable Diseases (NICD) India and in the Institute of Medicine (IoM) in Kathmandu. Of these, 54% (123/229) samples were positive for JEV antibodies. Five percent (11/229) were found positive for *P. falciparum.*

Moreover collaborative studies between the Ministry of Agriculture (MOA), MoH, US Armed Forces Research Institute of Medical Sciences (AFRIMS) Bangkok, a British Army Medical Team and the London School of Hygiene and Tropical Medicine, confirmed that JE virus was the etiologic agent during the 1985-86 epidemics of encephalitis in Nepal. JE virus isolates were obtained from human brain and cerebrospinal fluid samples, as well as from a sentinel pig and a pool of 100 *Culex* female species. One hundred

nineteen out of 124 suspected clinical JE infections were confirmed by IgM capture ELISA test to be JE (Gubler et. al., 1989). Virological studies of serum and CSF confirmed that JE virus was the causative agent of the 1986 epidemic of JE in Nepal (McCallum, J.D., 1991). This limited sample collection and test done for JE antibodies detection presumably was because of scarcity of reagents and slilled manpower in the country.

Based on clinical and epidemiological features of outbreaks and above occasional laboratory confirmations, it can be said with a fair degree of certainty that the outbreaks of encephalitis that starts from June to October (**Fig. 6**) every year, are related to hyperendemic transmission of JEV.

Fig. 6 Total No. of JE cases and deaths, Nepal 1978-1997



JE has prevailed as an important public health problem since the last twenty years (**Fig. 6**, above) imposing tremendous burden to the health system, as large number of patients who recover will suffer from varying degrees of brain damage and consequent sequelae. The disability requires life long care, either in specialized institutions or at home, thereby adding considerably cost to the health care system of the country.

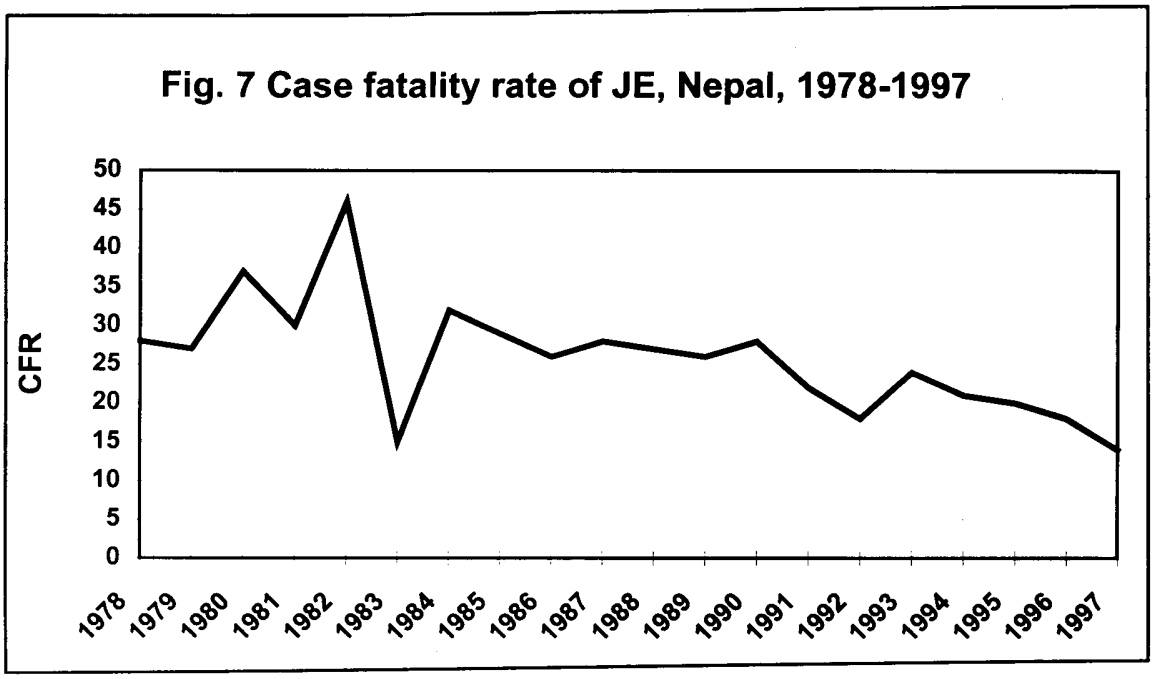
During 1978 to 1997, different hospitals in Nepal reported 17,172 cases and 3987 deaths of viral encephalitis (**Table 7**). The epidemiological analysis of the case-incidence trend, shows a clear step ladder pattern increase with an

epidemic peak in every 1-5 years (see **Table 2** and **Fig. 6**). Since 1978, each successive epidemic has generally been larger except the epidemic of 1988. Highest number of cases were reported in 1997 when 2953 cases with 407 deaths occurred. Annual incidence rate ranged from 0.2/100,000 population in 1981 to 25.3/100,000 in 1997, with the CFR ranging from 46.26 percent in 1982, to 13.78 in 1997 (**Fig. 7**, below).

Table: 7: Total Number of JE Cases, Deaths and Case Fatality Rate (CFR) (1978 - 1997)

Year	Cases	Deaths	CFR
1978	422	119	28.19
1979	182	49	26.92
1980	622	231	37.12
1981	54	16	29.62
1982	843	390	46.26
1983	242	36	14.87
1984	142	45	31.69
1985	629	183	29.09
1986	1615	415	25.69
1987	502	140	27.88
1988	1403	380	27.08
1989	868	227	26.15
1990	365	102	27.94
1991	650	114	22.3
1992	702	127	18.09
1993	446	108	24.21
1994	1836	383	20.86
1995	1246	255	20.38
1996	1450	260	17.93
1997	2953	407	13.78
Total	**17172**	**3987**	**23.2**

This successive increase in morbidity over the years may have resulted from different factors: 1) real increase in the number of JE cases; 2) increased awareness about the disease and its control methods among the residents of endemic areas leading to higher attendance of patients to the hospitals; 3) increased diagnostic and referral awareness among the health personnel working in the endemic areas, and 4) higher attendance of patients of JE to the hospitals because of the confidence they have developed in the hospitals. In this connection it is also important to review the JE prevention and control activities endorsed from the national vector borne disease control program for its appropriateness.



The decreasing trend of CFR may be the result of improved early service seeking behavior developed by the local residents and better case management provided in the different clinical institutions. Proper nursing care is critical for better case management. It leads into reduced mortality among JE patients and even comatose patients can be nursed in the general ward instead of CCU, thereby reducing the hospitalization costs significantly (Dr. Chan Kim Yong's experience in Singapore, personal communication). Different authors have encountered that Nursing Staff in hospitals of hyperendemic areas are well aware of proper and high quality nursing care and are keen to upgrade their knowledge and skills on this issue.

This study substantiates the findings of other studies (Prasad Rao et. al., 1982) that JE is prevalent in the rice-field ecosystem of rural agricultural areas, which makes an ideal breeding ground for *Culex* mosquitoes. Bankey, Bardia, Kailali, Rupandehi and Morang districts, which are hyperendemic for JEV transmission, also represent the paddy field ecosystem with abundant *Culex* species and amplifying hosts like pigs and migratory birds.

More than 24 districts of Nepal starting from Jhapa in the east to Kanchanpur in the far-west are constantly affected by Japanese Encephalitis (**Map 1**). The latter has established its endemicity in outer and inner terai areas of the country bordering with Bihar, Uttar-Pradesh and West Bengal states in India, which are also significantly affected by this disease

(Bhardwaj, 1981). JE has maintained enzootic forms under specific ecological conditions on either sides of the border (Joshi,1983; Sehgal,1989; Ogawa et. al., 1992). As per WHO classification (JE-Guidelines, WHO/SEARO, 1996), in Nepal, JE has acquired a regional-seasonal outbreak epidemiological pattern. It is evident that not only has the number of reported cases of JE increased, but the known geographical distribution of the virus in the Indian sub-continent has expanded as well. The reasons for this apparent expansion are not fully understood.

It is interesting to note that the case incidence is higher in the MWDR and FWDR than in the other regions. The following arguments need to be meticulously assessed for their objectivity in terms of explaining the preponderance of cases in MWDR and FWDR:

1) *Baduwa Majtoor* (Bonded labor) who work and reside in those regions. Because they stay long outdoors to work, are economically poor, are not well clothed and thus, their extremities and other body parts are exposed and are possibly malnourished, they carry a high risk of being bitten by infected mosquitoes and being infected with JE.

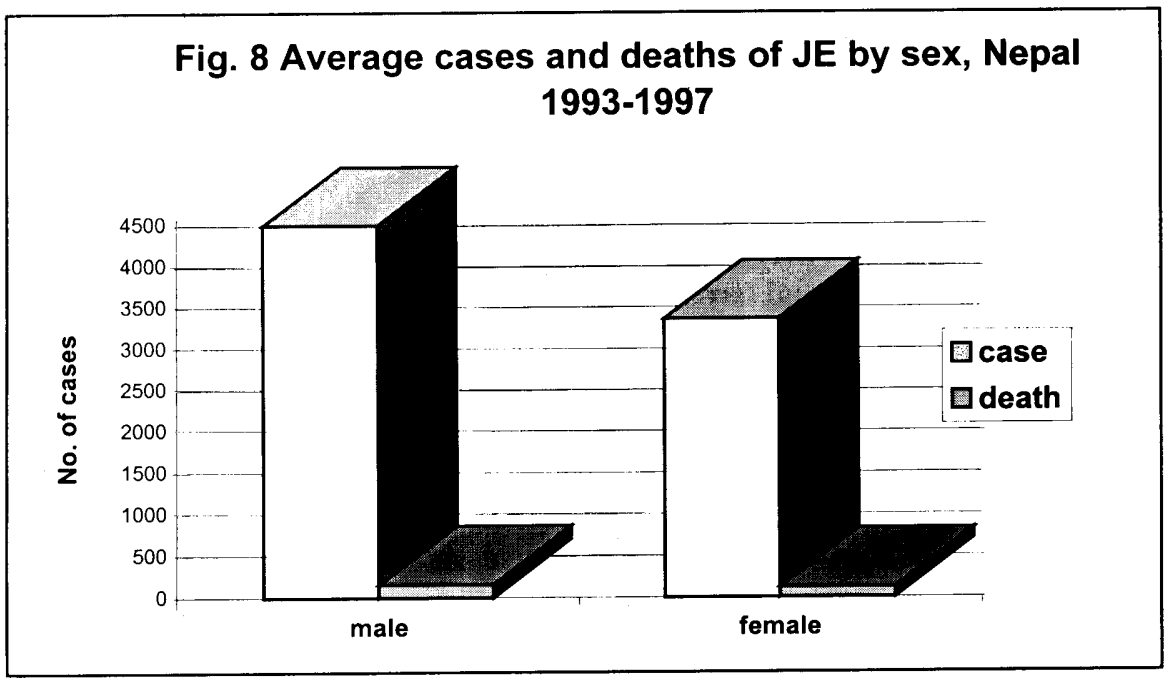
2) These regions may have relative abundance of amplifying hosts specifically pigs and birds.

3) These areas may have socio-cultural rituals and festivals taking place in dusk and dawn which maximize the chances of man-mosquito contact because of their enhanced mobility at that time.

Children bear the major brunt of this disease. JE is often severe and has a high mortality rate in young children and elderly people (Monath, T.P.,1986; Rosen, L., 1986). Neurological deficits and behavioral problems following encephalitis are well known (Goto, A., 1957; Piper, S.J.L., Kulan, L.T., 1958). This study revealed that mortality is higher in young children. Significant number of children died during the acute phase, mainly within the first three days of admission (personal communication with medical officers). Some children were found in the chronic phase developing neurological deficit and behavioral problems (personal communication with Dr. Kidwai, Nepalgunj hospital). The pre-school age (0-4 years) and the school age (5-14 years) groups were mainly affected. The findings of this study coincide with other studies as far as high mortality in the age group of

0-4 years is concerned. Majority of cases (>60%) and deaths (>55%) were concentrated in the age group below 15 years.

The average CFR for age group 0-4 years, 5-14 years and 15+ for the studied period was 20.6%, 15.5% and 15.4% respectively. The CFR for children below 15 years of age was 16.7%. There were some record of JE cases and deaths reported from two health institutions without specifying age group and gender, and while analysing, these figures were excluded (**Fig. 8**). Children's compromised immunity as a result of concurrent infections and infestations, compromised nutritional status and nudity of children in the rural areas, may have played a role for the increased burden of morbidity and mortality in this group.



Hilly areas also reported JE cases. Hospitals, namely Patan and Kanti Children Hospitals in Kathmandu, Palpa Hospital, Tansen, were found to be providing service to this kind of cases. This substantiates the changing pattern of JE with its sporadic incidence in Hills and Mountains concluded by other studies as well (Takashi, K. et.al., 1996).

Reports (Joshi, D.D. et. al., 1998; Reuben et. al., 1992) are there that *culincine* mosquitoes feed on bovines where there are no pigs and ducks.

This situation hypothesizes that the epidemiological pattern of the disease transmission could be cattle-mosquito-cattle cycle and buffallo-mosquito-bufallo cycle. In addition to the above since there was no confirmation of seropositivity against JE virus in sentinel pigs from Terai (Joshi D.D., 1998), which indicates the need of studying seroconversion status of animal reservoirs with their relation to possible change in pattern of endemicity in Nepal.

Case incidence was higher in males than in females (**Figs. 4 & 8**) which coincide with the findings of other studies (Joshi D.D. et. al., 1998). This is believed to happen because of the fact that males work outdoors more than females and their body parts are more exposed than females.

Each year outbreak of viral encephalitis occur consistently in the rainy season starting from June-July and reaches its peak in Auguest-September and thereafter, gradually subsides and this pattern has been observed throughtout the country (**Fig. 5**).

A rapid specific diagnosis of sporadic disease with JE is not yet possible in Nepal. In an epidemic situation, cases are diagnosed based on clinical history and findings of typical signs and symptoms, detailed clinical examination, CSF analysis and the epidemiological picture. For the final diagnosis of the aetiology of the epidemic, we need to have laboratory facilities in order to isolate the virus or demonstrate the presence of a rising titre of the specific antibodies which is considered confirmatory diagnosis of Japanese encephalitis (Burke, D.S., Leake, C.J., 1988).

Since the Terai areas of Nepal have free border with India and a large number of people cross the border freely every day, there is high chances of getting malaria infection in the coinciding period. Taking this into consideration blood slides from 187 patients were taken to exclude malaria out of which 17 were found to be positive *P. Falciparum* and 6 for *P. Vivax.* (IoM, unpublished data). So it would be advisable to have blood smear tested in each patient to exclude malaria infection as a routine process.

Japanese Encephalitis has established itself as an important public health problem in Nepal. Although the first epidemic was reported only in 1978, experts believe that JE infections were present in Nepal even before. It is

possible that JE virus has always been present in this country, but because of its occurence in animals and low severe disease incidence in humans, this disease was not given the status of clinical entity (Gubler et. al., 1989). But later, when major demographic changes occurred in 1960s and 1970s when massive influx of people took place from mountains to terai, the paddy ecosystem expanded dramatically, the JE problem and its impact became prominent.

This disease has raised public health concern not only because of its discernable morbidity and mortality over the years but also because of its impact on national development and socio-agricultural productivity. In an average more than 1500 clinical cases of JE occurred every year during 1993-1997. As mentioned earlier it is estimated that the ratio of apparent and inapparent infection is 1:20-1:1000. Thus, it can be estimated that 30,000 to 1,500,000 JE infections may have occurred every year in this study period. These infected people may not show severe neurological manifestations but may suffer from mild viral syndrom at least for some days. So the severe disease of more than 1500/year in number, death of about 300/yr and the above estimated pool of human infections may have a significant socio-economic impact in the rural community of Nepal which need further assessment through the development of appropriate resource propossal.

Japan and other countries have successfully controlled the problem of JE by applying immunization among risk groups by using different types of vaccines (**Annex 3**), incresing the living standard of residents, intermittent irrigation schemes (water management), air spray during epidemic and pre-epidemic periods, immunization of pigs and systematic piggery (Gubler et. al., 1989). Economic and technical resources of Nepal has not allowed us to consider the above all measures for the control of JE.

The proven effective method of JE prevention, i.e. immunization of children is the only way to be considered for implementation.After immunization annual number of cases have been found to be reduced more than 8-fold compared with previous years and upto 88% of JE cases detected after vaccination were found among the unvaccinated where as swine antibodies and mosquitoes population indicated continued transmission of virus in the study area (Tran Van Tien et. al., 1991-1992). But for a country like Nepal

cost-implication would be an issue of concern. China has been very suuccessful in producing and using cheaper vaccines. A cost effective (US$ 0.03 cents/dose) live attenuated vaccine made from the SA-14-14-2 strain, with its two doses has demonstrated efficacy of about 95%. Protection from the live attenuated vaccine lasted for at least 5 years following an immunization schedule for either one or two doses (Yu Yongxin, 1995). It would be feasible to implement childhood immunization (>60% of cases of JE belong to age group <15 yrs) with this vaccine meticulously considering the issues of virus strain, immunogenicity, cost implication, and objective delineation of the high risk areas with hyperendemic transmission of JE genuinely requiring vaccination. Experts (Chung Yeun Jun et. al., 1996) have concluded the evolutionary divergence of JE viruses isolated in Korea from the original Japanese and Chinese strains which further necessiates the need for carrying a specific evaluation study of immunization before incorporating it into childhood routine immunization program. This has tremendous implication as far as the effecacy of the vaccines under use is concerned.

Lately HMG/N through EDCD/DHS has considered to carry out an evaluation of the chinese vaccine to demonstrate its efficacy and effectiveness in the local context in a demonstration project before it is introduced into routine childhood immunization. This is in line with the recommendations made by National and International experts in the National Workshop of VBDs (Con. Recom National Workshop on VBDS 1997). The main objectives of this evaluation study are:

1. Demonstration of reduction of JE cases in a vaccinated district in comparision to otherwise similar unvaccinated district.
2. Measurement of risk of acute neurological infection due to the vaccine.
3. Compare immunogenicity and efficacy of a short interval (three months), two dose immunization schedule to conventional long interval (one year) to the schedule used in China.
4. Measure immune responses in infants vaccination at nine months:
   a) to evaluate effects of material immunity on immune response at this age and
   b) to determine if simultanous administration with measles vaccine is safe and if it interferes with the immune response to either antigens.

Despite the difficulties and resource constraints, National Program of Vector Borne Diseases have come up with some implementable recommendations for the control and prevention of JE which was throughly discussed and finalized by the experts in the field of control and prevention of JE (Con. Recom., National Workshop on VBDS, 1997). They are as follows:

Treatment and Management

Following steps are recommended for the management of Japanese encephalitis cases in Hospitals:

- No specific treatment is indicated.
- Manly supportive and symptomatic treatment is recommended.
- Meticulous nursing care for comatose patient is essential.
- Avoid indwelling catheter in conscious patient.
- A Ryle's tube should be introduced if the patient is unconscious.
- IV fluids should be avoided.
- Dextrose solutions should be considered in case of signs / symptoms of dehydration.
- No Antibiotics should be given unless there is a strong suspicious of secondary infection.
- Dexamethasone should be avoided.
- Mannitol should he used only in case raised intracranial pressure. It should be given in dose of 100 ml 20% Mannitol 8 hourly for 48 hours (Pediatric dose: 1.5 gm./kg.dose can be given 8 hourly).
- For convulsion give either Phenobarbitone or diazepam.

- Case management shouldn't be influenced by patients' relatives. Encourage the cooperation of the patients' party by making them aware of treatment policies like: no IV fluids, no antibiotics and no dexamethasone for which education materials should be developed for the country.

- Control trail in endemic areas should be undertaken at Bheri Zonal Hospital, Nepalgunj and Koshi Zonal Hospital, Biratnagar, to evaluate the effectiveness of dexamethasone and mannitol in case management of Japanese encephalitis.

- Continued Medical Education (CME) type of training for doctors working endemic areas should be given just before the outbreak season of Japanese encephalitis.

- Considering the workload during the months of outbreaks in district Hospitals provision of additional manpower should be made. This is recommended to be mobilized by the respective Regional Health Directorates within the region and if not possible request should be sent to the DG/DHGS for such support.

Prevention and Control

- Considering the wide dispersement of vectors, sporadic pattern of occurrence of JE cases and outdoor feeding behavior of JE vectors, insecticide spraying as a strategy to control JE vector was not recommended. However keeping in view the immediate suppression of infective vectors ultra low volume (ULV) or thermal fogging was recommended.

- So far, mass vaccination of children against JE has been the effective method of JE prevention in human population in many countries. Trial of vaccinating children in JE prone/endemic areas was recommended.

- In order to increase community participation, it was recommended that health education be given to people to create awareness on the seriousness of the JE problem and its consequences. The establishment of necessary coordination between the National Health Education Information and communication Center (NHEICC) and PHOs was

recommended for the development of IEC materials in Nepali and local languages. The notion of development of health education message with the purpose of developing early health seeking behavior of the residents of endemic areas was also accepted.

- Cleaning of urban and rural environments close to human dwellings draining out stagnant water and filling can be most helpful in avoiding mosquito-breeding places. This may help in curtailing the mosquito density and thus preventing or even stopping the JE transmission. Therefore it was advised that efforts be directed to encourage the local VDCs / Municipalities and District Development Committees to carry out such actions.

The current status of knowledge about JE does not leave any room for complacency for the planners, programmers and scientists engaged in the prevention and control of JE in Nepal. There are areas where much work needs to be done in coherence with the donor partners working in the research, prevention and control of JE. Some of the area which need meticulous attention are as follows:

1. Strengthening of epidemiological surveillance including diagnostic capacity and capability of cases with the development of geographical mapping of the foci of different level of endemicity
2. Isolation of local strains of JE virus which may have implication while considering the JE vaccination program in the country
3. Meticulous study of vector biology and bionomics to develop appropriate vector control methods
4. Appropriate design of a integrated Vector Control
5. Study of socio-economic factors associated with JE transmission.
6. Development of simple, sensitive and socio-culturally acceptable health education messages to impart necessary behavioral changes in the residents of JE endemic area by enhanced community participation. The latter has crucial role to play as far as non-chemical JE control strategies are concerned.
7. Coordination between Department Agriculture, Irrigation, Education and Health Services for the consideration of implementation of other possible measures of prevention and control of JE in Nepal.

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ANNEX 1

The typical case of encephalitis progress through 4 stages as follows:

Prodromal stage (2-3 days) - Characterized by an abrupt onset of high fever with headache; other non-specific symptoms include malaise, anorexia, nausea and vomiting.

Acute encephalitis stage (3-4 days) - After a few days if non-specific symptoms, during which the patient maintains a high-grade fever, signs and symptoms of neurological involvement appear. The essential features consist of a change of consciousness, ranging from mild clouding of mental status to confusion, delirium, disorientation, stupor, semicoma of coma. Convulsions, generalized or focal, also are a common presentation. Weakness of extremities and neck stiffness are frequently observed. Less common neurologic manifestations include tremor, abnormal movements, and cranial nerve palsies. Some patients present with thick, slow speech or abnormal behavior which may be interpreted as acute psychosis.

During this stage, there are signs of upper motor neuron involvement (hyper-reflexia, ankle clonus and extensor plantar responses) and sometimes, signs of meningeal irritation (neck stiffness and Kernig and Brudzinski signs). Papilledema is found in less than 10% of the patients. Hypertension id reported in a few patients.

Cerebrospinal fluid (CSF) examination reveals an elevated leukocyte count between 300-1,000 cells/mm^3 with a predominance of lymphocytes. CSF glucose usually is normal but the protein content can be slightly elevated. Fatal cases usually progress rapidly and deaths occurs in this stage.

Subacute stage (7-10 days) - In uncomplicated cases, fever defervescence and neurological involvement lessens over a period of one to two weeks. Improvement in neurological manifestations are seen in mild to moderate cases. In severe cases with paralysis of the extremities of in patients who do not gain consciousness, superimposed bacterial infections are common. Orthostatic pneumonia, urinary tract infections, and bed sores are among the most common infectious complications, and sometimes they became life-threatening if not treated properly.

Convalescent stage (4-7 weeks) - Further improvements on neurological deficits are seen during this stage. Mild cases may make a complete recovery. More than half of the patients have sequelae, which may be permanent, although they typically improve with time.

Outcome

The case-fatality ratio among cases in Thailand is now 15-20% and has declined from rates as high as 40% previously. Poor prognosis is reported in patients who are comatose on admission or have uncontrolled convulsions. Sequelae inlcude deficits in motor function, other neurologic deficits and changes in behavior and intellectual function, as shown in Table 1.

Table 1
Sequelae in patients recovery from Japanese encephalitis

Motor sequelae	Behavioral sequelae
Limb paralysis 34 - 44%	Aggressiveness 72%
Fine motor deficits 72%	Depression 38%
Abnormal movements 5.5 - 8%	Attention deficit 55%
Other neurologic sequelae	Intellectual sequelae
Epilepsy 16 - 20%	Abnormal intelligence 42 - 72%
Memory deficit 46%	Borderline intelligence 33%
Cranial nerve paralysis 16%	Mild mental retardation 11%
Blindness 2%	Moderate mental retardation 11%

ANNEX 2.

Protocol for the collection, storage and transportation of Human Specimens for the serological diagnosis of Japanese encephalitis.

Blood

Venous blood specimens should be collected from suspected JE cases as early as possible in the acute phase, immediately after the admission to the hospital or attendance at the clinic. A second convalescent specimen should be collected later on at the time of discharge.

- Collect 5 ml of blood aseptically.
- Keep the blood at room temperature for about 15 minutes to clot.
- Then at 4°C the clot is allowed to retract.
- Separate the serum and keep in a tightly stopped sterile container.
- Seal the container with adhesive type (patients name, identification number and the date of collection should be written clearly with a pencil or indelible ink or typewritten).
- Place the serum in a refrigerator for storage (not in deep fridge) prior to transportation to the laboratory.

CSF Specimen

It should be collected aseptically and placed in labeled container as mentioned above.

Storage and transportation of the specimens:

- Specimens should be placed in a refrigerator at 4°C as soon as possible after the collection. Do not fridge the specimen. They should be dispatched at the earliest possible opportunity in a large thermos or in a ice box to the National Public Health Laboratory, Teku, Kathmandu.
- They can either be airfreighted or sent by through a courier or hand.
- The courier should drain the water and replace ice as and when required during the journey.

ANNEX 3

Japanese Encephalitis Vaccines
(Adopted from JE, WHO/SEARO, 1996)

Vaccine Description	Substrate	Viral Strains	Manufactures
Inactivated	Mouse brain	Nakayama, Beijing-1 (P1)	India: Central Reserch Institute Japan: Biken, Chiba, Denka, Katetsu-ken, Kitasato, Saika-ken, Takeda Korea: Green Cross Taiwan: National Institute of Preventive Medicine Thailand: Government Pharmaceutical Organization
Inactivated	Primary hamster kidney cells	P3	Vietnam: National Institute of Hygiene People's Republic of China: Beijing, Shanghai, Wuhan and Changchun Institutes of Biological Products
Live, attenuated	Primary hamster kidney cells	SA14-14-2	People's Republic of China: Chengdu Institute of Biological Products

Annex 4

Insecticide suitable for residual spray application against mosquito vectors

Insecticide	Chemical type [a]	Dosage of ai.[b] (g/m)	Duration of effective action (months)	Insecticide action	Toxicity;[c] oral LD_{50} of ai. For body (weight)
bendiocard	C	0.1-0.4	2-6	contact & airborne	55
carbosulfan	C	1-2	2-3	contact & airborne	185
cyfluthrin	PY	0.025	3-6	contact	500
cypermethrin	PY	0.5	4 or more	contact	>4000 [d,e]
DDT	OC	1-2	6 or more	contact	113
deltamethrin	PY	0.05	2-3	contact	>2940 [d,e]
etofenprox	PY	0.1-0.5	6 or more	contact	>40000
fenitrothion	OP	2	3-6	contact & airborne	503
fenthion	OP	2	4-6	contact (outdoor only)	250
lindane (gaamma-HCH)	OC	0.2-0.5	3 or more	contact & airborne	100
lambda-cyhalothrin	PY	0.02-0.03	3-6	contact	79
malathion	OP	2	2-3	contact	>4000
permethrin	PY	0.5	2-3	contact	>4000 [d,e]
pirimiphos-methyl	OP	1-2	2-3 or more	contact & airborne	2018
propoxur	C	1-2	3-6	contact & airborne	95

[a] c= carbamate, OP= organophosphorus, PY= synthetic pyrethroid and OC= organochlorine compound

[b] a.i. = active ingredient.

[c] Toxicity and hazard are not necessarily equivalent; the factors influencing the latter are discussed in section 12.

[d] Dermal toxicity

[e] Because of their low dermal toxicity, and on the basis of experience with their use , these products have been classified in the WHO Hazard Classification in Class III.

Annex 5

Insecticides suitable as cold aerosol sprays and for thermal fogs for mosquito control

insecticide	Chemical type [a]	Dosage of a.i. [b] (g/ha)		Toxicity; [c] oral LD_{50} of ai [b] for rats (mg/kg of body weight)
		Cold sprays	Thermal fogs [d]	
bendiocard	C	4-60	-	55
bioresmethrin	PY	5-10	20-30	7000
chlorpyrifos	OP	10-40	150-200	135
cyfluthrin	PY	1-2		500
cypermethrin	PY	1-3	-	7180
cyphenothrin	PY	2-5	-	2250-2640
deltamethrin	PY	0.5-1.0	-	>2940 [e,f]
dichlorvos	OP	150	200-300	56
d-phenothrin	PY	5-10	-	>10000
etofenprox	PY	10-20	10-20	>40000
fenitrothion	OP	250-300	270-300	503
fenthion	OP	150	-	330 [f]
malathion	OP	112-693	500-600	>4000
naled	OP	56-280	-	430
permethrin [g]	PY	5-10	-	>4000 [e,f]
pirimiphos-methyl	OP	230-330	180-200	2018
propoxur	C	100	-	95
resmethrin	PY	7-16	-	2000
zeta-cypermethrin	PY	1-3	-	86

[a] c= carbamate, OP= organophosphorus, PY= synthetic pyrethroid and OC= organochlorine compound

[b] a.i. = active ingredient.

[c] Toxicity and hazard are not necessarily equivalent; the factors influencing the latter are discussed in section 12.

[d] The strength of the finished formulation applied depends on the performance of the sprayinf equipment used

[e] Because of their low dermal toxicity, and on the basis of experience with their use , these products have been classified in the WHO Hazard Classification in Class III.

[f] Dermal toxicity

[g] Also used in mixtures with knock-down agents or synergists.