# Japanese encephalitis vaccination impact on Japanese encephalitis national burden of disease in INDIA

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# Abstract

Background: Japanese Encephalitis (JE) virus was diagnosed in India on October 1955 (Vellore, TN). Incidences were increasing trend in India from 2001, after Afghanistan war and arrival of immigrant Herons. The JE vaccination was introduced in 2006. Murray had computed GBD in 1992 by taking 80 years (Japanese male e<sub>0</sub>) and 82.5 years (Japanese female e<sub>0</sub>) as full life for males and females respectively. In India, traditionally male's 80<sup>th</sup> birth day is being celebrated as *Sadabishekam* (Full life span as 1000 Lunar Months). JE National Burden of Diseases (NBD) was calculated from 2001 to 2011 for 10 years by taking 2006 as base year. Objectives: To find out vaccination impact by comparing JE NBD and CFR between Pre and Post five years. Methodology: JE NBD was calculated (DALYs) for 2001 to 2005 as Pre and 2007 to 2011 as Post vaccination period. DIS MOD II generated indicators were used for calculation of YLL and YLD. (DALY= YLL+YLD). The means of DALY and CFR% before and after vaccination was calculated for comparison of significance. Limitations: Data paucity, calculated DALYs were some extent crude. Results: The pre and post vaccination period mean NBD was 24897±16167.5 and 31002±7624.8 years respectively. The same of CFR% was 24.8±2.4 and 16.9±4.3%. Discussion: Before and after introduction of vaccination NBD was not significantly differed (P>0.05). But CFR was significantly reduced with difference of 7.9% (P<0.01). Conclusion: Vaccination has significantly reduced mortality. But morbidity is being stabilized without any impact. Keywords: JE Vaccination, CFR, NBD, Impact, DALY, YLL, YLD.</li>

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# **INTRODUCTION**

Japanese Encephalitis (JE) was clinically diagnosed in Japan, the sun rising country in 1871, among the Acute Encephalitis Syndrome (AES) cases and named as JE. Japanese Encephalitis Virus (JEV) originated from an ancestral virus in the area of the *Malay Archipelago* and spread across Asia<sup>1</sup>. In India, the virus was diagnosed at

Vellore in October 1955, Tamil Nadu. JE had spread over since 1972 as endemics/ out breaks to other states like West Bengal, Uttar Pradesh, Assam, Manipur, Bihar, Andhra Pradesh, Pondicherry, Karnataka, Goa and Kerala. In south India, the disease affected more among children <15 years. But in North India, all ages were affected. The incidence among males and females were 60% and 40% respectively [2and3]. At least 50 percent of children who survive illness are left with disabilities, including physical, cognitive, or psychiatric problems. These disabilities are typically life-long and cause significant burden within affected families and communities<sup>4</sup>. In India, JE was an increasing trend from 2001 as an endemic after Afghanistan war. The increasing trend of JE cases after 10<sup>th</sup> October (onset of war on 07-10-2001) reported in India may give us a hint regarding the role of these migratory birds in the causation of JE epidemics in India. The maintenance host of JEV (Herons) were immigrated and sustained. The spread of

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virus was amplified by infected mosquito biting pigs in North India. Japanese encephalitis virus is passed on by the bite of an infected mosquito that has previously sucked blood from an infected animal or person. Birds are the common hosts for several of the various encephalitis viruses. The Japanese encephalitis virus, in particular, is also able to replicate itself in pigs and birds. This means that the pig and bird populations constitute a reservoir of the disease that may be difficult to eradicate. The human is the dead end host of the JE<sup>5</sup>.

# Vaccination

*"Vaccination* Japanese against encephalitis is recommended if you intend to spend more than three to four weeks in a region where the disease is prevalent"<sup>o</sup>. The JE vaccine was recommended for those whose principal area of residence will be an area, where Japanese encephalitis was endemic or epidemic. Vaccination was started in India on 15<sup>th</sup> May 2006 in 11 districts of 4 States. During that campaign SA 14-14-2 live-attenuated JE vaccine was administered to nearly 9.3 million children all over 4 States. Nearly 50 million 1-15 vears of children were immunized until 2009 through vaccination campaign and routine immunization programme<sup>3</sup>. The protective effect of vaccine after 12–15 months was 98.5% (CI - 90.1-99.2%)<sup>7</sup>

#### **Burden of Disease**

Murray had made an attempt to the first global burden of disease-1990 in terms of Disability Adjusted Life Years (DALY) by taking the expectation of life at birth  $(e_0)$  of males as 80 years and females as 82.5 years<sup>8,9,10</sup>. The Japanese expectation of life at birth  $(e_0)$  80 years is the longest global longevity of human being. Biologically the females are 2.5 years greater than males. Traditionally in India, the Astronomers consider the full life of human being is 80 years and the 80<sup>th</sup> birth day of a male is being celebrated as Sadhabiseham. The concept of Sadhabiseham is, the individual has seen one thousand full or new moons (I<sup>st</sup> Millionth full moon) during his life span<sup>11</sup>. Human full life of 80 years was originated from India. The science of astronomy developed science of statistics with individual observations digested in to coherent theories<sup>12</sup>. Based on the above concepts, the following objectives were constituted to study the impact of JE vaccination in terms of burden of disease and case fatality in India.

# AIM

To study the impact of JE vaccination in health gap of disease burden of JE.

## **OBJECTIVES**

1. To find the effect of JE vaccination by comparing the morbidity (Health gap) before and after vaccination.

- 2. To find the effect of JE vaccination by comparing the Case Fatality Rate (CFR).
- 3. To recommend the strategies to be implemented to control and eradicate JE.

#### **METHODOLOGY**

The JE vaccination introduction and implementation year 2006 was taken as base year for comparison of JE Vaccination impact. The incidences of JE from 2001 to 2005 (Five years) have been taken as before vaccination and 2007-2011(5years) incidences in India have been taken as after vaccination for comparison. The NBD computing team might be consisting of an Epidemiologist, Economist, Bio- statistician and a part time Demographer. To fulfill the above task the author is Bio-statistician Economist and Demographer. The Epidemiologists helps were rendered then and there.. The data were selected from already published sources of Govt. of India. The health gap was calculated as Adjusted Life Years (DALYs). Disability The components of DALY are years of life lost due to premature deaths (YLL) and years of life lost due to disability (YLD). DALY= YLL+YLD.

# YLL Calculation

YLL was calculated by taking the five years age groups of mortality due to incidence of JE. In each age group the YLL was calculated with 3% discounting and uniform age counting by the following formula<sup>8,9</sup>. YLL= (N÷0.03) (1-e<sup>-0.03L</sup>). Where, N= No of deaths. And L = Standard life expectancy at the age of deaths in years. The summed up values of YLL of 0-4 to 85+ age groups were arrived the total of YLL for each year from 2001 to 2011.

#### **YLD Calculation**

Similar to YLL, the YLD was calculated for each year by adopting the following modality.  $YLD = I*DW (1-e^{-0.03L})$  $\div$  0.03. Where I= No of incident cases. DW= Disability weight. L=Average duration of the case until remission or death in years. DW (JE), Episodes= 0.616, Cognitive Impairment=0.468 and neurological sequelae=  $0.379^{8,9}$ The remission was calculated with the help of DIS MOD  $II^{13}$ . The software requires a minimum of three variables of particular cause of disease are to be entered as input. In this process, the gender wise data regarding incidence of JE, age wise total mortality and case fatality of JE were entered in to the window. In addition to that gender wise population was entered and the disease JE with ICD 10 (A83.0) code was selected. The model generated seven outputs such as incidence, remission, case fatality and mortality as hazards, prevalence as proportion, duration of disease in years and Relative Risk on total mortality. The components, which are required for calculation of YLD may be collected from the output of DIS MOD II. The National Burden of Disease (NBD) of JE was calculated in terms of DALYs. (Table-1)

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Veer	Deaths		YLL		Disability		YLD		
rear	М	F	М	F	М	F	Μ	F	DALTS (years)
2001	287	192	9902	6624	949	633	326	217	17069
2002	279	187	9626	6452	779	520	268	178	16524
2003	424	283	14628	9764	1117	744	384	255	25031
2004	220	147	7590	5072	798	532	274	182	13118
2005	1009	673	31311	19719	2992	1995	1029	684	52743
2006	395	263	13628	9074	1318	878	453	301	23456
2007	578	385	19941	13283	1837	1224	632	420	34276
2008	410	274	14145	9453	1903	1268	654	435	24687
2009	462	317	15939	10937	2518	1678	866	575	28317
2010	407	272	14042	9384	2693	1795	926	615	24967
2011	701	468	24185	16146	4248	2832	1461	971	42763

Table 1: Year wise gender wise JE DALYs in years from 2001-2011



Figure 1: Disease Model

## **Calculation of CFR**

The case fatality rate (CFR) of JE was calculated for the years 2001 to 2011. (Table-2)

Table 2: Year wise incidence of episodes and fatality from 2001-2012
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Year	Incidence	Deaths	CFR %	Year	Incidence	Deaths	CFR %
2001	2061	479	23.2	2007	4024	963	23.9
2002	1765	466	26.4	2008	3855	684	17.7
2003	2568	707	27.5	2009	4975	779	15.7
2004	1714	367	21.6	2010	5167	679	13.1
2005	6669	1682	25.2	2011	8249	1169	14.2

#### **Data analysis**

The health gap namely DALYs and CFRs for years 2001 to 2005 before JE vaccination implementation was compared with DALYs and CFRs for years 2007 to 2011 after implementation of JE vaccination. The student's 't'

test was used for comparison. The statistical package IBM SPSS-20 was used for calculation of test statistic and P-values. The P-value less than 0.05 (P<0.05) was considered as significant.

#### RESULTS

# Comparison of DALYs and CFR % in Pre and Post JE vaccination

Table 3: Comparison of DALYs and CFR % between pre and post JE vaccination

Health gap	Pre (2001- 05)		Post (2007-11)		Difference		DE	Cignificance
	Mean	SD	Mean	SD	Difference	L	DF	Significance
DALYs	24897	16167.5	31002	7624.8	6105	0.764	8	P>0.05
CFR %	24.8	2.4	16.9	4.3	7.9	3.595	8	P<0.01

The table 3 compares the JE DALYs and CFR % before and after JE vaccination. The mean DALYs before and after vaccination were  $24897 \pm 16167.5$  years and  $31002 \pm 7624.8$  years respectively. The difference between them was 6105 years and the same was not statistically significant (P>0.05). Whereas, the mean CFR % before and after vaccination were  $24.8 \pm 2.4$  and  $16.9 \pm 4.3$  respectively. The difference of CFR % 7.9 was statistically highly significant (P<0.01). The Fig-1 describes the trends of JE episodes, deaths and CFR through 2001to 2011. The episodes and deaths were fluctuating during the above period. Similarly the CFR



had fluctuated during the pre vaccination period and after

Figure 2: Year wise incidences, deaths and CFR/10000 (2001-2011)

# DISCUSSION

The JE vaccination has no impact on the incidence of JE before and after introduction, since the burden of JE prevalence showed no significant difference between Pre and Post vaccination periods (P>0.05). It was reported that around the world, the incidence has gone up from 44,000 in 2004 to 58,000 in 2009 with deaths ranged from 14000-16000 in the above years.<sup>14</sup> The CFR of JE after introduction of vaccination was significantly reduced than before introduction of vaccination in India (P<0.01) and it is conformed to 'the case fatality rate has been reduced from 25% in 2005 to 12% in 2010<sup>15</sup>.

## **CFR** Comparison between VBDs

Since 2003 December, the VBDs viz. Malaria, Kala-azar, Filariasis, Japanese Encephalitis and Dengue/Dengue Hemorrhagic Fever (DF/DHF) were brought under one umbrella namely National Vector Borne Disease Control Programme in India<sup>16</sup>. The post vaccination period of JE CFR was compared with the other umbrella programme of VBDs such as Malaria, Kala- azar and DF/DHF. The post vaccination period covers almost in 11<sup>th</sup> Five year plan period (2007-08 to 2011-12) with objectives of 'To reduce morbidity and Case Fatality Rate and to reduce frequency of outbreaks'. Among the VBDs, The mean case fatality rate 16929±4279.7 (/10000) of JE was significantly differed (P<0.001) with the other VBDs Mean CFR/10000 (Malaria=7.0±1.1, DF/DHF=75.7±32.7 and Kala- azar =  $37.8\pm8.7$ ) The Mean CFRs between the other VBDs were not differed significantly (P>0.05). Though 111 districts have already been covered under JE vaccination, 10 - 14% JE sero positivity was still being reported due to poor coverage of new cohorts under Routine Immunization<sup>17</sup>

# Recommendations

The results and discussions revealed that among VBDs the JE is the most dreadful disease while analyzing its fatality, Cognitive Impairment and neurological sequelae. As envisaged in 12<sup>th</sup> Five year plan the budg*et al*location (₹ 150 Crores) may not be sufficient for control and prevention of case fatality and out breaks<sup>18</sup>. More funds and new strategies may be devised for controlling the incidence. And to eradicate, steps and strategies like 0

polio and Pulse polio may be introduced for JE also since JE is a vaccine preventable disease.

# **CONCLUSION**

vaccination the trend was decreasing.

The 1983 Health Policy of India (HFA - 2000) emphasized to achieve the Net Reproduction Rate (NRR) unity to stabilize the Population of India in 2050. Most of the states next to Kerala and TN are getting momentum in achieving the NRR unity. At this context, JE incidents affect <15 aged children (75.1%) in UP, the biggest state of India. Among the affected children 60% and 40% were males and females respectively<sup>19</sup>. To stabilize our population, the girl children must be protected to maintain NRR unity at the context of already missed girl children. Nearly 50 percent of children who survive after illness of JE are left with disabilities, including physical, cognitive, or psychiatric problems. These disabilities are typically life-long and cause significant burden within affected families and communities<sup>4</sup>. After eradication of poliomyelitis, JE has gained increasing prominence as an important cause of disability of children in India. As envisaged in the 12<sup>th</sup> Five Year Plan proposal "Assess the impact of vaccination and guide the future strategies" the strategies may be devised to control and prevent the fatality and disability by means of eradicating the  $JE^{20}$ . "Small bite, big threat"

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