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Assessing Hepatitis A virus epidemics by stochastic model in six (Primary Health Care) centres in Thanjavur District, Tamil Nadu, South India

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Abstract

A stochastic model, two state Markov Chain, was applied to HAV seroprevelance data by age group from the Six Primary Health Centres (PHCs) *viz.*, Thirukkattupalli, Kurungulam, Pillaiyarnatham, Kudikadu, Kovilvenni and Budalur of the Thanjavur District, Tamil Nadu, South India. Age specific Risk Rate, Markov Risk Rate, (MRR) and its weighed sum, Total MRR were defined and used as novel measures to prioritize age groups for allocating vaccine and to decide in which PHC regions vaccine should be used to prevent Hepatitis A. All age groups whose MRR was over 20 are strongly recommended to be vaccinated first. Pillaiyarnatham and Budalur were predicted to be the PHC regions with a high risk of hepatitis A virus epidemic and therefore suggested that they should be under close surveillance.

Keywords: Age specific seroprevelance, Epidemiology Stochastic Process, Hepatitis A Virus, Markov process, Markov Risk Rate, PHC regions

INTRODUCTION

Hepatitis A (formerly known as infectious hepatitis) is caused by an enterovirus. It is clinically characterized by malaise, fever, nausea, vomiting and jaundice. The patient may recover completely in 3 to 6 weeks or in some cases, the patient's condition may worsen ending in coma and death. The disease is endemic throughout the world (Park, 1995).

This disease can be controlled/prevented by (i) Isolation of cases and disinfection of faeces and vomits (ii) Providing better hygienic and sanitary conditions, e.g., safe water supply, sanitary disposal of human excreta, promoting food hygiene, enforcing sanitary measures in hotels, restaurants and other eating establishments (iii) proper sterilization of needles and syringes and (iv) administration of human normal immunoglobulin to all contacts before or within a week of exposure (Park, 1995).

Hepatitis A creates worldwide public health problem. There has been growing interest over recent years in the survey of its seroprevelance. Using this information we may provide effective data for forecasting and controlling the hepatitis A epidemic.

To study the epidemiological features of Hepatitis A in the surroundings of Thanjavur District, Tamil Nadu, South India, six Primary Health Centres (PHCs) were investigated. A Stochastic Model, two-state Markov Chain, was applied to the age-specific hepatitis A seroprevelance data obtained from the six PHCs selected.

EPIDEMIC MATERIALS AND METHODS

Samples were taken randomly from the six PHC's and the sera were tested for the presence of specific anti-HAV antibody by an I_g-G-capture enzyme linked immunosorbent assay (ELISA). A positive result is a competitive rate > 40%.

Epidemiological Factors (Park, 1995)

(i) **Agent:** Hepatitis A virus (HAV), an enterovirus

(ii) **Source of infection:** Man is the only source of infection. Many infections are subclinical or mild, but all are sources of infection. There is no carrier state.

(iii) **Infective material:** Mainly human faeces. Blood is infective for a short period during the stage of viraemia.

(iv) **Age:** The disease is most common among children. By the age of 5 years, 90 percent of children have serological evidence of HAV infection.

(v) **Immunity:** Most people in endemic areas acquire infection through subclinical infection. An attack of hepatitis A generally provides protection against a second attack.

(vi) **Mode of transmission**: (i) **Faecal-oral route:** This is the most common route of spread, *via* contaminated water and food. (ii) **Direct contact**: Person to person contact can also spread the infection, via contaminated hands or objects in conditions, of poor sanitation and

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overcrowding. (iii)**Blood:** Hepatitis A is rarely transmitted by blood or blood products.

(vii) **Incubation period:** 15 to 50 days (usually 28 days).

MODEL

Multistep transmission matrix of Markov chain

Assume: $\{X_t = 0\}$: the rate of uninfected people at age t;

$\{X_t = 1\}$: the rate of infected people at age t;

P: Probability ,

$P_{ij}(t)$: Probability from state i to state j at age t, i, j = 0, 1.

Transmission probability of Hepatitis A infection process in 2´2 matrix (Medhi, 1994)

$$P=\begin{bmatrix} P_{00}(t) & P_{01}(t) \\ P_{10}(t) & P_{11}(t) \end{bmatrix}$$

All elements in matrix P are non-negative numbers:

$$\sum_{j=0}^{1} P_{ij}(t) = 1, \quad i = 0, 1$$

Infected peoples are not re-infected by Hepatitis A virus, (Medhi, 1994)

Then, we get

$$P_{10}(t) = 0$$

$$P_{11}(t) = 1$$

$$P_{01}(t) = 1 - P_{00}(t)$$

$$P_{00}(t) = \{X_{t+1} = 0 \mid X_t = 0\}$$

$$= P\{X_{t+1} = 0\} / P\{X_t = 0\} \quad \text{.....(1)}$$

Then we have

$$P^{(2)}(t) = P(t)\,P(t+1)$$

$$=\begin{bmatrix} P_{00}(t) & P_{01}(t) \\ 0 & 1 \end{bmatrix} \quad \begin{bmatrix} P_{00}(t+1) & P_{01}(t+1) \\ 0 & 1 \end{bmatrix}$$

$$=\begin{bmatrix} P_{00}(t)P_{00}(t+1) & 1-P_{00}(t)P_{00}(t+1) \\ 0 & 1 \end{bmatrix}$$

Using multistep transmission matrix we may write

$$P^{(n)}(t) = \begin{bmatrix} P_{00}^{(n)}(t) & P_{01}^{(n)}(t) \\ P_{10}^{(n)}(t) & P_{11}^{(n)}(t) \end{bmatrix}$$

$$= \begin{bmatrix} \prod_{k=1}^{t+n-1} P_{00}(k) & 1-\prod_{k=1}^{t+n-1} P_{00}(k) \\ 0 & 1 \end{bmatrix}$$

From (1), we get

$$P_{00}^{(n)}(t) = \prod_{k=t} P_{00}(k)$$

$$= P\{X_{t+n} = 0\} \,/\, P\{X_t = 0\} \quad \text{..... (2)}$$

So, the multistep transmission process can be obtained by $P\{X_t = 0\}$.

Method of calculation:

The original data of age distribution of Hepatitis A epidemic in Budalur PHC in 2010 were used to calculate multistep transmission process. Here 't' is the state of 'age group' and from equation (2)

We get

$$P_{00}(t) = P\{X_t = 0\}$$

So

$$P_{01}^{(t)}(0) = 1 - P_{00}(t)$$

$$= 1 - P\{X_t = 0\}$$

From table (1), the multistep transmission probability matrix can be calculated as follows (Medhi, 1994):

$$P^2(3) = \begin{bmatrix} P_{00}(3)P_{00}(4) & 1-P_{00}(3)P_{00}(4) \\ 0 & 1 \end{bmatrix}$$

$$= \begin{bmatrix} 0.988\times 0.967 & 1-0.988\times 0.967 \\ 0 & 1 \end{bmatrix}$$

$$= \begin{bmatrix} 0.955 & 0.045 \\ 0 & 1 \end{bmatrix}$$

From the multistep transmission probability matrix, an epidemic prediction can be obtained. So for t = 3 from table (1) we get $P_{01}(3) = 0.120$, from the above results, we get $P_{01}^{(2)}(3) = 0.605$. Therefore, those in the uninfected group will have the probability of infection of 0.120 between the ages of 20 – 29 and 0.045 between the ages of 30 – 39.

RESULTS

From the Stochastic Model, the MRR is set up as a new measure of infection risk. MRR_t the age-specific risk rate, varies as the product of the proportion susceptible at a given age' t' with the probability of becoming infected in two age / time steps, $P_{01}^{(2)}(t)$.

Its calculated formula is

$MRR_t = 100\ P\{X_t = 0\}\ P_{01}^{(2)}(t)$. [2]

Total MRR, another new index, is the weighed sum of these age-specific rates.

Its formula is

$$\text{Total MRR} = \int_0^{\infty} 0.1\ t\ MRR_{t-}\ dt.$$

$$= \sum 0.1\ t\ MRR_t.$$ [2]

Results of the models derived for each six PHCs studied are given in tables 1 to 6. In every table the last column shows that there is a wide variation in the MRR_t and the total MRR for the different PHC's.

CONCLUSION

The novel Index, MRR_t, varies as the product of the proportion susceptible at a given age t and the probability of becoming infected in two age/time steps, $P_{01}^{(2)}(t)$. Two-step transitions $P_{01}^{(2)}(t)$ are used in the novel index of MRR to show both age and time effects, which is validly based on the assumption that the age effects are stable over time. If there are novel seroprevelance data that suggest stationarity in average Hepatitis A virus is obsolete, the rates of the new data should be cited by the stochastic model. That is because the stationarity of age effects in time is relative to the cross-sectional seroprevelance surveys, and so only consecutive seroprevelance investigation at different time points can provide the data for separating age and time effects in the Hepatitis A virus epidemic process.

Another new index, the total MRR, provides a reasonable estimate of the disease burden in the whole PHC area. The total MRR is the weighed sum of age-specific rates. The weight co-efficient is based on the age group disease burden, which is positively correlated with age 't'. Therefore the authors assumed that the weighed co-efficient is positively correlated to age't'. The acquisition of infection by children is often asymptomatic with fewer consequences, both in terms of health care and work loss. However, when high rates

Table 1. Results of the model derived for the Thirukkattupalli PHC

Age	No.Examined	Anti-HAV (-)	t	$P\{X_t=0\}$	$P_{00}(t)$	$P_{01}(t)$	$P_{01}^{(t)}(0)$	(%)	MRR
Born	-	-	0	1.000	1.000	0.000	0.000	-	-
1 – 9	10	6	1	0.600	0.600	0.400	0.400	40	35.988
10 – 19	20	8	2	0.400	0.667	0.333	0.600	60	13.64
20 – 29	38	15	3	0.395	0.988	0.120	0.605	60	1.761
30 – 39	55	21	4	0.382	0.967	0.033	0.618	61	22.614
40 – 49	31	5	5	0.161	0.422	0.578	0.839	84	10.366
50 –	22	3	6	0.136	0.844	0.156	0.864	86	-
								Total	**21.09**

Table 2. Results of the model derived for the Kurungulam PHC

Age	No. Examined	Anti-HAV (-)	t	$P\{X_t=0\}$	$P_{00}(t)$	$P_{01}(t)$	$P_{01}^{(t)}(0)$	(%)	MRR
Born	-	-	0	1.000	1.000	0.000	0.000	-	-
1 – 9	100	60	1	0.600	0.600	0.400	0.400	40	36.024
10 – 19	200	80	2	0.400	0.666	0.334	0.600	60	13.36
20 – 29	300	120	3	0.400	1.000	0.000	0.600	60	0.0
30 – 39	500	200	4	0.400	1.000	0.000	0.600	60	25.68
40 – 49	350	50	5	0.143	0.358	0.642	0.857	86	10.01
50 –	250	30	6	0.120	0.839	0.161	0.88	88	-
								Total	**21.55**

Table 3. Results of the model derived for the Pillaiyarnatham PHC

Age	No.Examined	Anti-HAV (-)	t	$P\{X_t=0\}$	$P_{00}(t)$	$P_{01}(t)$	$P_{01}^{(t)}(0)$	(%)	MRR
Born	-	-	0	1.000	1.000	0.000	0.000	-	-
1 – 9	50	32	1	0.640	0.640	0.360	0.360	36	34.688
10 – 19	37	17	2	0.459	0.717	0.283	0.541	54	13.494
20 – 29	62	28	3	0.452	0.985	0.015	0.548	54	1.220
30 – 39	38	17	4	0.447	0.988	0.012	0.553	55	35.894
40 – 49	43	19	5	0.442	0.988	0.012	0.558	55	2.033
50 –	82	35	6	0.427	0.966	0.034	0.573	57	-
								Total	21.907

Table 4. Results of the model derived for the Kudikadu PHC

Age	No. Examined	Anti-HAV (-)	t	$P\{X_t=0\}$	$P_{00}(t)$	$P_{01}(t)$	$P_{01}^{(t)}(0)$	(%)	MRR
Born	-	-	0	1.000	1.000	0.000	0.000	-	-
1 – 9	130	126	1	0.969	0.969	0.031	0.031	03	11.724
10 – 19	200	176	2	0.880	0.908	0.092	0.120	12	19.976
20 – 29	340	255	3	0.750	0.852	0.148	0.250	25	11.55
30 – 39	220	164	4	0.745	0.993	0.007	0.255	25	0.968
40 – 49	176	124	5	0.704	0.944	0.056	0.296	29	7.884
50 –	98	65	6	0.663	0.941	0.059	0.337	33	-
								Total	12.96

Table 5. Results of the model derived for the Kovilvenni PHC

Age	No.Examined	Anti-HAV (-)	t	$P\{X_t=0\}$	$P_{00}(t)$	$P_{01}(t)$	$P_{01}^{(t)}(0)$	(%)	MRR
Born	-	-	0	1.000	1.000	0.000	0.000	-	-
1 – 9	128	92	1	0.718	0.718	0.282	0.718	71	21.755
10 – 19	97	67	2	0.697	0.971	0.029	0.303	30	6.273
20 – 29	83	54	3	0.653	0.937	0.063	0.347	34	8.031
30 – 39	62	38	4	0.612	0.937	0.063	0.388	38	12.852
40 – 49	55	28	5	0.517	0.844	0.156	0.483	48	13.493
50 –	42	19	6	0.453	0.876	0.124	0.547	54	-
								Total	17.769

Table 6. Results of the model derived for the Budalur PHC

Age	No.Examined	Anti-HAV (-)	t	$P\{X_t=0\}$	$P_{00}(t)$	$P_{01}(t)$	$P_{01}^{(t)}(0)$	(%)	MRR
Born	-	-	0	1.000	1.000	0.000	0.000	-	-
1 – 9	87	80	1	0.927	0.927	0.073	0.073	07	36.894
10 – 19	53	31	2	0.603	0.650	0.350	0.397	39	26.712
20 – 29	41	21	3	0.517	0.857	0.143	0.483	48	16.182
30 – 39	17	07	4	0.415	0.802	0.198	0.585	58	10.250
40 – 49	22	08	5	0.390	0.939	0.061	0.610	61	19.812
50 –	13	02	6	0.205	0.525	0.475	0.795	79	-
								Total	27.89

of HAV infection continues among older children and adults, or are deferred until older ages, the disease burden will be greater.

In some PHC regions the MRR_{1-} was high for children aged 1–9 followed by lower MRR for older people, the total MRR is the lowest as of those shown.

In some of the P.H.C. regions like Kudikadu, MRR_{10} – for aged group 10–19, is higher and MRR for other age groups is lower.

The authors suggest using total MRR to target whole P.H.C. regions for vaccination, and using age specific MRR_t to target the age groups to be vaccinated.

In 2010 MRR_{1-} in Budalur, Pillaiyarnatham, Kurungulam and the MRR_{10-} in Budalur were over 20. The total MRR in Budalur and Pillaiyarnatham were over 20 which was higher than the warning value. These PHC areas are of high risk areas and should be kept under closer surveillance.

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