

Calculating Prevalence of Hepatitis B in India: Using Population Weights to Look for Publication Bias in Conventional Meta-analysis

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ABSTRACT

Publication bias can result from the propensity of researchers to document what is unusual. This can distort the inferences drawn in systematic reviews. To measure the distortion, it has been suggested that a second analysis be done; using weights proportional to the size of the population from which the samples are drawn. We re-evaluate data from a published meta-analysis on prevalence of hepatitis B in India, to see how this approach alters the results. Prevalence of hepatitis B among tribal and non-tribal populations in different States was analyzed. Weights were then assigned according to population of the State. The overall country prevalence was then calculated. Using population-weights it is estimated that the point-prevalence of hepatitis B among non-tribal populations is 3.07% [95% CI: 2.5 - 3.64]. Among tribal populations it is 11.85% (CI 10.76 -12.93). Overall prevalence was 3.70 (CI: 3.17 -4.24) (corresponding to a chronic carrier rate of 2.96%). The present analysis using population-weights has resulted in the estimated prevalence among non tribal populations increasing by 24% and that among tribal populations decreasing by 25.5% when compared to figures of the meta-analysis published earlier. The advantages and drawbacks of this procedure are discussed. [Indian J Pediatr 2009; 76 (12) : 1247-1257] E-mail: Puliyel@vsnl.com

Key words: Hepatitis B

It has been suggested that when results of different studies are aggregated in a meta-analysis, it may sometimes be appropriate that they are given weights according to the size of the population they represent rather than the sample size. The concern was that large studies from small populations would get undue weightage otherwise.¹ We have recently completed a systematic search and conventional meta-analysis of studies on point-prevalence of Hepatitis B in India.² In this communication we revisit that data and perform a fresh analysis, using population weights, to see how this approach alters the results and the inferences drawn.

MATERIAL AND METHODS

The systematic search was performed looking for published papers on the point prevalence of Hepatitis B in India. Studies from high risk populations like sex

workers and health care workers were excluded. Details of the search strategy have been published elsewhere.² We included studies of voluntary blood donors (VBD) (altruistic donations) and replacement donors (RBD) (blood donated to replace blood utilized in specific patients – often friends or blood relations of the donor) and studies involving antenatal women and community studies.

We excluded studies from the following special groups who were assumed to be at high risk for hepatitis B: patients from sexually-transmitted-disease clinics, thalassaemia-clinics, hospitalised patients, professional blood donors, sex workers, drug abusers, dialysis patients, and hospital staff.

Briefly, 54 papers reporting data on 61 populations from 15 States in the country, qualified for inclusion [3-56]. In the first stage, the prevalence with its 95% confidence intervals was calculated for each individual study. Differences were noted in the prevalence between States and within the State between tribal and non-tribal populations (Fig. 1: forest plot). Initially, on account of the marked heterogeneity within the data-set, tribal and non-tribal populations were analyzed separately.

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[DOI-10.1007/s12098-009-0246-3]

[Received March 25, 2008 ; Accepted July 21, 2008]

Data from each of the 15 States was analyzed separately to determine the prevalence of hepatitis B in individual States among the tribal and non tribal populations. Prevalence was calculated as a weighted average of individual summary statistics. Weights at this stage are calculated by a method attributed to DerSimonian and Laird (depending on sample size). We used a random effects model.

In the next stage, analysis was performed giving weights to the State-prevalence, according to the population size. Two separate plots were obtained for the tribal and non-tribal populations.

Finally using population-weights, data from tribal and non-tribal groups were aggregated.

Presentation of Graphs and Tables of the Meta analysis: On account of the large number of studies included, the weights and confidence intervals of individual studies are listed in a table separate form the graph, to reduce the clutter and improve readability. All analyses were implemented on Stata 9.1. (Stata Corporation, 4905 Lakeway Drive, College Station, TX 77845, USA)

RESULTS

Fig. 2 (and the corresponding Table 2) shows data from studies among non tribal populations in different States. Fig. 3 (Table 3) shows the data for tribal populations.

The next stage of the analysis is shown in figures 4 and 5. Weights have been given in accordance with the group's population size (Census of India 2001 data). Fig. 4 (Table 4) relates to data from non tribal populations. Using these weights it is estimated that the prevalence among non tribal populations was 3.07% [CI 2.5 - 3.64]. Fig. 5 (Table 5) presents the same analysis for tribal populations. The prevalence for tribal populations was 11.85 (CI 10.76 -12.93)

Although heterogeneous, it is possible to combine the data from tribal populations and non-tribal populations, after attributing weights to the two groups according to their population size. Fig. 6 (Table 6) shows the analysis, having combined the data from the tribal and non-tribal populations using population weights. The overall prevalence was found to be 3.70% (CI: 3.17 -4.24)

DISCUSSION

We have previously recommended a new approach to meta analysis, using population weights to look for publication bias. Unfortunately in most circumstances,

TABLE 1. Forest plot of Prevalence Studies: Heterogeneity in Prevalence of Tribal and Non-Tribal Populations

Study by State	Prevalence (%)	95% C.I.	% weight
Andhra Pradesh			
Singh J (NT) 2001	3.256	1.975	4.538
Chandra M (T) 2003	5.004	3.571	6.436
State Sub-total	4.099	2.388	5.811
Tamil Nadu			
Singhvi A (NT) 1990	2.661	2.493	2.828
Sumathy S (NT) 1995	6.608	4.493	8.722
Chandrasekharan S (N) 2000	3.951	3.056	4.846
Kurien T (NT) 2005	5.543	4.535	6.551
State Sub-total	4.517	2.831	6.203
Delhi			
Nayak NC (NT) 1987	3.580	3.187	3.973
Panda SK (NT) 1991	2.080	1.775	2.385
Tandon BN (NT) 1991	1.952	1.087	2.817
Irshad M (NT) 1994	2.415	2.205	2.626
Manu A (NT) 1997	1.729	1.659	1.799
Prakash C (NT) 1998	9.398	7.683	11.113
Abass Faud (NT) 2001	0.819	0.606	1.031
Kaur R (NT) 2002	7.096	4.067	10.125
Sahni Mohit (NT) 2004	2.043	1.161	2.926
Singh B (NT) 2004	1.769	1.697	1.841
Varghese RM (NT) 2004	0.624	0.431	0.818
Chakravarthi (NT) 2005	4.079	2.140	6.017
Chakravarthi (NT) 2005	2.064	0.671	3.458
State Sub-total	2.255	1.880	2.630
Rajasthan			
Mukherjee M (T) 1990	10.261	7.692	12.830
Nijhawan S (NT) 1997	2.100	1.993	2.207
Ganju SA (NT) 2000	3.323	0.839	5.807
Ahmad B (NT) 2001	2.247	1.303	3.191
Garg S (NT) 2001	3.262	3.101	3.423
State Sub-total	3.349	2.401	4.296
West Bengal			
Chowdhury A (NT) 2005	2.786	2.417	3.154
State Sub-total	2.786	2.417	3.154
Uttar Pradesh			
Choudhury N (NT) 1995	2.373	0.686	4.059
Sharma R (NT) 1996	10.191	5.459	14.923
Sharma R (NT) 1996	5.096	1.656	8.535
Singh H (NT) 2003	1.868	0.886	2.850
Qamer S (NT) 2004	4.348	2.484	6.211
State Sub-total	3.918	2.013	5.823
Punjab, Haryana & Chandigarh			
Biswas SC (NT) 1989	2.300	1.371	3.229
Werner GT (NT) 1989	3.377	1.572	5.181
Kaur H (NT) 2001	1.510	1.413	1.607
Gupta N (NT) 2004	0.461	0.398	0.525
Sharma RR (NT) 2004	0.805	0.769	0.841
State Sub-total	1.195	0.779	1.611
Karnataka			
Singh J (NT) 2001	4.167	2.796	5.538
State Sub-total	4.167	2.796	5.538
Maharashtra			
Khatri JV (NT) 1980	0.627	0.194	1.060
Mukherjee M (T) 1990	8.973	6.842	11.103
Elavia AJ (NT) 1991	1.835	1.578	2.093
Satoskar (NT) 1992	4.535	3.803	5.267
Nandi J (NT) 1994	6.227	1.342	11.111
Mohite JB (NT) 1999	2.111	1.238	2.984
Sub-total	3.441	2.030	4.852
Gujarat			
Bhagyalaxmi A (NT)	1.233	0.417	2.050
State Sub-total	1.233	0.417	2.050
Andaman & Nicobar islands			
Murhekar MV (T) 2000	23.302	20.853	25.752
Murhekar MV (T) 2002	22.165	19.431	24.898
Murhekar MV (T) 2002	37.903	22.271	53.535
Murhekar MV (T) 2002	31.052	19.144	42.960
Murhekar MV (T) 2002	3.528	-3.431	10.488
Murhekar MV (T) 2003	18.681	9.132	28.230

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Murhekar MV (T) 2004	22.448	20.386	24.509	1.26
State Sub-total	21.071	17.016	25.126	3.56
Himachal Pradesh				
Thakur TJ (NT) 1991	0.536	0.135	0.937	2.70
State Sub-total	0.536	0.135	0.937	2.70
Jammu & Kashmir				
Makroo RN (NT) 1989	1.114	0.882	1.345	2.78
State Sub-total	1.114	0.882	1.345	2.78
Madhya Pradesh				
Joshi SH (T) 1990	15.677	13.711	17.643	1.33
Mukherjee M (T) 1990	14.286	9.202	19.370	0.33
State Sub-total	15.496	13.663	17.330	1.66
Arunachal Pradesh				
Prasad SR (T) 1983	8.446	5.278	11.614	0.72
State Sub-total	8.446	5.278	11.614	0.72
Overall	3.660	3.350	3.971	100.00

T = Tribal

NT = Non tribal

prevalence of hepatitis B and is made up of mostly non tribal populations. However in view of its status as the national capital city, it got a disproportionate amount of attention from researchers. Delhi accounted for 29.5% of the total tests performed (Table 1), although it represents 1.89% of the population of the areas studied (Table 6). The large number of studies from an area with low prevalence resulted in an unduly low prevalence estimate, when using conventional meta-analysis methods.

Among tribal populations, the situation was reversed. A very large number of studies were undertaken in the Andamans and Nicobar islands, because of interest in this population with very high endemicity of Hepatitis B. In fact 49% of all tests reported from tribal populations were performed from this area (Table 3) whereas the population of these islands represents a small proportion tribal population of country (0.8%) (Table 5). Use of population weights was able to correct the distortion due to this bias.

A chronic carrier is defined as one who is HbsAg positive on testing two times, with an interval of at least 6 months between tests.⁵⁷ Most studies reported here were done on convenience samples – from women attending ante-natal clinics and blood donors - and as such, only a single sample was available from most people. Thus the prevalence reported represents the point prevalence rather than the chronic carrier rate of the country. It is estimated that the chronic carrier rate is about 80% of the point prevalence.⁵⁷ The chronic carrier rate in the country thus works out to be 2.46% among non tribal populations and 9.5% among tribal populations in the country. This chronic carrier rate is more crucial than the point prevalence because long term consequences like the development of chronic active hepatitis, cirrhosis and hepatocellular carcinoma, occur in chronic carriers. The chronic carrier rate using the traditional meta-analysis was 1.9% and 12.7% among non tribal and tribal populations respectively.

We have seen from the forest plot that the prevalence

TABLE 2. State-Wise Prevalence among Non-tribal Population (Conventional Meta-analysis)

Study (Year)	Prevalence (%)	95% C. I.	% Weight
Andhra Pradesh			
Singh J (2001)	3.256	1.975	4.538
Sub-total	3.256	1.975	4.538
Tamil Nadu			
Singhvi A (1990)	2.661	2.493	2.828
Sumathy S (1995)	6.608	4.493	8.722
Chandrasekharan S (2000)	3.951	3.056	4.846
Kurien T (2005)	5.543	4.535	6.551
Sub-total	4.517	2.831	6.203
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Sub-total	2.255	1.880	2.630
Rajasthan			
Nijhawan S (1997)	2.100	1.993	2.207
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Ahmad B (2001)	2.247	1.303	3.191
Garg S (2001)	3.262	3.101	3.423
Sub-total	2.635	1.730	3.540
West Bengal			
Chowdhury A (2005)	2.786	2.417	3.154
Sub-total	2.786	2.417	3.154
Uttar Pradesh			
Choudhury N (1995)	2.373	0.686	4.059
Sharma R (1996)	10.191	5.459	14.923
Sharma R (1996)	5.096	1.656	8.535
Singh H (2003)	1.868	0.886	2.850
Qamer S (2004)	4.348	2.484	6.211
Sub-total	3.918	2.013	5.823
Punjab, Haryana & Chandigarh			
Biswas SC (1989)	2.300	1.371	3.229
Werner GT (1989)	3.377	1.572	5.181
Kaur H (2001)	1.510	1.413	1.607
Gupta N (2004)	0.461	0.398	0.525
Sharma RR (2004)	0.805	0.769	0.841
Sub-total	1.195	0.779	1.611
Karnataka			
Singh J (2001)	4.167	2.796	5.538
Sub-total	4.167	2.796	5.538
Maharashtra			
Khatri JV (1980)	0.627	0.194	1.060
Elavia AJ (1991)	1.835	1.578	2.093
Satoskar (1992)	4.535	3.803	5.267
Nandi J (1994)	6.227	1.342	11.111
Mohite JB (1999)	2.111	1.238	2.984
Sub-total	2.462	1.189	3.736
Gujarat			
Bhagyalaxmi A (2005)	1.233	0.417	2.050
Sub-total	1.233	0.417	2.050
Himachal Pradesh			
Thakur TJ (1991)	0.536	0.135	0.937
Sub-total	0.536	0.135	0.937
Jammu & Kashmir			
Makroo RN (1989)	1.114	0.882	1.345
Sub-total	1.114	0.882	1.345
Overall	2.444	2.159	100.00

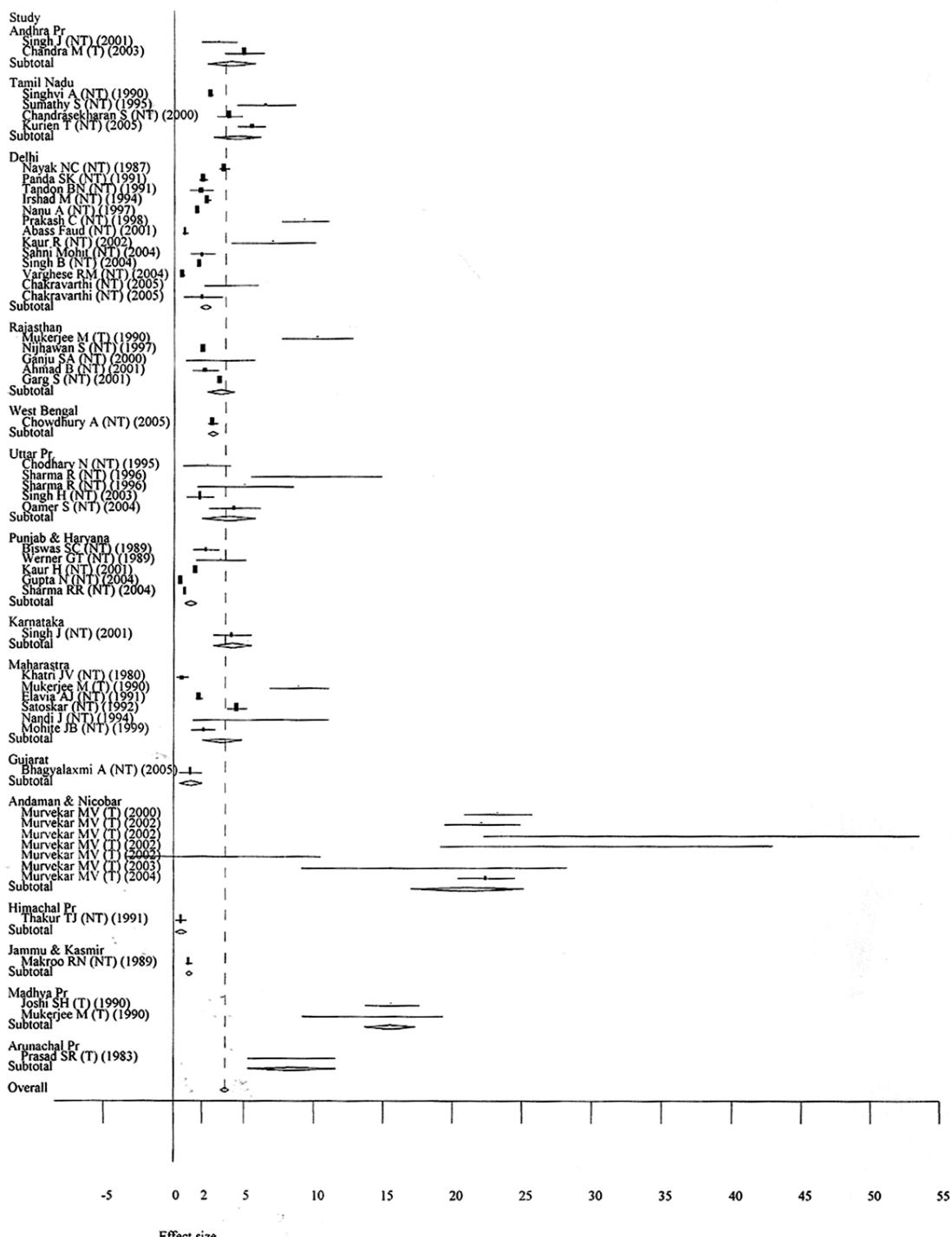


Fig. 1. Forest plot of Prevalence Studies: Heterogeneity in Prevalence of Tribal and Non-Tribal Populations.

it is difficult to estimate the size of the populations from which samples are drawn. Meta analysis of data on point prevalence of hepatitis B from different parts of the country however, lends itself easily to test this new approach. We applied this novel method for analysis,

to see how much difference the new method makes to the inferences drawn.

This meta analysis includes data from 884,052 hepatitis B antigen (HbsAg) tests done all over the country. Data was available from 15 of the 29 States in

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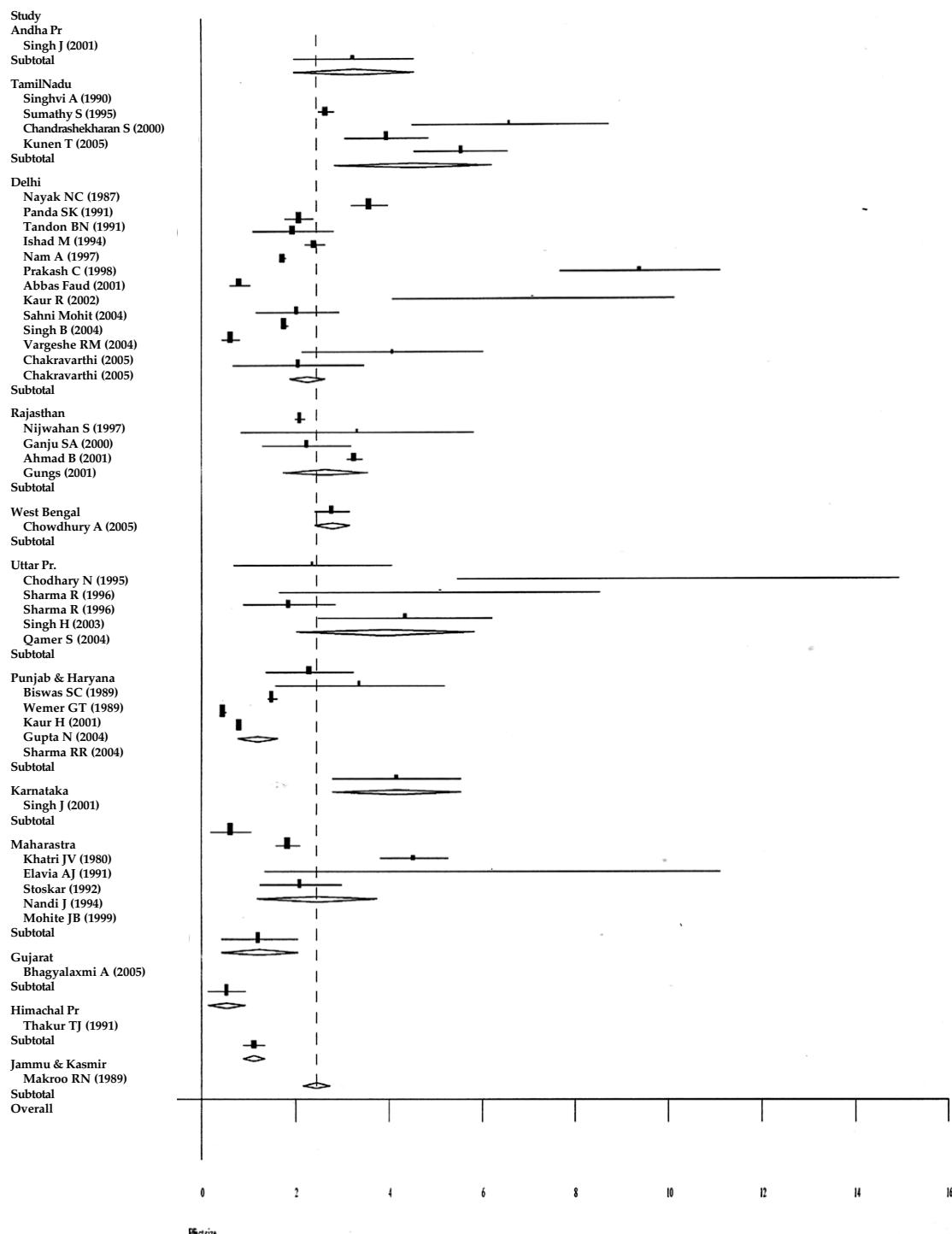


Fig. 2. Non Tribal Populations in Different States (Conventional Meta-analysis)

the country. (Some of the data is available from the State of Madhya Pradesh before separation of the new State of Chhattisgarh. Both States have been clubbed as one State in this analysis. Uttar Pradesh and Uttranchal, Punjab, Haryana and the union territory of Chandigarh were also taken together and as such the

country has been categorized as having 29 States in this analysis, rather than the present number of 32 States). Most of the large States were included, such that the population of these 15 states constitutes 78% of the population of the country. The point prevalence of Hepatitis B was found to be 3.07% among non tribal

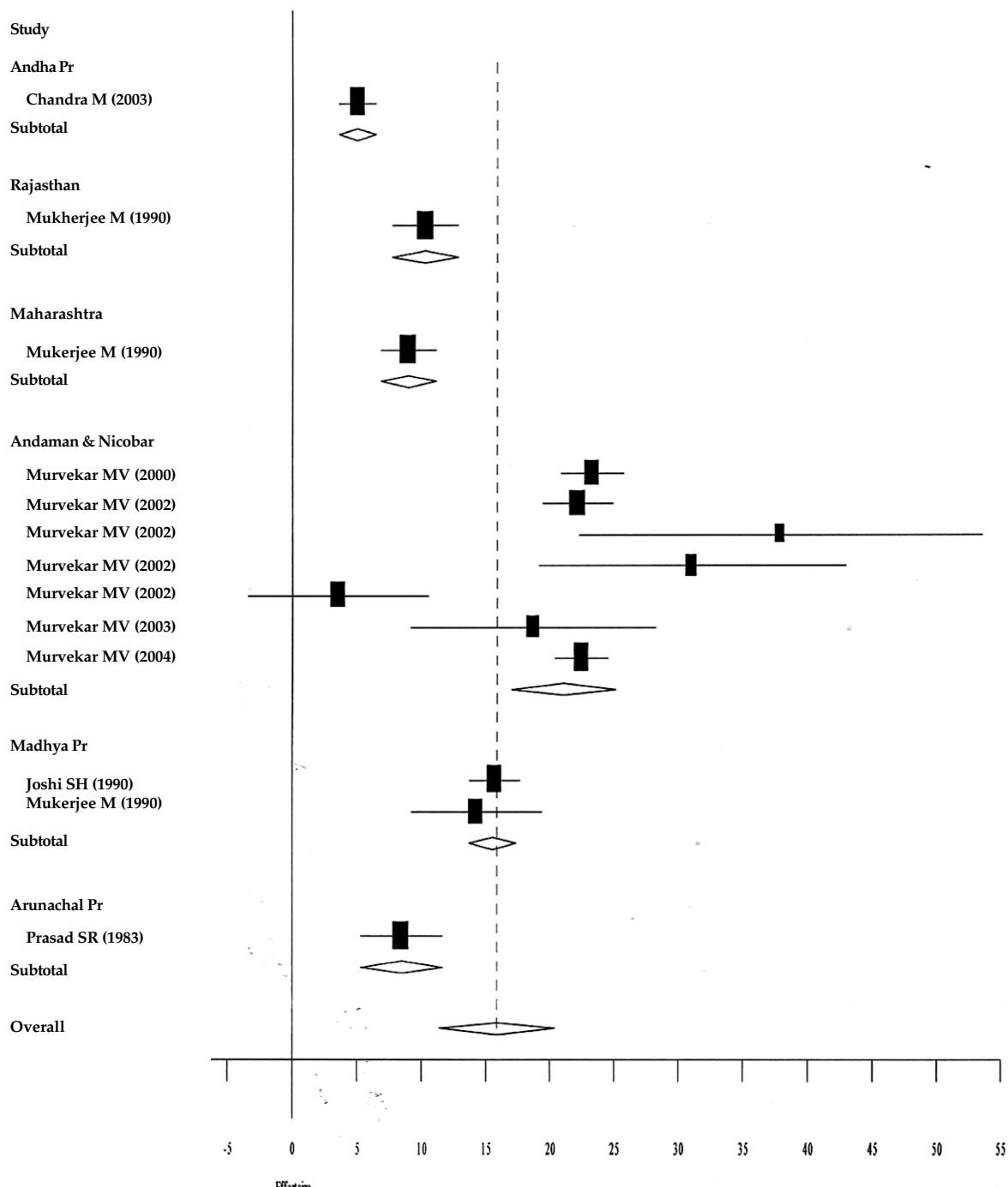


Fig. 3. State-Wise Prevalence among Tribal Populations (Conventional Meta-analysis).

populations and 11.85% among tribal population in the country.

The previous analysis, using conventional meta-analysis techniques (without employing population weights) on the same data base had found the point prevalence among non tribal populations was 2.4% (CI: 2.2 – 2.7) and in tribal populations it was 15.9% (CI 11.4

– 20.4). The present analysis using population-weights has resulted in a 24% increase in the estimated prevalence among non tribal populations and a 25.5% decrease in the estimated prevalence among tribal populations. This increase among non-tribal and decrease among tribal populations highlights the importance of employing this strategy of utilizing population weights. Delhi, for example, has a low

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TABLE 3. State-Wise Prevalence among Tribal Populations (Conventional Meta-analysis)

Study (Year)	Prevalence (%)	95 %	C.I.	Weight %
Andhra Pradesh				
Chandra M (2003)	5.004	3.571	6.436	8.73
Sub-total	5.004	3.571	6.436	8.73
Rajasthan				
Mukerjee M (1990)	10.261	7.692	12.830	8.56
Sub-total	10.261	7.692	12.830	8.56
Maharashtra				
Mukherjee M (1990)	8.973	6.842	11.103	8.64
Sub-total	8.973	6.842	11.103	8.64
Andaman & Nicobar islands				
Murhekar MV (2000)	23.302	20.853	25.752	8.58
Murhekar MV (2002)	22.165	19.431	24.898	8.53
Murhekar MV (2002)	37.903	22.271	53.535	4.27
Murhekar MV (2002)	31.052	19.144	42.960	5.44
Murhekar MV (2002)	3.528	-3.431	10.488	7.27
Murhekar MV (2003)	18.681	9.132	28.230	6.30
Murhekar MV (2004)	22.448	20.386	24.509	8.65
Sub-total	21.071	17.016	25.126	49.05
Madhya Pradesh				
Joshi SH (1990)	15.677	13.711	17.643	8.66
Mukherjee M (1990)	14.286	9.202	19.370	7.92
Sub-total	15.496	13.663	17.330	16.58
Arunachal Pradesh				
Prasad SR (1983)	8.446	5.278	11.614	8.44
Sub-total	8.446	5.278	11.614	8.44
Overall	15.866	11.371	20.361	100.00

TABLE 4. Population Weighted Prevalence for the Country among Non-tribal Populations

State	Prevalence (%)	95% C. I.	Weight %
Andhra Pradesh	3.256	1.975	4.538
Tamil Nadu	4.517	2.831	6.203
Delhi	2.255	1.880	2.630
Rajasthan	2.635	1.730	3.540
West Bengal	2.786	2.417	3.154
Uttar Pradesh	3.918	2.013	5.823
Punjab, Haryana &			25.57
Chandigarh	1.195	0.779	1.611
Karnataka	4.167	2.796	5.538
Maharastra	2.462	1.189	3.736
Gujarat	1.233	0.417	2.050
Himachal Pradesh	0.536	0.135	0.937
Jammu & Kashmir	1.114	0.882	1.345
Overall	3.070	2.500	100.00

TABLE 5 . Population Weighted Prevalence among Tribal Population for the Country

State	Prevalence (%)	95% C. I.	Weight %
Andhra Pradesh	5.004	3.571	6.436
Rajasthan	10.261	7.692	12.830
Maharastra	8.973	11.10	22.11
Andaman & Nicobar islands	21.071	17.016	11.103
Madhya Pradesh	15.496	13.663	17.330
Arunachal Pradesh	8.446	5.278	11.614
Over all	11.848	10.764	12.932

TABLE 6. Combined overall (Tribal & Nontribal) Population Weighted Prevalence for the Country

Study	Prevalence (%)	95% C.I.	Weight %
Andhra Pradesh (NT)	3.256	1.975	4.538
Andhra Pradesh (T)	5.004	3.571	6.436
Tamil Nadu (NT)	4.517	2.831	6.203
Delhi (NT)	2.255	1.880	2.630
Rajasthan (NT)	2.635	1.730	3.540
Rajasthan (T)	10.261	7.692	12.830

West Bengal (NT)	2.786	2.417	3.154	10.37
Uttar Pradesh (NT)	3.918	2.013	5.823	23.87
Punjab, Haryana &				
Chandigarh (NT)	1.195	0.779	1.611	6.35
Karnataka (NT)	4.167	2.796	5.538	6.91
Maharashtra (NT)	2.462	1.189	3.736	12.02
Maharashtra (T)	8.973	6.842	11.103	1.24
Gujarat (NT)	1.233	0.417	2.050	5.90
Andaman & Nicobar islands (T)	21.071	17.016	25.126	0.80
Himachal Pradesh (NT)	0.536	0.135	0.937	1.38
Jammu & Kashmir (NT)	1.114	0.882	1.345	0.04
Madhya Pradesh (T)	15.496	13.663	17.330	2.59
Arunachal Pradesh (T)	8.446	5.278	11.614	0.10
Overall	3.704	3.167	4.240	100.00

of Hepatitis B in India is different in the different regions of the country. The overall carrier rate is often quoted as being 4.7%.⁵⁸ The calculations undertaken to arrive at this figure are not clear but it appears to be a median of the point prevalence seen in different regions of the country. Lodha et al did a systematic review of literature and concluded that the true prevalence of Hepatitis B in India was 1 to 2%.⁵⁹ No statistical tool was used in the systematic review to synthesize the results of the different studies. Our previous analysis was the first systematic review of prevalence of Hepatitis B in India to use meta-analysis tools. The present analysis employing the same data set has found that using population weights, allows one to arrive at a more realistic estimate of the overall prevalence.

One can attempt a meta analysis on any data, but synthesizing various studies is not appropriate if there is considerable heterogeneity. One indication of the

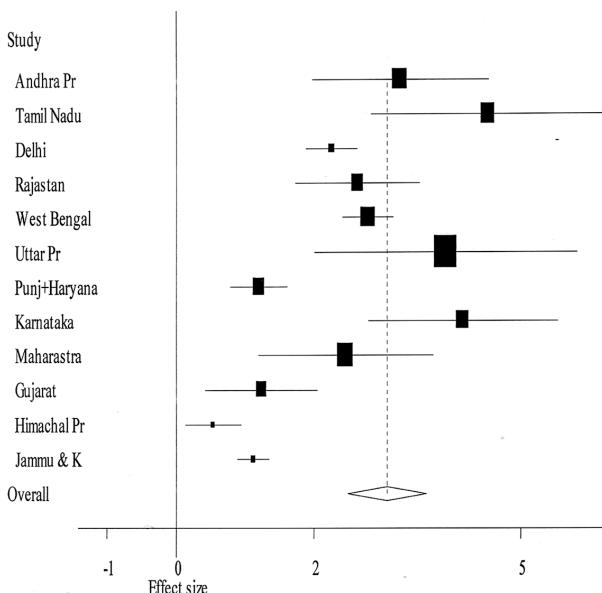


Fig. 4. Population Weighted Prevalence for the Country among Non-tribal Populations.

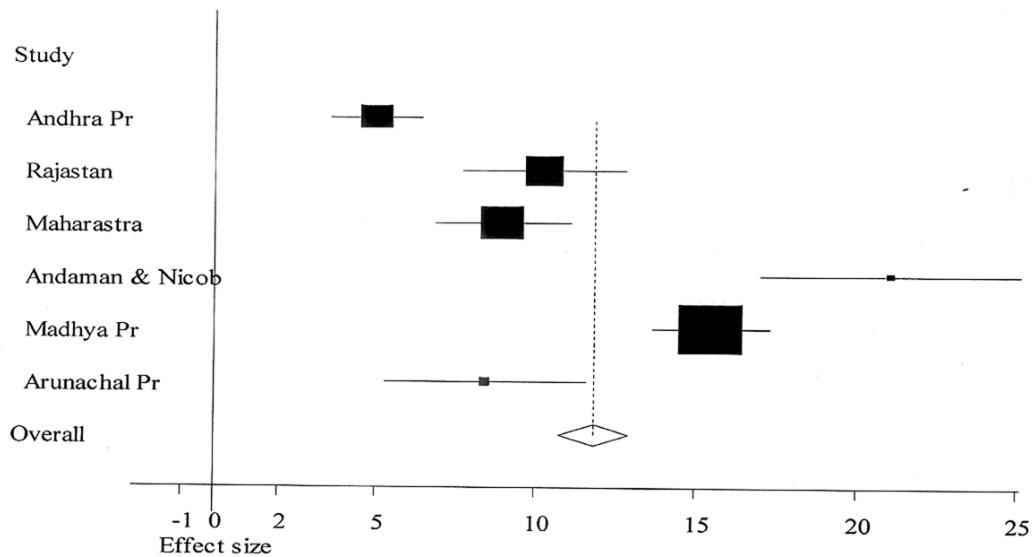


Fig. 5. Population Weighted Prevalence among Tribal Population for the country.

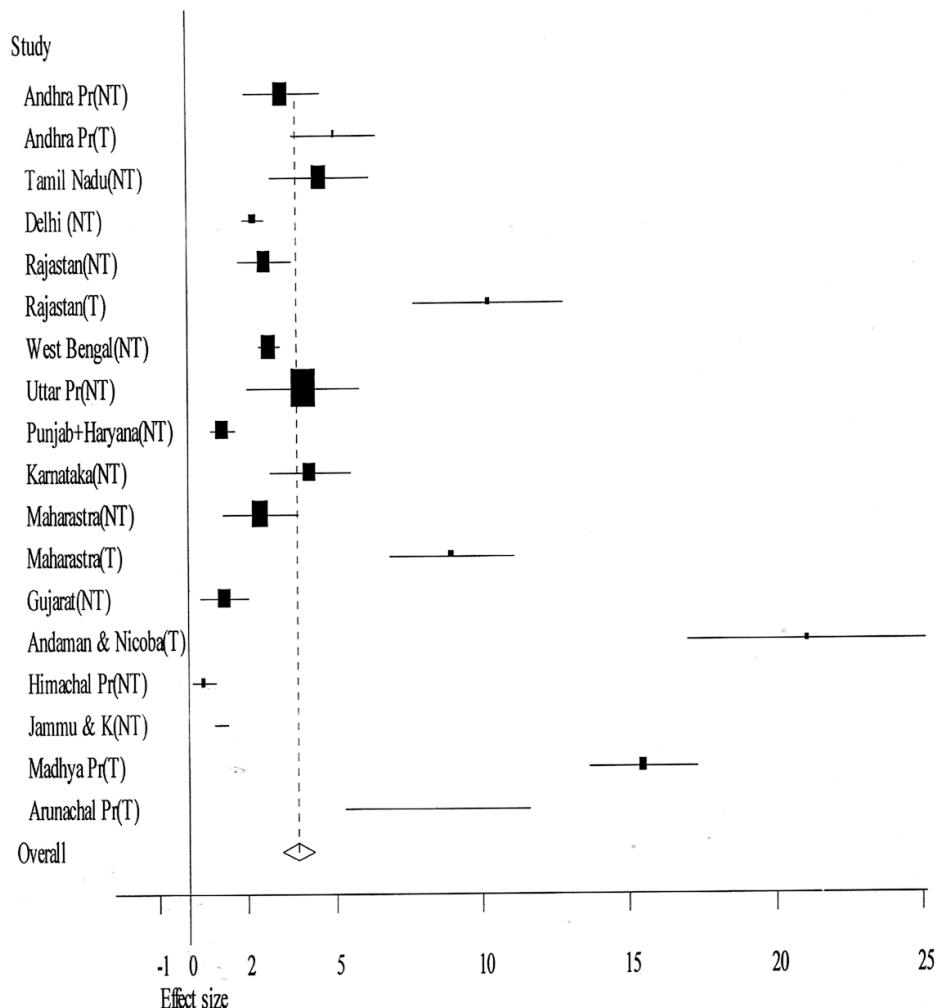


Fig. 6. Combined overall (Tribal & Nontribal) Population Weighted Prevalence for the Country.

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heterogeneity in the data is available from the forest plot. Our results as seen in fig. 1 revealed that tribal population clearly formed a separate group with higher prevalence. Another index of heterogeneity among the studies is the I^2 , which varied from 68% to 98% in different States with more than one study. The overall I^2 was observed to be 98.8%, indicating that there was considerable variability not only in all the studies combined, but also within each State. This is expected as the tribal population has higher prevalence as compared to non-tribal population. Accordingly, a separate meta-analysis was performed for tribal and non-tribal populations. An advantage of using population weights is that it is possible to combine the two analyses (tribal and non-tribal) after giving the tribal population weights in accordance to their representation in the population as a whole. In this study the overall prevalence, combining the data from tribal and non-tribal populations, was 3.7 (Table 6). With its very high prevalence of hepatitis B, tribal populations in India need special attention. Although the use of population weights allows such synthesis of disparate data sets, it has the disadvantage that the tribal group's distinctly higher prevalence, gets submerged in the data of the majority and thus this group may not get the special attention it deserve. The data in the two groups is therefore best analyzed separately as done in the traditional meta-analysis.

Drawbacks of the study and corrective measures

A meta-analysis can only be as good as its component studies. Detection of the true national prevalence will need an epidemiologically representative sample survey from all the different cross sections of society and from all regions of the country. In the absence of such a study, our meta-analysis provides the best retrospective analysis that is available. Half of the States in the country, representing 78% of the national population, have been included in this analysis and as such it should be reasonable to extrapolate this data on to the rest of the country.

Although population weights can correct for distortions due to some forms of publication bias, it can also introduce errors of another type. For example a study of a small sample, which is not representative of the population of a State, may get undeserved weightage from the large population of the State and this can skew the data. In the present study, the aggregate data base from each state was sufficiently large, as indicated by the small confidence intervals seen in the forest plot. Distortion due to small sample sizes can be circumvented, if the forest plots of data from states are screened to ensure that the confidence intervals are acceptably narrow before attributing population weights.

Researchers tend to concentrate on areas with unusual data, and this result in bias in meta analysis. Use of population weights compensates for the bias. This novel method of analysis, resulted in substantial changes in the estimates of prevalence of Hepatitis B in India.

Acknowledgements

The authors acknowledge with thanks the help received from the Indian Medical Association (IMA) 'Subcommittee on Immunization' and the experts who came for the consultation. We also acknowledge the financial support provided by 'Plan International (India)' to the IMA that helped to conduct the experts consultation.

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