

A Bayesian Meta-Analysis and Systematic Review On Global And Local Prevalence Of Hepatitis B

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Abstract

Background: HBV is a global threat, more prevalent in Asia, Latin America, Africa and southern Europe. Pakistan is one of most prevalent countries with approximately 9 million infected. Researchers are trying to investigate the HBV prevalence worldwide but it is too expensive and time consuming to investigate a disease in millions of population.

Methods: We carried out a systematic review of the online literature from 2000-2013 from the six populated continents with a special focus on Pakistan and its neighbors.

Results: The pooled prevalence rate was found to be 30.49, while in stratified analysis with respect to Pakistan vs neighboring countries, only India (10.23) and china (4.13) were observed to be less prevalent than Pakistan. The OR of Pakistani population was 0.19 (95% CI 0.09%-0.35%) against India 0.05(95% CI 0.03-0.08), China 0.006 (95% CI 0.005%-0.007%), Iran 0.24 (95% CI 0.03%-0.76%), Afghanistan 0.44(95% CI 0.05%-0.92%) and Bangladesh 0.22 (95% CI 0.03-0.70%). A significant heterogeneity was observed among pattern of results from the collected data. The Egger's Regression of overall study was -4.53(-22.73 to 13.67) while in Pakistani population it was 22.72(4.18-41.26).

Conclusion: It is to be understood that only a huge countrywide epidemiological study can answer to the general prevalence of HBV in a country like Pakistan with population more than I billion. It is therefore recommended that, the increased risk of HBV among Pakistani population and other related populations needs an effective testing system and proper legislation should also prepared to protect public health.

Keywords: HBV, Hepatitis B, prevalence, meta-analysis

Introduction

HBV is an ever-present virus with worldwide distribution, much more prevalent in Asia, Latin America, Africa and southern Europe. It can cause chronic and acute liver diseases, leads to cirrhosis

and finally hepatocellular carcinoma. Annually, about 1 million death cases are reported from this fatal infection and according to a global estimated more than 2 billion people have been diagnosed of HBV infection [1-4]. The HBV infection may be either symptomatic or asymptomatic, depend upon the

severity and body condition of the infected individual and varies from person to person as well. Chronic hepatitis B leads to cirrhosis then hepato-cellular carcinoma and may cause death [2].

Pakistan also lies among the most common prevalent countries with an estimate of 9 million infected people. The number is increasing steadily day by day due to multiple reasons including lack of awareness, unavailability of proper health facilities and low financial standings for proper management of common contagious diseases including HBV [6-9].

Scientists are trying worldwide to accurately investigate the prevalence of Hepatitis B, in Pakistan also many studies from different regions have been reported to evaluate safety and preventive measures against HBV among Pakistani population to help the government to somehow minimize the HBV infection. But still it is too costly and time consuming on a national level to investigate the prevalence of a disease in millions of population, so the best way to analyze the available data and to obtain the desired results is to use Meta analysis.

Most of the published studies were based on small target groups with a few clinical indications, therefore are unable to precisely reflect the general prevalence. In the current study, a multi-dimensional analysis was performed on a large data set of HBV studies from different ethnic groups of the world to present a clear picture of HBV prevalence in different ethnic groups.

Materials and Methods

Published studies in the English were collected from the online resources including PubMed, the Cochrane library clinical trials registry, ISI Web of Science, CNKI (China National Knowledge Infrastructure) and Google Scholar from 2000 to 2013. Studies fulfilling our inclusion criterion were collected from the six continents (Asia, Africa, Americas, Australia and Europe) with a special focus on Pakistan and its all neighboring countries (Afghanistan, Bangladesh, Iran, India and China). Literature search was performed with the key words, hepatitis, hepatitis B, HBV, HBV epidemiology, HBV in Pakistan and Global Prevalence of Hepatitis B. The meta-analysis was performed through the Comprehensive Meta analysis software Version 2.0 (14 North Dean Street, Englewood, NJ 07631, USA).

The studies fulfilling the following inclusion criteria were included in the present analysis, (1) total number of studied patients with positive and negative individuals (2) cases and none cases number must be confirmed (3) same pattern studies from all continents. Studies that were not in accordance with the inclusion criteria were excluded e.g. if (1) the study do not have both positive and negative samples (2) incomplete data information (3) with less number of patients (5) editorial articles letters, reviews and meta-analysis (Figure-1). Because we conducted a meta-regression, we did use exclusion criteria, and all studies addressing this topic were considered, so that effect estimates (*i.e.*, odds ratios) were available or could be calculated.

An initial draft of the article was sent to the domain experts who were invited to extend the

review if possible, the draft was then modified accordingly. Overall this new study includes data

from a total of 144 studies identified in 133 published papers.

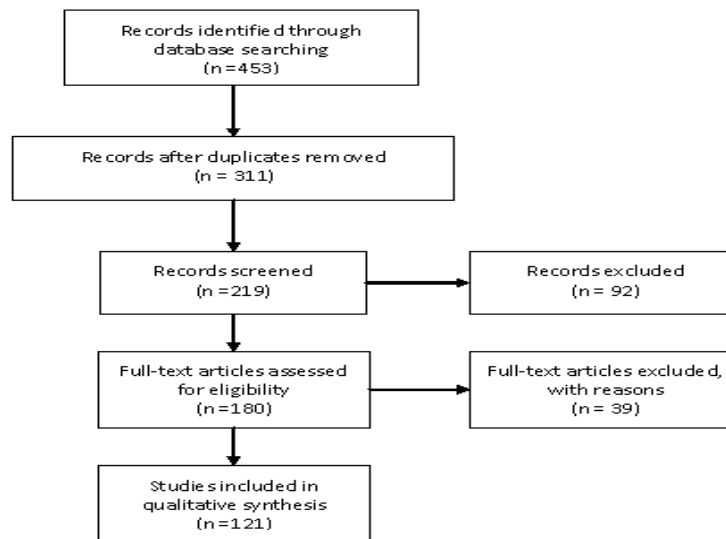


Figure 1: Flow chart for Meta analysis.

Required data was extracted from the published studies by using standardized criteria. Data with the features, author name/s, year of publication, country of research, ethnicity of the sampled population, study design, numbers of cases and none cases, were selected from each study (Table-1). The positive and negative reported individuals were calculated through the odd ratios (ORs) with 95% Confidence Intervals (CI). Funnel plots was used to evaluate the publication biasness. Linear regression was systematically applied to measure asymmetry of funnel plot using a natural logarithm of Odd Ratios to evaluate publication bias [15].

Results

A total of 121 articles were finally selected and included in our study. Some of these studies were also consisted of more than one report, so a total of 144 studies from these 121 research papers

were extracted. The scrutinizing steps are shown in Figure 1.

The prevalence rate of all collected studies was found to be 30.49. In stratified analysis with respect to Pakistan vs neighboring countries, only India (10.23) and china (4.13) were observed to be less prevalent, while Iran (36.84), Afghanistan (47.40) and Bangladesh (31.27) were high in prevalence rate than Pakistan (29.70).The OR results of meta-analysis of Pakistani population was 0.19 (95% CI 0.09%-0.35%) against India 0.05(95% CI 0.03-0.08), China 0.006 (95% CI 0.005%-0.007%), Iran 0.24 (95% CI 0.03%-0.76%), Afghanistan 0.44(95% CI 0.05%-0.92%) and Bangladesh 0.22 (95% CI 0.03-0.70%). The P-Value of Pakistani studies (0.00) was same as to India and china while Iran (0.33), Afghanistan (0.85) and Bangladesh (0.25) were not the same. The Egger’s Regression of overall study was -4.53(-22.73 to 13.67) while in Pakistani population it was 22.72(4.18-41.26), India

9.62(0.34-18.90), China -48(-14.24-4.73), Iran -3.5(-192.56-185.49), Afghanistan 55.12(-140.04-250.28) and Bangladesh -36.04(-90.11-18.02). In sub-group analysis stratified by ethnicity, Asians were compared with other populations. We processed our data to analyze the prevalent ratio of Asians (54.33), Europeans (66.53), Americans (North South) (66.90), Australians (29.04) and Africans (83.95). Among these ethnic groups African were at high risk while the ratio was less in Australian population. The OR values and 95% CI was found as Asian

(0.57(0.30-0.80)), European (0.77(0.43-0.93)), American (North South) (0.66(0.42-0.84)) and African (0.89(0.79-0.94)) population. The Egger's Regression was also performed on all ethnic groups where we observed Asian (-1.18(-49.74-47.36)), European (-27.15(-66.05-11.74)), American (North South) (6.02(-7.77-19011)) and African (4.20(-3.76-12.18)) population. The P-Value in ethnic comparison The Australian and African studies showed null value (0.00) while Asian, European and American were 0.67, 0.45 and 0.62 respectively

Table 1.

Table 2: Pooled analysis of HBV Prevalence on the basis of collected data.

Total	No.	Positive/Negative	Prevalence Rate	OR 95%CI	Kendalls Tau	Egger's Regression
	144	1263490/7840996	30.49	0.13(0.08-0.20) I ² =99.99 P=0.00	0.98 2TP=0.08	-4.53(-22.73-13.67) 2TP=0.62
Pakistan VS neighbors						
Pakistan	26	18308/470725	29.70	0.19(0.09-0.35) I ² =99.94 P=0.00	-0.25 2TP=0.07	22.72(4.18-41.26) 2TP=0.02
India	29	5393/371584	10.23	0.05(0.03-0.08) I ² =99.73 P=0.00	-0.06 2TP=0.67	9.62(0.34-18.90) 2TP=0.04
China	35	8284/1417769	4.13	0.006(0.005-0.007) I ² =99.77 P=0.00	-0.07 2TP=0.57	-48(-14.24-4.73) 2TP=0.32
Iran	3	21495/122662	36.84	0.24(0.03-0.76) I ² =99.54 P=0.00	-0.33 2TP=0.6	-3.5(-192.56-185.49) 2TP=0.85
Afghanistan	4	722/1488	47.40	0.44(0.05-0.92) I ² =99.65 P=0.00	0.66 2TP=0.174	55.12(-140.04-250.28) 2TP=0.34
Bangladesh	4	170989/32292	31.27	0.22(0.03-0.70) I ² =99.9 P=0.00	0.00 2TP=1.0	-36.04(-90.11-18.02) 2TP=0.1
Ethnicity/Populations						
Asian	25	1072308/164648	54.33	0.57(0.30-0.80) I ² =99.9 P=0.00	0.06 2TP=0.67	-1.18(-49.74-47.36) 2TP=0.96
European	8	102339/5981	66.53	0.77(0.43-0.93) I ² =99.9 P=0.00	0.21 2TP=0.45	-27.15(-66.05-11.74) 2TP=0.14
American (North+South)	8	1523/1460	66.90	0.66(0.42-0.84) I ² =98.78 P=0.00	0.14 2TP=0.62	6.02(-7.77-19011) 2TP=0.32
Australia	2	1019/2489	29.04	0.31(0.25-0.38) I ² =76.54 P=0.04		
African	9	4090/586	83.95	0.89(0.79-0.94) I ² =97.54 P=0.00	-0.11 2TP=0.67	4.20(-3.76-12.18) 2TP=0.080.28

2TP = 2 tailed P value

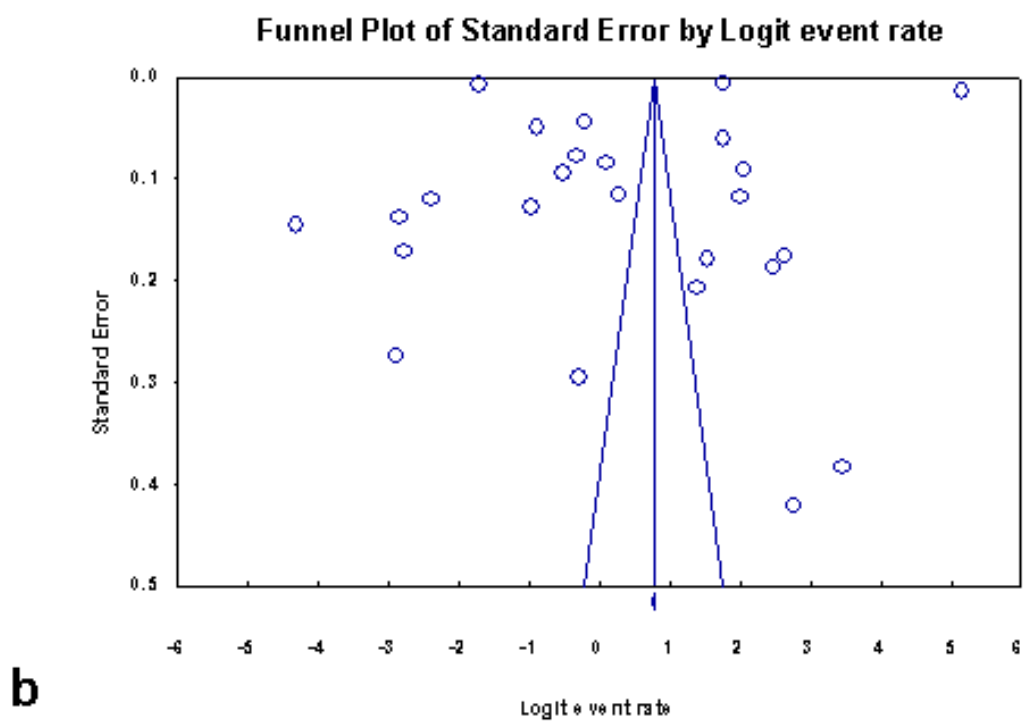
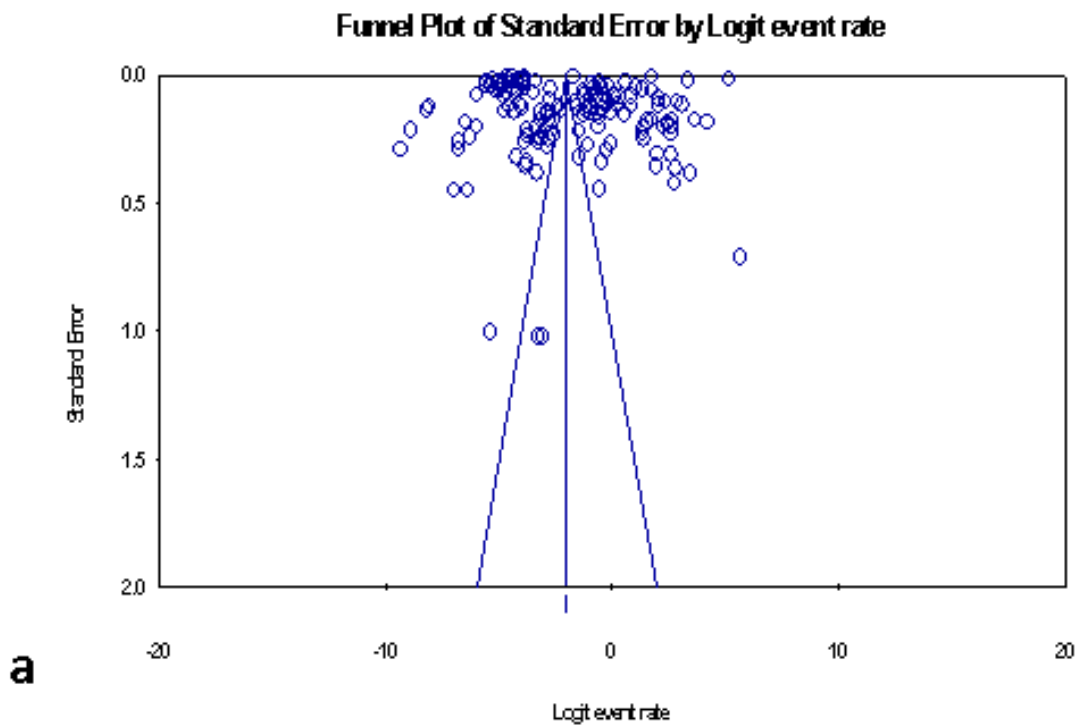


Figure 2. Funnel plot analysis to evaluate publication bias

- a. heterogeneity in pooled worldwide data.
- b. heterogeneity in pooled data from Asia

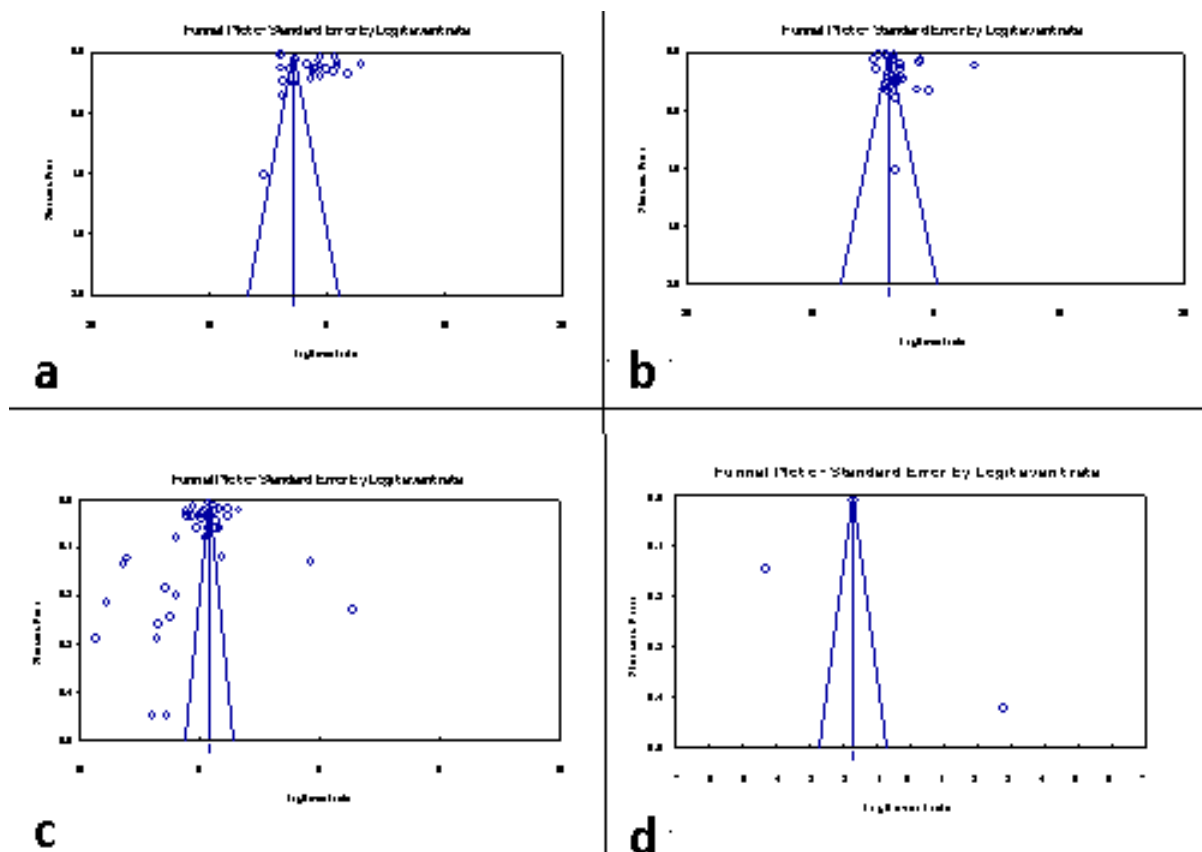


Figure 3. Funnel plot analysis to evaluate publication bias in country wise data. The plots shows heterogeneity in pooled data from, a. Pakistan b. India c. China and d. Iran

Discussion

In the current analysis there were a lot of variations observed in the collected data from different populations. In sub-group analysis stratified with reference to Pakistan and its neighbors, a significant heterogeneity was observed among the included studies and similar pattern of results was observed in different ethnic groups from different continents. The heterogeneity as observed in our analysis is not surprising because of the difference in methods, kits, antigens etc used in the prevalence assessment. Meta-analysis is therefore helpful in providing a comprehensive sketch and informative idea of the global and local prevalence. Almost every included study is a cross-sectional one and

is thus analytical of the disease occurrence. However many ways for the prevalence may be used to obtain its accurate estimate.

In our results we found that, the OR results of meta-analysis of Pakistani population was 0.19 (95% CI 0.09%-0.35%) against India 0.05(95% CI 0.03-0.08), China 0.006 (95% CI 0.005%-0.007%), Iran 0.24 (95% CI 0.03%-0.76%), Afghanistan 0.44 (95% CI 0.05%-0.92%) and Bangladesh 0.22 (95% CI 0.03-0.70%). The P-Value of Pakistani studies (0.00) was same as to India and china while Iran (0.33), Afghanistan (0.85) and Bangladesh (0.25) were not the same. While The Egger's Regression of overall study was -4.53(-22.73 to 13.67) while in Pakistani population it was 22.72(4.18-41.26), India

9.62(0.34-18.90), China -48(-14.24-4.73), Iran -3.5(-192.56-185.49), Afghanistan 55.12(-140.04-250.28) and Bangladesh -36.04(-90.11-18.02). In the same study we also had to analyze the data from different continents in which we concluded that The OR values and 95% CI in Asian was 0.57(0.30-0.80), European 0.77(0.43-0.93), American (North South) 0.66(0.42-0.84) and African 0.89(0.79-0.94). The Egger's Regression was also performed on all ethnic groups where we observed Asian (-1.18(-49.74-47.36)), European (-27.15(-66.05-11.74)), American (North South) (6.02(-7.77-19.01)) and African (4.20(-3.76-12.18)) population.

The same studies have also been seen conducted by other workers; they have analyzed the data only from a single country, while we have collected a sample data from six different countries and six continents as well. A better example is the study of Liu et al., 2013 [10], who designed a study for the estimation of prevalence of HBsAg positive and HBV occult infection in Chinese blood donors through meta-analysis. They identified 571227 positive and 5957412 negative donors in OBI group and HBsAg group respectively. The pooled prevalence of HBsAg group was 1.085% (95% CI 0.859%, 1.398%) and OBI group was 0.094% (95% CI 0.0578%, 0.1655%) respectively. They also found in their analysis that, developed regions have a comparatively lower prevalence rate than the under developed areas. other countries has an obvious lower prevalence e.g. France has 0.12% [12], UAE has 0.23% [13], UK has 0.004%, even most of the Latin American countries has

prevalence rates less than 0.5% [14] and China (1.085%) also as compared to the prevalence of Pakistani population. We also compared our study with that of Batham et al 2007 [11] who evaluate the point prevalence of different parts of India through Meta-analysis. They observed prevalence rate of 15.9 % (CI: 11.4% -20.4%) in tribal populations and 2.4% (95% CI: 2.2% - 2.7%) in non-tribal populations, which is showed variation from our analysis.

Careful examination of the forest plots from the neighbors to Pakistan and Asia versus other continents, all studied populations have prevalence rate close to the overall mean and it seems suitable that all these groups are integrated in this comprehensive systematic review and meta-analysis. This is not confirmed that all the published articles were surely being included in this study because of the limited keywords used for the identification and collection of data. Therefore to minimize this we directly traced research papers through their proper references but still a systematic attempt was made to get sample representative studies from the selected countries. It is understood that only a huge countrywide epidemiological study be able to answer to the general prevalence of HBV in Pakistan.

The elevated incidence of HBV contamination among Pakistani population needs an effective testing system. Legislation should be prepared to shield therapeutic welfare of human resources in both public and private sectors to minimize HBV infection. It is also needed in a country like Pakistan to improve health education at the basic

level among the communalities and also to encourage more sensitive detection technologies in diagnostics. Most importantly, input are needed collectively from the central government along with provisional Governments of Pakistan for the construction of public health system/schemes in general and specifically in under developed areas as an indispensable way out to improve blood safety against HBV infection.

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