

A Systematic Review and Meta-analysis of Injecting Drug Use as a Risk Factor of HIV in Bangladesh

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Abstract

HIV is a new, transpiring problem, especially, among injecting drug users (IDU) in Bangladesh. Although HIV prevalence in Bangladesh compared to the neighboring countries is still low, ongoing high-risk behaviors among injecting drug users could facilitate the more extensive transmission of HIV to the general population. This study aims to assess the relationship between HIV and injecting drug use. Through a systematic review, we included 19 studies that met the inclusion/exclusion criteria. Pooled prevalence, odds ratio, 95% CI, and measures of heterogeneity were calculated by the random-effects model. Publication bias was examined by funnel plots and Egger's test. We found the overall pooled prevalence was 3.65% (95% CI: 2.10-5.56%) which indicates that Bangladesh is on the brink of a concentrated epidemic. IDUs were 6.085 times more likely to be HIV-positive than non-IDUs (pooled OR: 6.085; 95% CI: 4.654-7.956). The pooled prevalence for males was reported to be 2.44% (95% CI: 1.51-3.57%), which was significantly higher than those for females with a pooled prevalence of 0.26% (95% CI: 0.00-1.19%). This meta-analysis revealed that injecting drug use is a significant risk factor for HIV in Bangladesh. Moreover, while the HIV prevalence in female IDUs was found to be very low, it was much higher in male IDUs.

Keywords: Meta-analysis, Injecting Drug Use, HIV, AIDS, Risk Factor.

I. Introduction

AIDS is an acquired immune deficiency syndrome caused by the human immunodeficiency virus (HIV) that spreads through blood, semen, vaginal secretions, and breast milk¹. Unprotected sexual intercourse with an HIV-positive partner is the most common method of transmission. Other methods include transfusion of blood or blood products, tissue or organ transplants of a HIV infected person, use of contaminated needles and syringes, mother-to-child transmission during pregnancy, birth, or breastfeeding¹. Bangladesh is one of the countries with a low HIV prevalence but is still considered to be at high risk because of the presence of many risk factors for the spread of HIV, in particular injecting drug use. The overall prevalence of HIV in Bangladesh is less than 1%, however, among the key populations (for example, IDUs, sex workers, men who have sex with men, and truck drivers), high levels of HIV have been found among injecting drug users (IDUs)². For example, according to the latest serological surveillance, 7% of all IDUs living in Dhaka's Old City tested positive for HIV exceeding the threshold of 5% for being an epidemic condition³.

Injecting drug use is a method of illicit drug use. In this method, users inject drugs into the body via needle and syringe. Any means of contaminated drug injection equipment can transmit any blood-borne viruses⁴. According to UNODC (United Nations Office on Drugs and Crime), around 15.9 million people inject drugs illicitly, and among them, approximately 3 million are HIV-

positive⁵. In 2008, the estimated number of IDUs was 20,000- 40,000, and at least 5,000 among them were the inhabitants of Dhaka city⁷⁻⁸. Drug users spread the disease more rapidly by using non-sterile injecting equipment among themselves and also through sexual contact.

Since 1998, Bangladesh has been implementing a national HIV surveillance system based on UNAIDS guidelines. Behavioral surveillance has previously been undertaken by ICDDR, B (International Centre for Diarrhoeal Disease Research, Bangladesh) but is now run by other key institutions. The population groups consider to be most-at-risk for HIV prevalence include: female and male sex workers, males who have sex with males (MSM), transgender (hijras), injecting drug users (IDU), heroin smokers, truckers, dockworkers, launch workers, rickshaw pullers, etc. According to Azim et al.⁹ after the fourth round of national serological surveillance, HIV prevalence remained below 1% in all groups except IDUs. IDUs were found to have the highest HIV prevalence in all rounds. She reported that there had been a significant rise in HIV prevalence in IDUs from the needle/syringe exchange programs (NEP) in Central Bangladesh between the last three rounds (P-value= 0.035) and the rate (4%) was close to the concentrated epidemic mark¹⁰.

The sixth round of national HIV serological surveillance included female IDUs as a separate group for the first time in surveillance, and HIV prevalence was zero¹¹. HIV rate in IDUs had been steadily rising over the years and now, after the 6th round, it was found to be 4.9%¹¹. HIV prevalence

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remained low, less than 1%, amongst most of the other key populations sampled¹¹. The ninth round of national serological surveillance showed that the prevalence of HIV was less than 1% among all population groups tested, except for IDUs. The prevalence of HIV in the cluster of IDUs increased from 4% in 2002 to 7% (in one locality of central Dhaka) in 2007-2008, which fell to 5.3% in 2010. Also, the prevalence of HIV in female IDUs was found to be 1.13%^{7,12}.

HIV prevalence rates were reported to be the highest among the IDU population since the first surveillance in 1998¹³. As mentioned in the foregoing discussions, although there are numerous individual studies to assess the prevalence of HIV among IDUs in Bangladesh, no systematic review and meta-analysis has yet been implemented to determine the significance of injecting drug use as a risk factor of HIV in Bangladesh. Therefore, the primary research objective of this study was to aggregate the evidence of injecting drug users impact on HIV in Bangladesh. Our aim was to conduct a systematic review and meta-analysis of studies to assess the HIV prevalence among IDUs by calculating a combined pooled prevalence and, to check the association between HIV and injecting drug use through a combined pooled odds ratio.

II. Methods and Materials

Search strategies and data extraction

The inclusion criteria for this study were: 1) biological confirmation of HIV status, 2) clear description of HIV-risk population, 3) provision of raw numbers of subjects exposed and unexposed by injecting drug use, 4) studies must report sufficient statistical information to compute effect sizes, 5) studies must be conducted in Bangladesh region. Several sources were used to access data for this review. Initially, PubMed and Google Scholar were searched for published articles from 1998 to 2019 using the search terms: “all in the title: Bangladesh HIV OR AIDS”. The reference lists from relevant review articles and all eligible studies were also searched manually. Other relevant articles and reports released by ICDDR, B and the Ministry of Health and Family of Bangladesh were utilized. The initial search process resulted in the identification of 563 articles (471 in Google scholar and 92 in PubMed) with potential for inclusion in the meta-analytic database. There were three levels of screening. In the first two rounds of screening, only the titles and abstracts were checked while the third round consisted of a review of full-text articles. These levels of screening were performed by several investigators. Investigators simultaneously extracted data from the articles in the third level which is discussed in the next section. Thus, the articles were narrowed down to 19

studies^{2,6-7,11-12,20-21,28-36}. The data of first three serological surveillance can be found in the ninth round technical report of National HIV serological surveillance⁷.

The selection process is documented with a flow chart in Figure 1 to illustrate how the inclusion and exclusion criteria were applied to the available studies, and how the final studies were selected. Two general categories of information were extracted: study descriptors and effect size information. For each eligible study, the following information were obtained: 1) first author's name, 2) year of publication, 3) year of study, 4) sampled population (e.g., brothel-based sex workers, injecting drug users, adolescents, etc.), 5) Study design (e.g., Cohort/Cross-sectional/Case- control), 6) study location, 7) mean/average age of the participants (if mean/average age is not mentioned, age- group was reported), 8) the total number of participants in the study (overall sample size), 9) the number of HIV positive, 10) overall effect size, 11) the total number of injecting drug users, 12) the number of injecting drug users who are HIV positive (without considering gender), 13) effect size without considering gender, 14) the number of male and female Injecting drug users, 15) number of male and female injecting drug users who are HIV positive, and 16) effect size for male and female separately.

Effect size computation and choice of model

The effect size can be described as a number that encodes the magnitude of the relationship between two variables. The summary effect is the weighted mean of the individual effects^{14,15}. Our primary outcome was the proportion/prevalence of injecting drug users who developed HIV. This was calculated as the number of HIV-positive persons divided by the total number of injecting drug users. Besides using proportion/prevalence as the effect size, we calculated the odds ratio for assessing the association between HIV and injecting drug use.

Barendregt et al.¹⁶ discussed methods of a meta-analysis of prevalence and also some transformations to stabilize the variance. Individual study weights can be obtained by using the binomial equation for variance:

$$Var(\hat{p}) = \frac{\hat{p}(1 - \hat{p})}{N},$$

where p is the prevalence, and N is the population size. Therefore, the pooled prevalence estimate P becomes

$$\hat{P} = \frac{\sum_i \frac{\hat{p}_i}{Var(\hat{p}_i)}}{\sum_i \frac{1}{Var(\hat{p}_i)}}$$

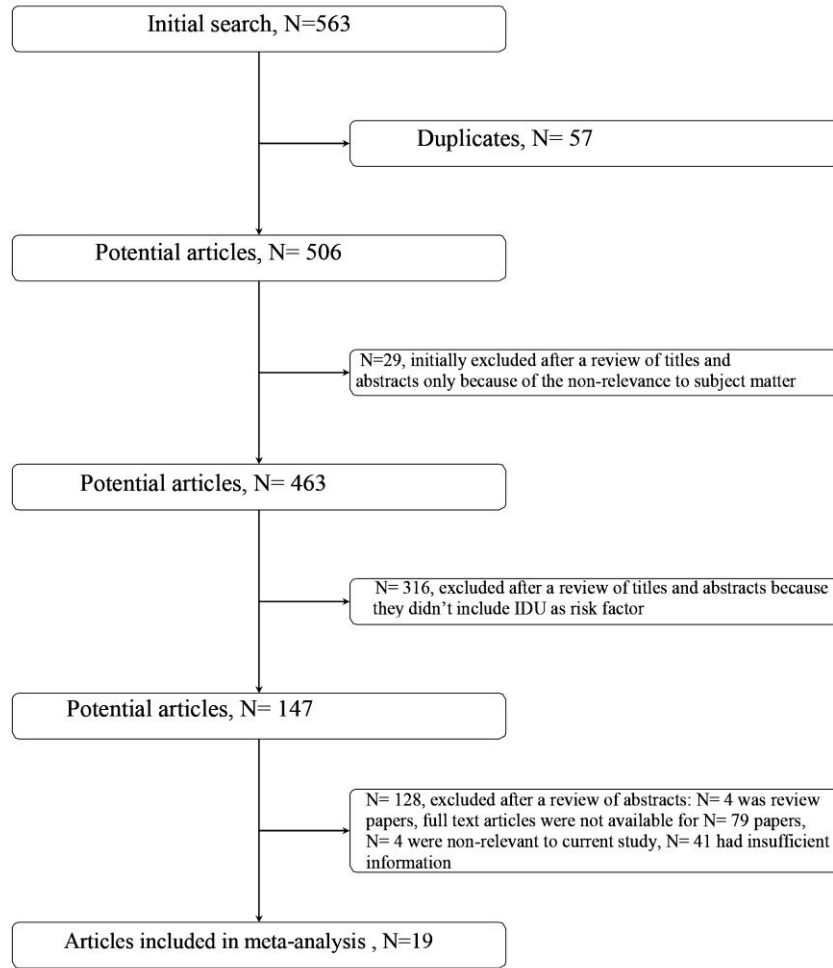


Fig.1. A flow chart illustrating how the inclusion and exclusion criteria were applied to the available studies and how the final studies were selected. with SE

$$SE(\hat{P}) = \sqrt{\sum_i \frac{1}{\text{Var}(\hat{p}_i)}}$$

Although this works well for the value of proportion around 0.5, problems arise when it becomes close to the limits of the [0,1] range. Hence, we used Freeman-Tukey double arcsine transformation, which is more reliable¹⁶. For data from a prospective study where the data were reported as the number of events and non-events in two groups, researchers typically compute either risk ratio or odds ratio, or risk difference¹⁵. To measure the association between injecting drug use (risk factor) and HIV (disease), we calculated the odds ratio as effect size.

For aggregating individual effect sizes, we chose a random-effects model because it provides a more conservative estimate than a fixed-effects model of variance. This approach draws reliable conclusions since it recognizes the selected studies as a sample of all potential studies and

incorporates between-study variability in the overall pooled estimation. The random-effects framework postulates that each study summary statistic, Y_i , is a draw from a distribution with a study-specific mean, θ_i , and variance, s_i^2 ,

$$Y_i | \theta_i, s_i^2 \stackrel{\text{indep.}}{\sim} N(\theta_i, s_i^2).$$

Assessing heterogeneity and publication bias

We carried out a chi-squared test of the hypothesis of homogeneity of effects using Cochran’s Q statistic to quantify if the observed and expected effects are equal. According to Borenstein et al.¹⁵, the first step in partitioning the variation is to compute Q, defined as,

$$Q = \sum_{i=1}^k W_i(Y_i - M)^2,$$

where W_i is the study weight ($\frac{1}{V_i}$), Y_i is the study effect size, and M is the summary effect and k is the number of studies.

We also estimated I^2 which was proposed by Higgins¹⁷ to serve as a measure of heterogeneity independent of scale and to quantify the proportion of the observed variance that reflects the real differences in effect size. While systematic reviews and meta-analyses have the potential to produce reliable parameter estimates of treatment effects, they are not free from bias¹⁸. Publication bias was assessed using funnel plot and its asymmetry was examined by using Egger’s method¹⁹. Stata version 14.1 was used for the statistical analysis.

III. Analysis and Results

A total of 19 studies published from 1998 to 2018 were included in the meta-analysis. These 19 studies generated a sample size of 97059 subjects where the injecting drug user sample size was 26259. Among these 19 studies, only 15 studies contained information on male and female sample sizes and that yielded a male sample size of 24478 and a female sample size of 973. Only 12 studies contained information on both IDUs and non-IDU groups, consisting of a sample of 23235 and 70800 subjects, respectively. The subject’s age range was 15-50 years.

HIV prevalence among IDUs was used to pool the overall prevalence with 19 studies using the DerSimonian- Laird

random-effects method. This process was also used to calculate pooled HIV prevalence among male and female injecting drug users with 13 studies and 7 studies, respectively. The Freeman-Tukey double arcsine transformation of proportions/prevalence was performed to stabilize the variance. 12 studies containing information on both IDUs and non-IDUs were used to calculate the pooled odds ratio, and perform a Z test with a null hypothesis, H_0 : Pooled OR = 1.

The pooled prevalence of HIV among IDUs in Bangladesh was found to be 3.65% (95% CI: 2.10-5.56%) which means that among the injecting drug users, 3.65 out of 100 individuals were found to be HIV positive. From the forest plot in Figure 2, we get an idea of the relative weights given to each study and the precision of those studies. Here, the squares indicate the effect sizes for each study and the size of them indicates their weights. Studies with more weights are represented by a bigger square. The effect size of each study is bounded by a confidence interval which measures the uncertainty of the effect size. The confidence interval for the study “Urmi et al.(2015)” is narrower than that for the study “Matin et al.(2011)”, reflecting the fact that the “Urmi et al.(2015)” study has greater precision. The pooled effect size (3.65%) is represented by a diamond here with a confidence interval of (2.10-5.56%).

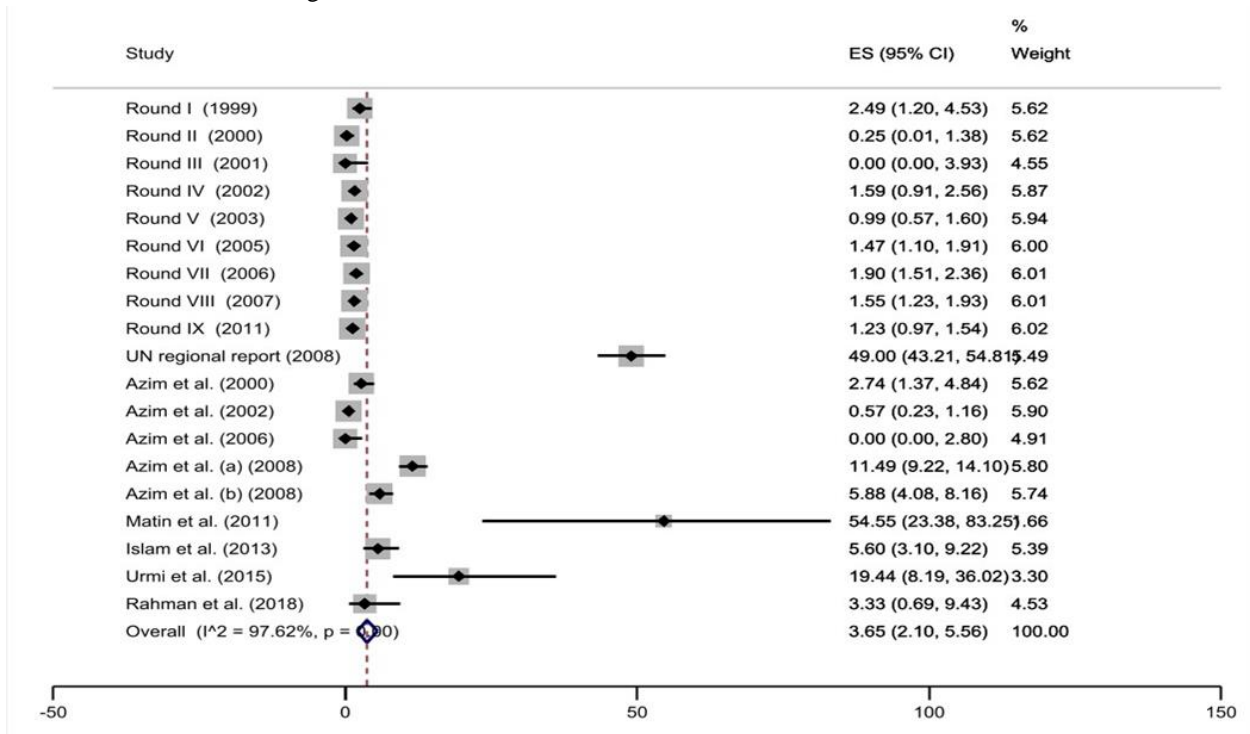


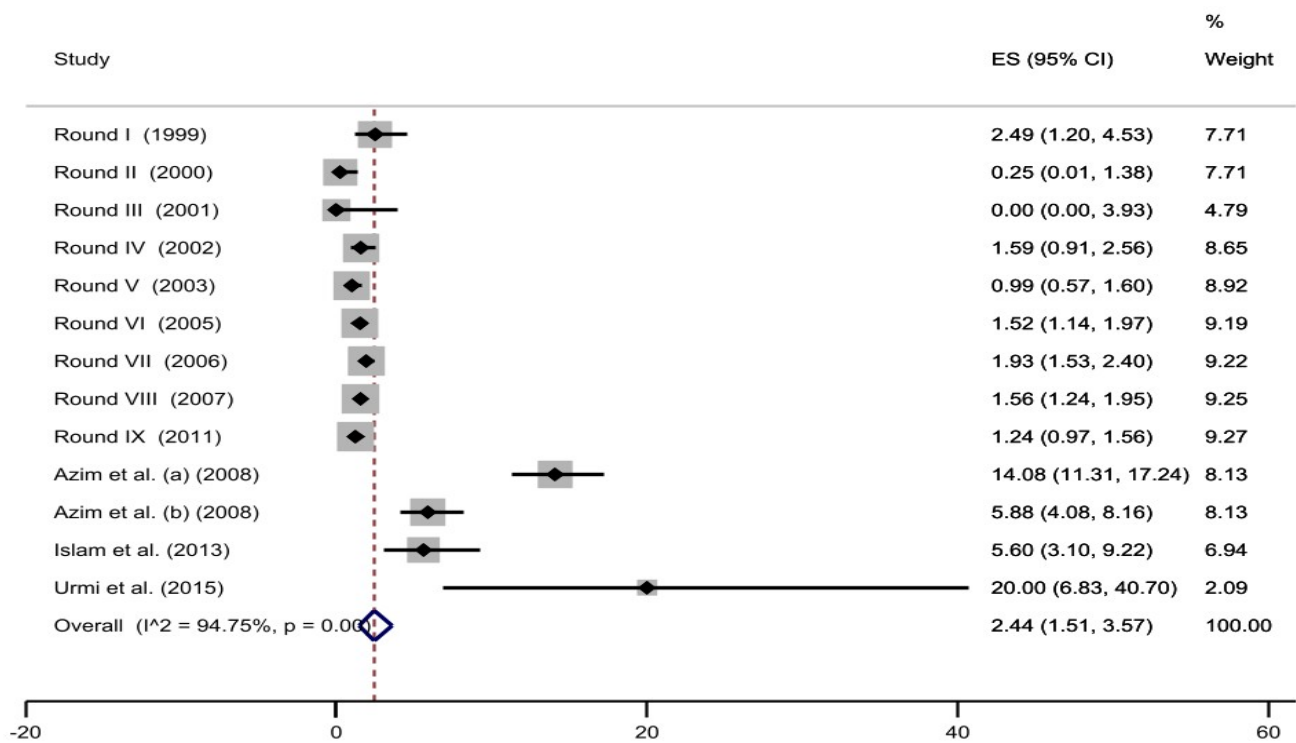
Fig. 2. Forest plot for overall HIV-prevalences from random-effect meta-analysis with 19 studies.

The I^2 was found to be 97.62% which means that 97.62% variation in the effect size was due to heterogeneity among studies. From Cochran's Q test, heterogeneity chi-squared (Q statistic) was 757.12 with degrees of freedom 18, and thus the test of heterogeneity yielded a p-value of 0.00 meaning that heterogeneity among the studies is significant. The estimated between-study variation τ^2 for this random effect model was found to be 0.03.

From the forest plots in Figure 3, we get an idea of the relative weights given to each study and the precision of those studies for both the meta-analyses conducted for male and female IDUs separately. We also see that the pooled prevalence of HIV among male IDUs in Bangladesh was 2.44% (95% CI: 1.51-3.57%) which means that among the male injecting drug users, 2.44 out of 100 individuals were found to be HIV positive, whereas the pooled prevalence of HIV among female IDUs in Bangladesh was 0.26% (95% CI: 0.00-1.19%) indicating 0.26 out of 100 female injecting drug users were found to be HIV positive.

The number of HIV-positive individuals among IDUs, the number of HIV-positive individuals among non-IDUs, effect sizes (here, odds ratio), 95% confidence intervals, and weights in percentage for each study were presented in Figure 4. The pooled odds ratio was 6.085 (95% CI: 4.654-7.956) which means IDUs were 6.085 times more likely to be HIV-positive than non-IDUs. Test of significance of the association between HIV and injecting drug use yielded a p-value of 0.00 which indicates there was a significant association between HIV and injecting the drug.

Four funnel plots are shown in Figure 5 to assess the publication bias of the four meta-analyses we conducted. For the overall HIV-prevalence analysis, 2 studies are out of the dashed region is almost 89% of the studies are inside the region. The effect has direction to the right, so non-significant studies would have been on the left bottom of the plot if we had been able to locate them. For the overall odds ratio analysis, we took the odds ratios and standard errors in the log scale as suggested.



(a)

Fig. 3. Forest plots for (a) male HIV-prevalence from random effect meta-analysis with 13 studies

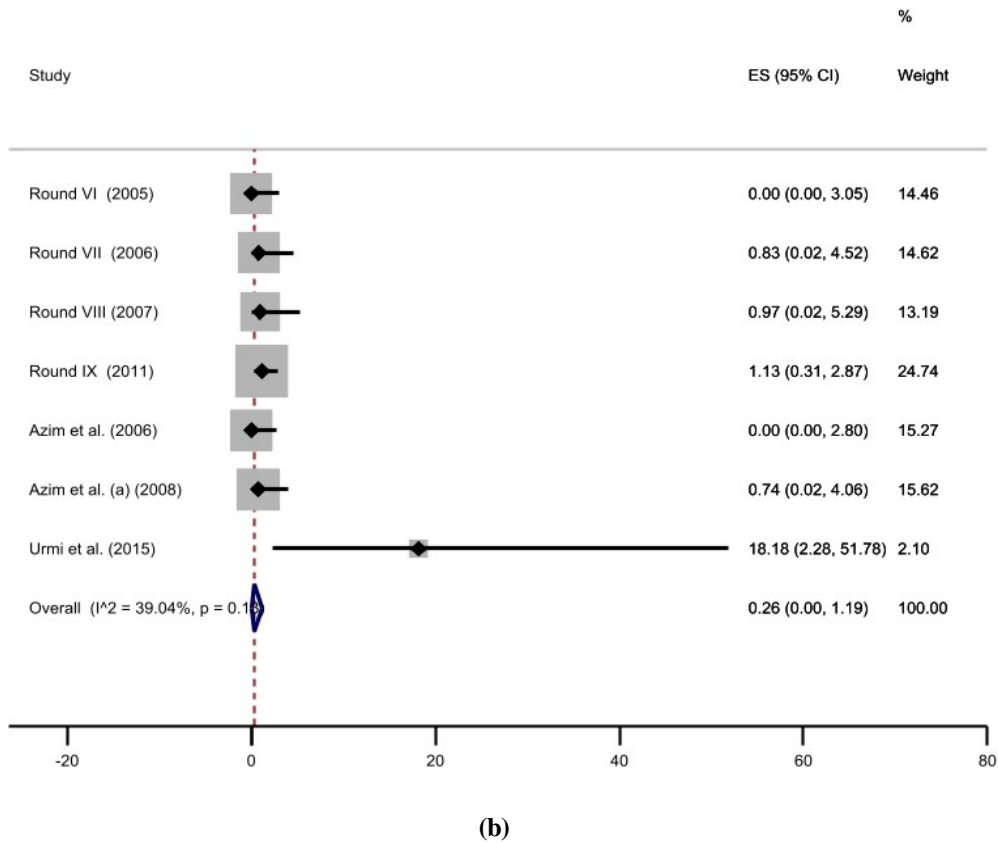


Fig. 3. Forest plots for (b) female HIV-prevalence from random effect meta-analysis with 7 studies.

Here, all studies are inside the region which indicates no bias. We found the p-value for Egger’s test of publication

bias for all four analyses is < 0.05 which indicates that there are no small-study effects for the analyses.

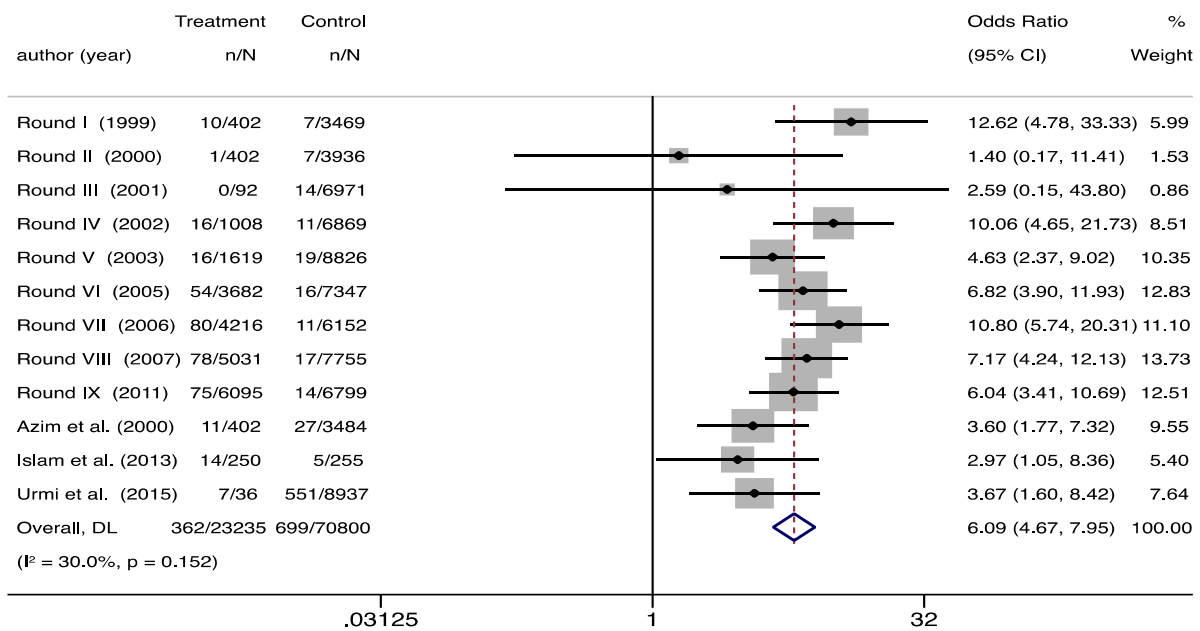


Fig. 4. Forest plot for odds ratios from random-effect meta analysis with 12 studies.

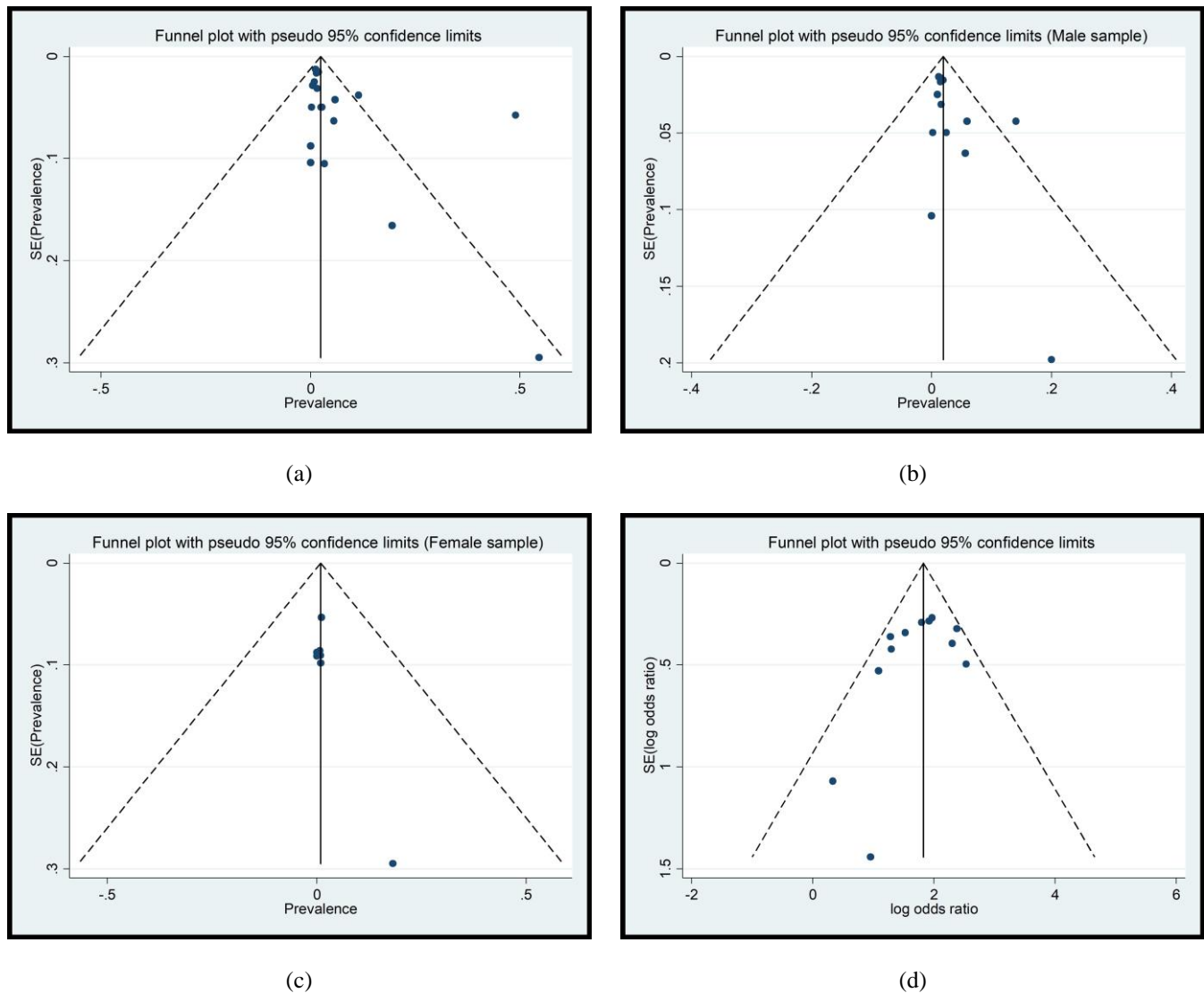


Fig. 5. Funnel plots for (a) overall HIV-prevalence from random effect meta-analysis with 19 studies, (b) male HIV-prevalence from random effect meta-analysis with 13 studies, (c) female HIV-prevalence from random effect meta-analysis with 7 studies, and (d) overall odds ratio from random effect meta-analysis with 12 studies.

IV. Discussion and Conclusion

In the present meta-analysis, we have quantified the association between injecting drug use and HIV in Bangladesh which has yielded statistically significant findings by extracting its strength from the pooled estimates for a large combined sample size of subjects ($N = 97059$) which eventually increased the statistical power to study the effects of interest.

This meta-analysis showed that Bangladesh is on the brink of a concentrated epidemic among people who inject drugs (pooled prevalence: 3.65%; 95% CI: 2.10-5.56%). While the HIV prevalence in female IDUs was found to be very low (pooled prevalence: 0.26%; 95% CI: 0.00-1.19%), in male IDUs, it was much higher (pooled prevalence: 2.44%; 95% CI: 1.51-3.57%). Also, this meta-analysis revealed that injecting drug use is a significant risk factor for HIV. People who inject drugs were

6.085 times more likely to be HIV-positive than people who do not inject drugs (pooled odds ratio: 6.085; 95% CI: 4.654-7.956).

The prevalence of HIV in female IDUs was comparatively lower than in male IDUs which was expected because of the socio-cultural factors of Bangladesh. Women using illicit drugs are more stigmatized compared to their male counterparts, and therefore more hidden. Hence, inability to detect female injecting drug users in Bangladesh could also attribute to this low prevalence of HIV among female IDUs. However, our findings echo those of other authors. Azim et al.²⁰ found that no one had HIV among 130 female IDUs but she suggested that female IDUs are vulnerable to HIV through their injection and sexual risk behaviors and sex worker IDUs appear especially vulnerable.

Very little is known about female IDUs in Bangladesh, and intervention programs are not accessing them in large numbers². The high prevalence of HIV in male IDUs also reflects the

vulnerable situation of marginalized male injecting drug users in Bangladesh. The data from the HIV surveillance survey²² reported a rapid rise of HIV among male IDUs in Dhaka city which has significantly increased from 5.3% in 2011 to 22% in 2016 which is the explainable consequence of our pooled result that included national surveillance reports from 1998 to 2011.

Another finding of our study was injecting drug use is a significant risk factor for HIV. This makes sense because injecting drug users are at the highest risk of exposure to HIV than the other key populations because of their prevalent immune nutritional deficiencies^{23,24}, and behavioral risk factors such as sharing of needles, multiple sex partners, unprotected sex practices, use of immunosuppressive morphine derivatives, etc.^{3,25}. This is coupled with continuing high-risk behaviors, such as increased sharing of injecting equipment and a decline in condom use in sexual encounters with female sex workers in Bangladesh¹³. The IDU population is well integrated into the surrounding community, socially and sexually, increasing concern about the spread of HIV from this most at-risk population. It has been documented that the largest number of AIDS cases in developing countries occurs in IDUs^{24,26}. According to WHO, injecting drug use was the second most common mode of HIV transmission in the South-East Asia region²⁷. Also, there was evidence of continuing high transmission among people who inject drugs²⁷.

HIV among injecting drug users is increasing alarmingly in Bangladesh and requires long-term, comprehensive, and effective interventions and prevention. The numerous analyses completed for this study may not necessarily delineate complex differences in HIV epidemic dynamics, but bring further indication of a high HIV prevalence rate among injecting drug users. HIV surveillance efforts should consider the high density of HIV among this key population and expand surveillance approaches to locate hidden populations. Social science, epidemiological, and behavioral research should be more involved in research to assess the prevalence of HIV risk behaviors, awareness about HIV, and social and sexual network interactions, hence strengthening our capability to cross-examine various studies. Research works, surveillance and prevention efforts should be in sync together to improve and propagate currently available strategies targeting the key populations in Bangladesh. Many pragmatic strategies are being implemented in Bangladesh but need further assessment.

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