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Review article

Rates of hepatitis B and C in patients with schizophrenia: A meta-analysis

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ABSTRACT

Objective: Schizophrenia is associated with increased infectious disease comorbidity and mortality. Individuals with schizophrenia have increased risk of infectious hepatitis, potentially due to substance use comorbidity, sexual behaviors, and immunologic factors. We performed a systematic review and meta-analysis of the association between schizophrenia and hepatitis B and C.

Method: We searched major electronic databases from inception until January 2019 for prevalence and case-control studies of infectious hepatitis in patients with schizophrenia. Random effects meta-analyses calculating odds ratios (ORs) and 95% confidence intervals (CIs) for case-controls studies, prevalence and 95% CIs, and meta-regression analyses were performed.

Results: Twenty-one studies met the inclusion criteria. In case-control studies, there was an over 3-fold increased odds of hepatitis C in patients with schizophrenia (OR = 3.29, 95% CI 1.50–7.23, p = 0.003), and a prevalence of 6% (ES = 0.06, 95% CI 0.04–0.08). In case-control studies, there was an over 2-fold increased odds of hepatitis B in patients with schizophrenia (OR = 2.36, 95% CI 1.61–3.47, p < 0.001) and a prevalence of 7% (ES = 0.07, 95% CI 0.03–0.11).

Conclusion: We found an approximately 3-fold increased odds of hepatitis B and C in patients with schizophrenia. This association may be due to an increased prevalence of environmental risk factors, increased susceptibility to infections, or both. Findings suggest that screening for infectious hepatitis may be germane to the clinical care of patients with schizophrenia and relevant risk factors.

1. Introduction

Patients with schizophrenia have a dramatic increase in premature mortality, including deaths from both infection and liver disease [1]. There is evidence for an increased prevalence of hepatitis in patients with schizophrenia compared to the general population [2]. Multiple factors may contribute to this risk, including an increased prevalence of substance use disorders, including injection drug use, [3] as well as increased high-risk sexual behaviors (including hypersexual behavior during acute psychosis, unprotected sex, multiple sexual partners, or sex work/trading) [4] in individuals with schizophrenia, which are associated with risk of major infections. Hepatitis B and hepatitis C are viral infections that affect the liver and can cause acute and chronic disease, including hepatocellular carcinoma, cirrhosis, and liver failure. They are transmitted through contact with the blood or other body fluids of an infected person, which may occur though injection drug use, unsafe sexual practices, and the transfusion of unscreened blood and blood products. In 2018, an estimated 257 million people worldwide were living with hepatitis B infection, and 71 million people worldwide were found to be living with hepatitis C. Among people with infectious hepatitis, 20–30% will develop chronic liver disease, including cirrhosis and/or liver cancer [5,6]. Therefore, individuals with schizophrenia may have an increased risk of infectious hepatitis.

In addition to these social determinants of health, a confluence of evidence also supports an association between immune dysfunction and schizophrenia. Psychotic symptoms can be triggered by inflammation affecting the brain through central nervous system (CNS)-reactive antibodies, or by CNS infections [7]. There is evidence for abnormal levels of blood inflammatory markers and autoantibodies, in patients with schizophrenia compared to controls [8–10]. There is also a growing body of evidence suggesting an association between infections and schizophrenia. A population-based study in Denmark showed that infections requiring hospitalization, as well as infections treated with anti-infective agents, were associated with increased risk of schizophrenia-spectrum disorders [11]. Previous studies have also found an increased prevalence of urinary tract infections in acutely ill patients with schizophrenia [12,13]. A meta-analysis found a 1.7-fold increase in risk of positive Toxoplasma gondii IgM antibodies, a marker of

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acute/recent exposure, persistent infection, or reinfection, in patients with acute psychosis compared with controls [14]. Several studies have also found an increased prevalence of active viral [15–17] and chlamydial [18] infections in patients with acute psychosis. Furthermore, patients with schizophrenia may have abnormal function of neutrophils and natural killer cells [19–21], and the resulting impaired host defense may increase susceptibility to infections. These findings raise the possibility that infections may be associated with both schizophrenia risk and comorbidity.

A previous meta-analysis [22], which included studies published through 2012, investigated the prevalence of hepatitis B and C in individuals with serious mental illness (broadly-defined to include psychotic disorders, (unipolar and bipolar) affective disorders, and substance use disorders.) They found a 2.6% prevalence of hepatitis B and a 3.0% prevalence of hepatitis C in this population. Although patients with schizophrenia may have increased risk of infectious hepatitis, the extent of this association is unclear, in part due to heterogeneous findings. For example, two studies in the United States reported a positive association between schizophrenia and hepatitis C among veteran populations [23,24]. However, a study in Taiwan [25] and one in Belgium [26] failed to find this association. Meta-analysis can bring increased clarity to an area of research with significant heterogeneity, and thus is well suited to the study of infectious hepatitis and schizophrenia. To date, there has not been a systematic, quantitative review of studies to clarify the association with infectious hepatitis in individuals with schizophrenia, which is important given its potential contributions to disease comorbidity and mortality. The objective of the present study was to perform a systematic review and meta-analysis of this association. We hypothesized that there is an increased prevalence of infectious hepatitis (B and C) in patients with schizophrenia.

2. Materials and methods

2.1. Study selection

This systematic review was conducted in accordance with the PRISMA statement [27]. Studies of comorbid hepatitis B or hepatitis C and schizophrenia were identified by systematically searching Medline (PubMed, National Center for Biotechnology Information, US National Library of Medicine, Bethesda, Maryland), PsycInfo (via Ovid, American Psychological Association, Washington, DC), Web of Science (Science Citation Index and Social Sciences Citation Index, Thomson Reuters, Charlottesville, Virginia), and the reference lists of studies that met the inclusion/exclusion criteria for the meta-analysis in January 2019. The primary search strategy was: (schizophrenia OR psychosis OR schizoaffective OR “non-affective psychosis”) AND (hepatitis OR “hepatitis B” OR “hepatitis C” OR HBV OR HCV). Using the filters “human subjects” and “English”, we identified 585 potential studies. The majority of initial matches were excluded because the studies investigated non-infectious (e.g., antipsychotic-induced) hepatitis, the study population was not primarily patients with schizophrenia, or were case reports or review articles.

The inclusion criteria were case-control or prevalence studies of comorbid hepatitis B and hepatitis C in patients with schizophrenia and other non-affective psychoses (either 100% of the total sample, or stratified data on the subset of patients with schizophrenia in the study were available). Case-control studies were defined as observational studies that compared the prevalence of hepatitis (B and/or C) between two defined groups—patients with schizophrenia and controls without this disorder. Prevalence studies were defined as observational studies that reported the prevalence of hepatitis (B and/or C) in patients with schizophrenia. We defined non-affective psychosis to include schizophrenia, schizophreniform disorder, brief psychotic disorder, delusional disorder, schizoaffective disorder, and psychotic disorder not otherwise specified. Exclusion criteria were 1) (stratified) data on subjects with schizophrenia or other non-affective psychoses not available, or 2) data

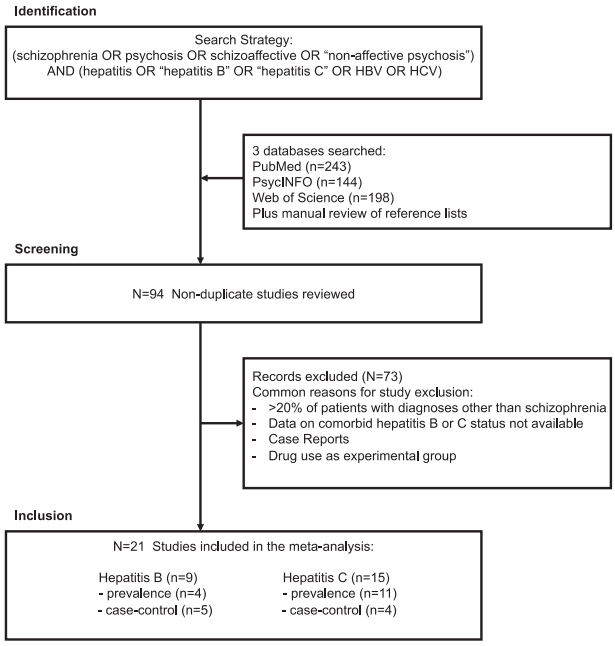

Fig. 1. Flow chart of the study selection process.

(raw counts) on comorbid hepatitis B or C status by subject group not available (after attempting to contact the study authors). After independent search and review of study methods, 21 studies met the inclusion/exclusion criteria [23–26,28–49], including 9 studies of hepatitis B (4 prevalence studies and 5 case-control studies), and 15 studies of hepatitis C (11 prevalence studies and 4 case-control studies). Three studies contributed data on both hepatitis B and C.

A flowchart summarizing the study selection process is presented in Fig. 1. Details of the included studies are also presented as Table 1. A diagnosis of schizophrenia in the majority of included studies was made by (non-standardized) clinical interview; other studies utilized either chart review or linkage to patient registries/databases. A diagnosis of hepatitis B was based on laboratory testing (hepatitis B surface antigen [HBsAg]) in 8 of 9 studies; the other study used linkage to national disease registers. A diagnosis of hepatitis B was based on laboratory testing (anti-hepatitis C antibodies [HCV Ab]) in 9 of 15 studies; the other studies used linkage to disease registries or databases.

2.2. Data extraction and meta-analysis

Data were extracted (number of subjects with schizophrenia [and controls for case-control studies] with and without comorbid hepatitis B or C, as well as other demographic variables) for each study that satisfied the inclusion and exclusion criteria. One author (EL) extracted all data, which was verified by another author (BJM). For case-control studies, effect size estimates (odds ratios [ORs] and 95% confidence intervals [95% CIs]) were calculated using the random effects method of DerSimonian and Laird [45] for hepatitis B and C, separately. The independent variable was subject group (schizophrenia versus control), and the dependent variable was hepatitis B or C, separately. For studies with data on the prevalence of hepatitis B and C in patients with schizophrenia, which includes both prevalence and case-control studies, effect size estimates (prevalence and 95% CIs) were calculated, also using random effects meta-analysis. The independent variable was subject group (schizophrenia), and the dependent variable was hepatitis B or C, separately. Random effects methods are considered to be more representative of real-world data in comparison to the alternative fixed effect approach [46]. For case-control studies, the null hypothesis was that the OR for the prevalence of hepatitis B or C in individuals with schizophrenia equals 1.0 (i.e., no significant increase in prevalence

Table 1
Studies of hepatitis B and C in schizophrenia.

1a. Hepatitis C

					Schizophrenia			Hepatitis C	
Study	Country	Study design	Age	% male	(n)	Diagnostic criteria	Diagnostic method	Positive (n)	Diagnostic method
Baur-Staeb 2017	Sweden	Prevalence	48	66	21,232	ICD-8,9,10	Inpatient or outpatient records	1194	Linkage to national registers
Carney 2006	US	Case-control	40	47	1074	ICD-9	Insurance claims database	7	Insurance claims database
Chiu 2017	Taiwan	Case-control	43	52	6097	ICD-9	Clinical interview	128	Linkage to national registers
Cividini 1997	Italy	Prevalence	60	76	423	ICD-9	Clinical interview	47	HCV Ab, HCV RNA
De Hert 2009	Belgium	Prevalence	37	95	595	DSM-IV	NS	4	HCV Ab
Dinwiddie 2003	US	Prevalence	38	61	153	NS	NS	14	HCV Ab, HCV RNA
Freudenreich 2007	US	Prevalence	45	74	98	NS	Clinical interview	8	HCV Ab, HCV RNA
Fuller 2011	US	Case-control	57	94	6521	ICD-9	VA medical center database	17	VA medical center database
Himelhoch 2009	US	Prevalence	55	95	89,189	ICD-9	VA national psychosis registry	6287	VA health services database
Huckans 2006	US	Case-control		93	2207	DSM-IV	VA medical center database	219	VA medical center database (HCV Ab or HCV RNA or HCV RIBA, or HCV genotype)
Hung 2012	Taiwan	Prevalence	42	59	588	DSM-IV	NS	11	HCV Ab
Nakamura 2004	Japan	Prevalence	50	71	455	ICD-10	Interview by two psychiatrists	28	HCV Ab
Rosenburg 2005	US	Prevalence		68	495	NS	NS	90	HCV Ab, HCV RIBA
Sockalingam 2010	Toronto	Prevalence	45	68	110	DSM-IV	Clinical interview	3	HCV Ab, HCV RIBA
Tabbian 2008	US	Prevalence	49	98	19	DSM-IV	Clinical interview	2	HCV Ab

1b. Hepatitis B

					Schizophrenia			Hepatitis B	
Study	Country	Study design	Age	% male	(n)	Diagnostic criteria	Diagnostic method	Positive (n)	Diagnostic method
Bauer-Staeb 2017	Sweden	Prevalence	48	66	21,232	ICD-8,9,10	Inpatient or outpatient records	112	Linkage to national registers
Chaudhury 1993	India	Case-control	50	100	60	DSM-IIIR	Interview by two psychiatrists	1	HBsAg
Chaudhury 1994	U.S.	Case-control	54	100	100	DSM-IIIR	Interview by two psychiatrists	11	HBsAg
Esquivel 2005	Mexico	Case-control	30	67	33	ICD-10	NS	4	HBsAg (all) and HBsAb (patients)
Hung 2012	Taiwan	Prevalence	42	59	570	DSM-IV	NS	59	HBsAg
Said 2001	Jordan	Case-control	38	55	192	DSM-IV	NS	14	HBsAg
Tabbian 2008	US	Prevalence	49	98	19	DSM-IV	Clinical interview	1	HBsAg, HBsAb, HBcAb
Wang 2016	China	Case-control	19	52	415	DSM-IV	NS	28	HBsAg, HBsAb, HBV DNA
Zhu 2015	China	Prevalence	33	46	1649	ICD-10	Interview by two psychiatrists	181	HBsAg, HBsAb, HBV DNA

of hepatitis B or C in schizophrenia versus controls). We also hypothesized that the prevalence of hepatitis B or C in schizophrenia would not differ based on study design (case-control versus prevalence studies).

The meta-analysis procedure also calculates a χ^2 value for the heterogeneity in effect size estimates, which is based on Cochran's Q-statistic [47], and I^2, the proportion of the variation in effect size attributable to between-study heterogeneity. Between-study heterogeneity χ^2 was considered significant for $p < 0.10$ [48]. For case-control studies of hepatitis C, and prevalence studies of hepatitis B and C, between-study heterogeneity χ^2 was significant, so we performed a sensitivity analysis. This was done by removing one study at a time and repeating the meta-analysis procedure, to examine its impact on the effect size estimates and between-study heterogeneity [49]. If between-study heterogeneity remained significant after removing each individual study, we then removed all combinations of two different studies and repeated the meta-analysis procedure. Given the significant heterogeneity in results, we also performed a series of meta-regressions to explore possible moderating variables to account for such heterogeneity. Meta-regression assesses and adjusts the effects of potential moderating variables on the effect size estimate from the meta-analysis. A positive slope (i.e., regression coefficient) means that the effect size estimate from the meta-analysis and the moderator variable change in the same direction, and a negative slope means they change in the opposite direction. The effects of age, sex (as percentage of males in the study sample), geographic region, and year of publication were assessed in meta-regression analyses. Sex and geographic region were modeled as categorical variables, and age and publication year were modeled as continuous variables. The potential for publication bias was examined by means of Sterne's funnel plot analysis [50] and Egger's regression intercept [51]. All statistical analyses were performed in Stata 10.0 (StataCorp LP, College Station, TX), and p-values were considered statistically significant at the $\alpha = 0.05$ level.

3. Results

Twenty-one studies met the inclusion criteria, including n = 15 studies for hepatitis C (n = 11 prevalence studies and n = 4 case-control studies) and n = 9 studies for hepatitis B (n = 4 prevalence studies and n = 5 case-control studies). Three studies included data on both hepatitis B and C. For case-control studies of hepatitis C, there was an over 3-fold increased odds of hepatitis C in patients with schizophrenia (OR = 3.29, 95% CI 1.50–7.23, p = 0.003; see Fig. 2). Between-study heterogeneity was significant ($\chi^2 = 336.25$, $I^2 = 98.8\%$, $p < 0.001$). In sensitivity analyses, between-study heterogeneity remained significant after removing all combinations of two studies. A funnel plot and results of Egger's test ($p > 0.05$) showed no evidence of publication bias. In univariate meta-regression analyses, sex, age, and geography were all unrelated to the association between comorbid hepatitis C and schizophrenia ($p > .05$ for each).

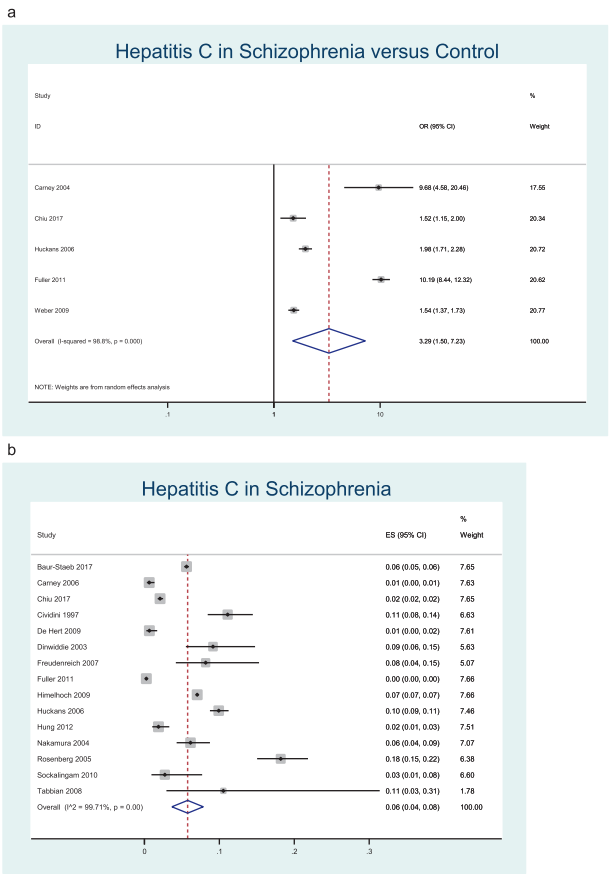

Fig. 2. Meta-analyses of hepatitis C in schizophrenia.

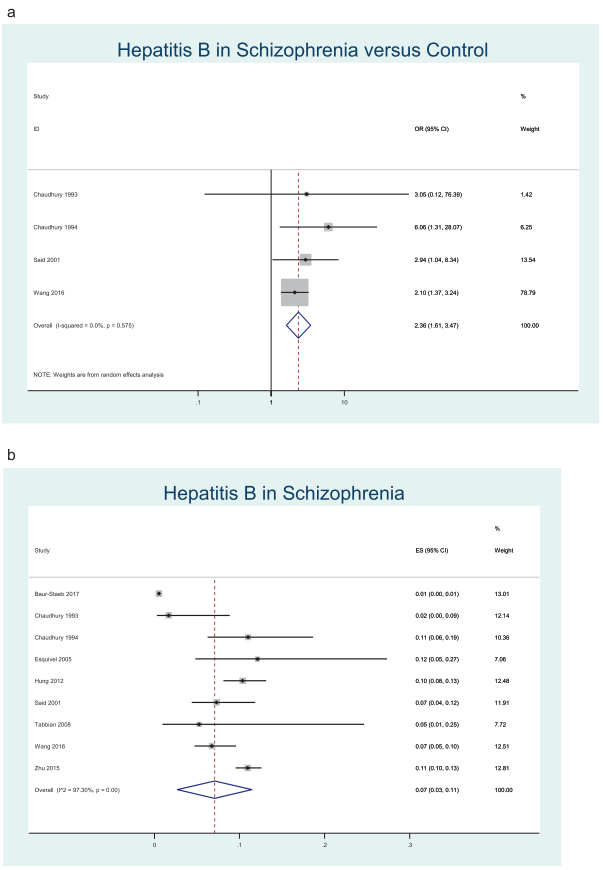

Fig. 3. Meta-analyses of hepatitis B in schizophrenia.

For all studies, the prevalence of hepatitis C in patients with schizophrenia was 6% (ES = 0.06, 95% CI 0.04–0.08; see Fig. 2). Between-study heterogeneity was significant ($\chi^2 = 4782.63$, $I^2 = 99.71\%$, $p < 0.001$). In sensitivity analyses, between-study heterogeneity remained significant after removing all combinations of two studies. In a subgroup analysis, the prevalence of hepatitis C in patients with schizophrenia was non-significantly higher (7%, ES = 0.08, 95% CI 0.04–0.10) in studies with laboratory testing. A funnel plot and results of Egger's test ($p > 0.05$) showed no evidence of publication bias. In univariate meta-regression analyses, age, sex and geography were both unrelated to the association between hepatitis C and schizophrenia ($p > .05$ for each). When considered separately by study design, the prevalence of hepatitis C was 3% in case-control studies (ES = 0.03, 95% CI 0.01–0.05, $p < 0.01$) and 7% in prevalence studies (ES = 0.07, 95% CI 0.05–0.08, $p < .01$).

For case-control studies of hepatitis B, there was an over 2-fold increased odds of hepatitis B in patients with schizophrenia (OR = 2.36, 95% CI 1.61–3.47, $p < 0.001$; see Fig. 3), and between study heterogeneity was not significant ($\chi^2 = 1.99$, $I^2 = 0.0\%$, $p = 0.58$). A funnel plot and results of Egger's test ($p > 0.05$) showed no evidence of publication bias. In univariate meta-regression analyses, sex, age, and geography were all unrelated to the association between comorbid hepatitis B and schizophrenia ($p > .05$ for each).

For all studies, the prevalence of hepatitis B in patients with schizophrenia was 7% (ES = 0.07, 95% CI 0.03–0.11; see Fig. 3). Between-study heterogeneity was significant ($\chi^2 = 296.26$, $I^2 = 97.30\%$, $p < 0.01$). In sensitivity analyses, between-study heterogeneity remained significant after removing all combinations of two studies. In a subgroup analysis, the prevalence of hepatitis B in patients with schizophrenia was non-significantly higher (8%, ES = 0.08, 95% CI 0.05–0.11) in studies with laboratory testing. A funnel plot and results of Egger's test ($p > 0.05$) showed no evidence of publication bias. In univariate meta-regression analyses, sex, age, and geography were all unrelated to the association between comorbid hepatitis B and schizophrenia ($p > .05$ for each). When considered separately by study design, the prevalence of hepatitis B was 7% in both case-control studies (ES = 0.07, 95% CI 0.00–0.14, $p = 0.07$) and in prevalence studies (ES = 0.07, 95% CI 0.03–0.10, $p < 0.01$)

4. Discussion

We found meta-analytic evidence of an over three-fold increased odds (OR = 3.29) of hepatitis C in patients with schizophrenia compared to controls, and a 6% prevalence of hepatitis C in these patients. There was an over two-fold increased odds (OR = 2.36) of hepatitis B in patients with schizophrenia compared to controls, and a 7% prevalence of hepatitis B in these patients. There was significant between-study heterogeneity regarding these associations, which were not moderated by age, sex, or geography.

A strength of our study was that we included a large cumulative sample size of patients with schizophrenia and comorbid infectious hepatitis. Another strength is that we performed meta-regression analyses to consider a number of potential moderating factors. There are always limitations to studies. One limitation is that data on viral load for subjects with hepatitis were not available, therefore the prevalence of patients with active viremia is unknown. Data on other potential confounding and/or moderating behavioral factors—such as sexual behaviors and substance use comorbidity—that are known to influence risk of infectious hepatitis were also generally not available

It is important to note that study weights are more similar in random effects meta-analysis (i.e., large studies lose influence while small studies gain influence). As a result, the raw prevalence of hepatitis B in all studies (2%) was substantially lower than prevalence

estimate derived from the meta-analysis (7%). However, when one outlying study was excluded (Bauer), the raw prevalence of hepatitis B was 10%. Excluding this study from the meta-analysis did not change the prevalence estimate (7%). By contrast, both the raw and meta-analysis- derived prevalence estimates for hepatitis C were 6%. It is reassuring that the prevalence of infectious hepatitis in patients with schizophrenia was broadly consistent between the two different study designs, as well as studies that used laboratory (versus database/registry)-based diagnosis of infectious hepatitis. The prevalence of hepatitis C was 3% in case-control studies and 7% in prevalence studies. There was high concordance for hepatitis B, with a prevalence of 7% in both case-control and prevalence studies. According to the World Health Organization, hepatitis B and C are both found worldwide, although the prevalence varies by geographic region [18,19]. The prevalence of hepatitis C ranges from 0.5 to 2.3%, and the prevalence of hepatitis B ranges from 0.7 to 6.2%, based on region. There was a 3% prevalence of hepatitis B and C, respectively, in controls in our meta-analysis, which is also broadly consistent with these estimates. Interestingly, geography did not moderate the association between schizophrenia and infectious hepatitis, although there may not have been enough geographical diversity in the included studies to detect such an association.

Although we found an increased prevalence of infectious hepatitis in patients with schizophrenia, the mechanism of this association remains unclear. One important possibility is that the increased prevalence of substance use comorbidity, including injection drug use, is associated with increased risk of infectious hepatitis. The lifetime prevalence of a comorbid substance use disorder in individuals with schizophrenia is 25–50% [52,53]. Consistent with this hypothesis, Rosenberg and colleagues [39] found that among a population of hepatitis C positive individuals, 75% reported using injection drugs. Likewise, Klinkenberg and colleagues [54] found that those with a diagnosis of both severe mental illness and hepatitis C were reported to be more likely to have a history of injection drug use or diagnosis of substance use disorder compared to those without hepatitis C infection.

Risky sexual behavior is, in turn, another important potential risk factor for infectious hepatitis comorbidity in schizophrenia. In a birth cohort from New Zealand followed to age 21, compared to individuals with no psychiatric disorder, those with schizophrenia-spectrum disorder had an over 2-fold increased risk of early sexual intercourse, sexual intercourse in the past year, and lifetime history of sexually transmitted disease [4]. A survey of 42 individuals with schizophrenia who had been sexually active in past 6 months found that over half had multiple sexual partners, used drugs during sex, traded sex (for money, drugs, or other goods), and had never used condoms [55]. Another sample of 67 sexually active young adults with first-episode psychosis found that 75% had multiple (> 3) sexual partners, 38% had never used condoms, and 17% had traded sex. [56].

Another possibility that is not mutually exclusive is that patients with schizophrenia have abnormal immune cell function that confers an increased susceptibility to infection. One study found a significant decrease in natural killer cell activity—first-line defenders against infections, including viruses—in patients with schizophrenia [19], although this finding warrants replication. To our knowledge, there are no in vitro studies comparing susceptibility of cells to infection in patients with schizophrenia and controls. Future studies investigating these potential mechanisms are warranted.

In conclusion, patients with schizophrenia have an increased prevalence of infectious hepatitis, which may be due to behavioral factors, immunologic factors, or both. Given the impact of chronic liver disease on morbidity and mortality, our findings suggest that screening for infectious hepatitis may be germane to the clinical care of patients with schizophrenia and relevant risk factors.

Role of the funding source

Not applicable.

Contributors statement

Dr. Miller designed the study. Ms. Lluch managed the literature searches and data extraction, which were replicated/checked by Dr. Miller. Dr. Miller performed the data analysis. Both authors contributed to the writing of the manuscript.

Declaration of competing interest

Ms. Lluch has nothing to disclose.

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References

[1] Olfson M, Gerhard T, Huang C, Crystal S, Stroup TS. Premature mortality among adults with schizophrenia in the United States. JAMA Psychiat 2015;72:1172–81.
[2] Leucht S, Burkard T, Henderson J, Maj M, Sartorius N. Physical illness and schizophrenia: a review of the literature. Acta Psychiatr Scan 2007;116:317–33.
[3] Regier DA. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. JAMA 1990;264:2511–8.
[4] Ramrakha S. Psychiatric disorders and risky sexual behaviour in young adulthood: cross sectional study in birth cohort. BMJ 2000;321:263–6.
[5] Hepatitis B Retrieved from https://www.who.int/news-room/fact-sheets/detail/hepatitis-b; 2018, July 18.
[6] Hepatitis C Retrieved from https://www.who.int/news-room/fact-sheets/detail/hepatitis-c; 2018, July 18.
[7] Benros ME, Mortensen PB. Role of infection, autoimmunity, atopic disorders, and the immune system in schizophrenia: evidence from epidemiological and genetic studies. Curr Top Behav Neurosci 2019. https://doi.org/10.1007/7854_2019_93. [In press].
[8] Ezeoke A, Mellor A, Buckley P, Miller B. A systematic, quantitative review of blood autoantibodies in schizophrenia. Schizophr Res 2013;150:245–51.
[9] Goldsmith DR, Rapaport MH, Miller BJ. A meta-analysis of blood cytokine network alterations in psychiatric patients: comparisons between schizophrenia, bipolar disorder and depression. Mol Psychiatry 2016;21:1696–709.
[10] Miller BJ, Culpepper N, Rapaport MH. C-reactive protein levels in schizophrenia: a review and meta-analysis. Clin Schizophr Relat Psychoses 2014;7:223–30.
[11] Köhler-Forsberg O, Petersen L, Gasse C, Mortensen PB, Dalsgaard S, Yolken RH, et al. A nationwide study in Denmark of the association between treated infections and the subsequent risk of treated mental disorders in children and adolescents. JAMA Psychiat 2018;76:271.
[12] Graham KL, Carson CM, Ezeoke A, Buckley PF, Miller BJ. Urinary tract infections in acute psychosis. J Clin Psychiatry 2014;75:379–85.
[13] Miller BJ, Graham KL, Bodenheimer CM, Culpepper NH, Waller JL, Buckley PF. A prevalence study of urinary tract infections in acute relapse of schizophrenia. J Clin Psychiatry 2013;74:271–7.
[14] Monroe JM, Buckley PF, Miller BJ. Meta-analysis of anti-toxoplasma gondii IgM antibodies in acute psychosis. Schizophr Bull 2015;41:989–98.
[15] Ahokas A, Rimón R, Koskiniemi M, Vaheri A, Julkunen I, Sarna S. Viral antibodies and interferon in acute psychiatric disorders. J Clin Psychiatry 1987;48:194–6.
[16] Krause D, Matz J, Weidinger E, et al. The association of infectious agents and schizophrenia. World J Biol Psychiatry 2010;11:739–43.
[17] Srikanth S, Ravi V, Poornima KS, Shetty KT, Gangadhar BN, Janakiramaiah N. Viral antibodies in recent onset, nonorganic psychoses: correspondence with symptomatic severity. Biol Psychiatry 1994;36:517–21.
[18] Fellerhoff B, Laumbacher B, Mueller N, Gu S, Wank R. Associations between Chlamydophila infections, schizophrenia and risk of HLA-A10. Mol Psychiatry 2007;12:264–72.
[19] Abdeljaber MH, Nair MP, Schork MA, Schwartz SA. Depressed natural killer cell activity in schizophrenic patients. Immunol Invest 1994;23:259–68.
[20] Rwegellera GG, Fernando KA, Okong'o O. Bactericidal activity of neutrophils of schizophrenic patients. Med J Zambia 1982;16:21–2.
[21] McAdams C, Leonard BE. Neutrophil and monocyte phagocytosis in depressed patients. Prog Neuropsychopharmacol Biol Psychiatry 1993;17:971–84.
[22] Hughes E, Bassi S, Gilbody S, Bland M, Martin B. Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness: a systematic review and meta-analysis. Lancet Psychiatry 2016;3:40–8.
[23] Fuller BE, Rodriguez VL, Linke A, Sikirica M, Dirani R, Hauser P. Prevalence of liver disease in veterans with bipolar disorder or schizophrenia. Gen Hosp Psychiatry 2011;33:232–7.

[24] Himelhoch S, Mccarthy JF, Ganoczy D, Medoff D, Kilbourne A, Goldberg R, et al. Understanding associations between serious mental illness and hepatitis C virus among veterans: a national multivariate analysis. Psychosomatics 2009;50:30–7.
[25] Hung C, Loh E, Hu T, Chiu H, Hsieh H, Chan C, et al. Prevalence of hepatitis B and hepatitis C in patients with chronic schizophrenia living in institutions. J Chin Med Assoc 2012;75:275–80.
[26] De Hert M, Franic T, Vidovic M, Wampers M, Van Eyck D, Van Herck K, et al. Prevalence of HIV and hepatitis C infection among patients with schizophrenia. Schizophr Res 2009;108:307–8.
[27] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62:1006–12.
[28] Bauer-Staeb C, Jörgensen L, Lewis G, Dalman C, Osborn DP, Hayes JF. Prevalence and risk factors for HIV, hepatitis B, and hepatitis C in people with severe mental illness: a total population study of Sweden. Lancet Psychiatry 2017;4:685–93.
[29] Carney CP, Jones LE, Woolson RF. Medical comorbidity in women and men with schizophrenia: a population-based controlled study. J Gen Intern Med 2006;21:1133–7.
[30] Chaudhury S, Chandra S, Chopra GS, Augustine M. Australia antigen (HBsAG) in institutionalized schizophrenics. Indian J Psychiatry 1993;35:31–2.
[31] Chaudhury S, Chandra S, Augustine M. Prevalence of Australia antigen (HBsAg) in institutionalised patients with psychosis. Br J Psychiatry 1994;164:542–3.
[32] Chiu Y, Lin H, Kao N, Kao S, Lee H. Increased risk of concurrent hepatitis C among male patients with schizophrenia. Psychiatry Res 2017;258:217–20.
[33] Cividini A, Pistorio A, Regazzetti A, Cerino A, Tinelli C, Mancuso A, et al. Hepatitis C virus infection among institutionalised psychiatric patients: a regression analysis of indicators of risk. J Hepatol 1997;27:455–63.
[34] Dinwiddie SH, Shicker L, Newman T. Prevalence of hepatitis C among psychiatric patients in the public sector. Am J Psychiatry 2003;160:172–4.
[35] Esquivel CA, Angel M, Valenzuela A, Suarez MFM, Andrade FE. Hepatitis B virus infection among inpatients of a psychiatric hospital of Mexico. Clinical Practice and Epdemiology in Mental Health 2005;1:10.
[36] Freudenreich O, Gandhi RT, Walsh JP, Henderson DC, Goff DC. Hepatitis C in schizophrenia: screening experience in a community-dwelling clozapine cohort. Psychosomatics 2007;48:405–11.
[37] Huckans MS, Blackwell AD, Harms TA, Hauser P. Management of hepatitis C disease among VA patients with schizophrenia and substance use disorders. Psychiatr Serv 2006;57:403–6.
[38] Nakamura Y, Koh M, Miyoshi E, Ida O, Morikawa M, Tokuyama A, et al. High prevalence of the hepatitis C virus infection among the inpatients of schizophrenia and psychoactive substance abuse in Japan. Progress in Neuro-Psychopharmacology and Biological Psychiatry 2004;28:591–7.
[39] Rosenberg SD, Drake RE, Brunette MF, Wolford GL, Marsh BJ. Hepatitis C virus and HIV co-infection in people with severe mental illness and substance use disorders. AIDS 2005;19:S26–33.
[40] Said WM, Saleh R, Jumaian N. Prevalence of hepatitis V virus among chronic schizophrenia patients. La Revue de Sante de La Mediterrannee Oirentale 2001;7:526–30.
[41] Sockalingam S, Shammi C, Powell V, Barker L, Remington G. Determining rates of hepatitis C in a clozapine treated cohort. Schizophr Res 2010;124:86–90.
[42] Tabibian JH, Wirshing DA, Pierre JM, Guzik LH, Kisicki MD, Danovitch I, et al. Hepatitis B and C among veterans on a psychiatric ward. Dig Dis Sci 2007;53:1693–8.
[43] Wang Y, Yu L, Zhou H, Zhou Z, Zhu H, Li Y, et al. Serologic and molecular characteristics of hepatitis B virus infection in vaccinated schizophrenia patients in China. The Journal of Infection in Developing Countries 2016;10:427.
[44] Zhu H, Liu X, Xue Y, Shen C, Li Y, Wang A, et al. Seroepidemiology of hepatitis B virus infection among Chinese schizophrenia patients. The Journal of Infection in Developing Countries 2015;9:512.
[45] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.
[46] Hunter JE, Schmidt FL. Fixed effects vs. random effects meta-analysis models: implications for cumulative research knowledge. International Journal of Selection and Assessment 2000;8:275–92.
[47] Cochran WG. The comparison of percentages in matched samples. Biometrika 1950;37:256.
[48] Song F, Sheldon TA, Sutton AJ, Abrams KR, Jones DR. Methods for exploring heterogeneity in meta-analysis. Eval Health Prof 2001;24:126–51.
[49] Higgins J, Green S. Cochrane handbook for systematic review of interventions. 2011. [20 5.1.0 11].
[50] Sterne JA, Egger M. Funnel plots for detecting bias in meta-analysis. J Clin Epidemiol 2001;54:1046–55.
[51] Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34.
[52] Buckley PF, Miller BJ, Lehrer DS, Castle DJ. Psychiatric comorbidities and schizophrenia. Schizophr Bull 2009;35:383–402.
[53] Nesvåg R, Knudsen GP, Bakken IJ, Høye A, Ystrom E, Surén P, et al. Substance use disorders in schizophrenia, bipolar disorder, and depressive illness: a registry-based study. Soc Psychiatry Psychiatr Epidemiol 2015;50:1267–76.
[54] Klinkenberg WD, Caslyn RJ, Morse GA, Yonker RD, McCudden S, Ketema F, et al. Prevalence of human immunodeficiency virus, hepatitis B, and hepatitis C among homeless persons with co-occurring severe mental illness and substance use disorders. Compr Psychiatry 2003;44:293–302.
[55] McKinnon K, Cournos F, Sugden R, Guido JR, Herman R. The relative contributions of psychiatric symptoms and AIDS knowledge to HIV risk behaviors among people with severe mental illness. J Clin Psychiatry 1996;57. (506-153).
[56] Brown A, Lubman DI, Paxton S. Sexual risk behaviour in young people with first episode psychosis. Early Interv Psychiatry 2010;4:234–42.