

## Original Research Reports

# Increased Risk of Chronic Liver Disease in Patients with Schizophrenia: A Population-Based Cohort Study

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**Objective:** To investigate the prevalence and incidence of chronic liver disease in patients with schizophrenia in Taiwan. **Methods:** We used a random sample of 661,266 subjects aged  $\geq 18$  from the National Health Research Institute database in the year 2000. Subjects with at least one primary diagnosis of schizophrenia (The International Classification of Diseases, Ninth Revision, Clinical Modification: 295) in 2000 were selected. Patients with a primary or secondary diagnosis of chronic liver disease (The International Classification of Diseases, Ninth Revision, Clinical Modification: 571) were also defined. We compared the prevalence and associated factors of chronic liver disease between patients with schizophrenia and the general population in 2000. We also compared the incidence of chronic liver disease in patients with schizophrenia and the general population from 2001 through 2010. **Results:** The prevalence of chronic liver disease in patients with schizophrenia (7.0%) was 1.27

times as high as that of the general population (6.1%) in 2000. The average annual incidence of chronic liver disease in patients with schizophrenia from 2001–2010 was also higher than that of the general population (2.9% vs 2.5%, risk ratio, 1.15; 95% confidence interval, 1.07–1.24). Younger patients with schizophrenia were found to have a much higher prevalence and incidence than those in the general population, and diabetes was a risk factor for patients with schizophrenia in developing chronic liver disease. **Conclusions:** Patients with schizophrenia exhibited a significantly higher prevalence and incidence of chronic liver disease than those in the general population, and younger patients with schizophrenia have a much higher prevalence and incidence than those in the general population. Co-morbidity with diabetes was the primary risk factor for patients with schizophrenia to develop chronic liver disease.

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## INTRODUCTION

Concurrent medical conditions make caring for patients with schizophrenia more complex and difficult. With respect to the gastrointestinal system, chronic liver disease<sup>1</sup> is an important medical problem among patients with schizophrenia. Chronic liver disease usually occurs insidiously without vivid or typical symptoms and signs before reaching the complications of hepatic decompensation or even failure. Jimba et al.<sup>2</sup> conducted a general health examination program and reported that the

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# Chronic Liver Disease in Patients with Schizophrenia

prevalence of nonalcoholic fatty liver disease (NAFLD) was 29% in Japan. It had also been reported that as many as one-third of the adult Taiwanese population with NAFLD have elevated liver enzymes.<sup>3</sup> Thus, the early detection and monitoring of liver diseases are important.

Interestingly, schizophrenia and hepatic dysfunction share certain abnormal biochemical and biological characteristics, such as increased blood and central nervous system (CNS) levels of biogenic amines and low CNS levels of gamma-aminobutyric acid (GABA).<sup>4</sup> One case-control study from 1996–2001 demonstrated that persons with schizophrenia were 4.42 times more likely to have liver disease.<sup>5</sup> One large-scale retrospective study found a higher prevalence of liver disease (22.4% vs 3.2%; odds ratio [OR], 8.73) and alcohol-related cirrhosis (1.6% vs 0.4%; OR, 3.82) in veterans with schizophrenia.<sup>6</sup> Furthermore, a community-based study for patients with serious mental illness provided an OR of 2.69 in comparing patients with schizophrenia to a reference group with liver problems.<sup>7</sup>

According to our previous studies, we have found that patients with schizophrenia have a higher prevalence of diabetes and hyperlipidemia than those in the general population.<sup>8,9</sup> However, no comprehensive epidemiologic study of chronic liver disease in Taiwanese patients with schizophrenia has been reported during recent years. In this study, we first compared the prevalence of chronic liver disease between patients with schizophrenia and those in the general population (persons without schizophrenia). Second, we analyzed the associated factors for the prevalent cases of chronic liver disease in persons with schizophrenia in 2000. Third, we also compared the incidence of chronic liver disease in patients with schizophrenia and those in the general population from 2001 through 2010. Finally, we analyzed the risk factors for chronic liver disease in patients with schizophrenia during this same period.

## METHODS

### Sample

The National Health Research Institute medical claims database includes data on ambulatory care, hospital inpatient care, and prescription drugs. The Institute provided a randomly sampled database of 1,000,000 for this study. From this database, we

examined the 661,266 individuals aged  $\geq 18$  years in 2000. This study was approved by the Institutional Review Board of Jianan Mental Hospital. The diagnosis of schizophrenia was coded according to the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic criteria in the National Health Insurance (NHI) program of Taiwan.<sup>1</sup> Study subjects with one primary diagnosis of schizophrenia (ICD-9-CM: 295) for either outpatient or inpatient care during 2000 were identified.<sup>10,11</sup> No statistically significant differences in age, sex, or average insured payroll-related amount were present between the sample group and all enrollees.

### Definition of Chronic Liver Disease

Study subjects with one primary or secondary diagnosis of chronic liver disease (ICD-9-CM: 571) for either outpatient or inpatient care were identified in the study period. Chronic liver disease included alcoholic fatty liver (571.0), acute alcoholic hepatitis (571.1), alcoholic cirrhosis of the liver (571.2), alcoholic liver damage, unspecified (571.3), chronic hepatitis (571.4), cirrhosis of the liver without mention of alcohol (571.5), biliary cirrhosis (571.6), other chronic non-alcoholic liver disease (571.8), and unspecified chronic liver disease without mention of alcohol (571.9). Viral hepatitis (ICD-9-CM: 070) was excluded in this study.

With regard to the prevalence of chronic liver disease in the general population and patients with schizophrenia, the numerator was the number of prevalent cases of chronic liver disease, and the denominator was the total number of study subjects recruited to each of the 2 groups in 2000. With regard to the incidence of chronic liver disease, we identified new cases of chronic liver disease from 2001–2010. Subjects with newly-diagnosed chronic liver disease and no chronic liver disease diagnosis before 2001 comprised the group with incident chronic liver disease, and we calculated the incidence from 2001–2010. The numerator was the number of incident cases of chronic liver disease, and the denominator was the number of person-years contributed by the study subjects.

### Definition of Diabetes

Study subjects who had at least one prescription (oral hypoglycemic agents or insulin) for the treatment of diabetes in 2000 for either outpatient or inpatient care were considered to have a diagnosis of diabetes.<sup>9</sup>

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