# Catatonic Schizophrenia: A Cohort Prospective Study

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*Background:* In the 20th century, catatonia was usually deemed a subtype of schizophrenia. Recently, the nature and classification of catatonia are being reconsidered. This study is the first to describe catatonia using prospectively collected data and to examine how catatonic schizophrenia differs from, or resembles, other types of schizophrenia. *Methods:* Data were analyzed in a cohort of 90 079 offspring followed from birth till ages 29–41 years. Proportional hazards models were used, calculating time to first psychiatric hospital admission, to compare risk factors for catatonic schizophrenia vs "other schizophrenia." *Results:* Of 568 cases of schizophrenia, 43 (7.6%) had catatonic schizophrenia. The sexes were equally at risk for catatonic schizophrenia in contrast to other schizophrenia, for which the incidence was higher in males (1.70, 1.42–2.03, $P <$ .0001). Advancing paternal age had no influence on the risk of catatonic schizophrenia in contrast to other schizophrenia, in which the risk to offspring of fathers age 35+ was 1.27 (1.03–1.57, $P =$ .03) compared with those of younger fathers. Those with catatonic schizophrenia were somewhat more likely to have older mothers (aged 35+) (relative risk = 2.14, 0.85–5.54) while maternal age was not related to other schizophrenia. Both were equally affected by parental history of schizophrenia. Patients with catatonia were significantly more likely to attempt suicide ($P =$ .006). *Conclusion:* Patients with catatonic schizophrenia show a somewhat different profile of risk factors from those with other types of schizophrenia in this cohort and are more likely to attempt suicide. This lends some support to the hypothesis that catatonic schizophrenia may have a distinct etiology.

*Key words:* sex differences/suicide/paternal age/cohort

## Introduction

Since the early 20th century, catatonia has been regarded primarily as a subtype of schizophrenia. This view was first put forth by Kraeplin and Bleuler[1] and is currently upheld in both the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV )* and the *International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10)*.[2,3] In the past several decades, however, the many descriptions of catatonia as a syndrome in patients with mood disorders, medical disorders, and toxicities have put the syndrome in a new light. Some authors argue that catatonia should be considered as a separate syndrome,[1,4–6] or not exclusively as a subtype of chronic schizophrenia,[4] pointing out that catatonia presents more frequently in psychiatric inpatients diagnosed with mood disorders than in those with schizophrenia.[2] Catatonic symptoms also co-occur with other psychiatric diseases and with general medical conditions.[2,3]

Although the nature, proper diagnostic classification, and treatment of catatonic schizophrenia are under debate, there are no population-based studies of this condition, in which the data were collected prospectively. To meet this need, we analyzed information from a large birth cohort for the purpose of quantifying demographic and clinical features of patients with catatonic schizophrenia within a population and assessing whether established risk factors for schizophrenia (sex, parental age, and family history of psychiatric disease)[7–11] might affect catatonic schizophrenia in the same way as other subtypes.

## Methods

### Subjects

We used data from the Jerusalem Perinatal Study, a population-based cohort derived from all 92 408 births

in 1964–1976 to mothers resident in West Jerusalem. The cohort includes linkages within nuclear families and a 29- to 41-year follow-up. Core information from the notification of birth was supplemented with other data from multiple sources. The methods and the characteristics of the population were described in detail by Harlap *et al.* in 2007.[12] The cohort has been linked with Israel's population registry to trace and verify identity (ID) numbers, dates of birth, and basic demographic characteristics and to ascertain vital status and dates of death.

Information on psychiatric morbidity was drawn from Israel's national Psychiatric Registry, to which the cohort has been linked. Run by the Ministry of Health since 1950,[13] the Registry contains a record of all admissions to psychiatric wards and day facilities and includes dates of admission and discharge and a single discharge diagnosis for each episode, assigned by a board-certified psychiatrist. These diagnoses are coded with the ICD; codes from earlier years have been updated to 10th Revision (ICD-10), and those for psychotic disorders have been validated recently.[14] This validation, however, must be considered in light of the fact that the diagnoses in the whole registry are compared with diagnoses in subjects selected for research. Israel's Psychiatric Registry includes a separate rubric for whether a suicide attempt was made in the 60 days prior to admission. The research was approved by institutional review boards at Hebrew University, Jerusalem, and at New York University Medical Center and exempted from the requirement for written informed consent.

*Operational Definitions*

Catatonic schizophrenia was defined as a record of at least 1 hospital admission prior to January 1, 2005 with a discharge diagnosis coded in ICD-10 as F20.2 ("catatonic schizophrenia"). "Other schizophrenia" was defined by at least 1 record of admission for F20 but no admissions for F20.2. For the purposes of this study, the diagnoses did not have to be at first admission or consistent over all admissions. Note that schizophrenia spectrum disorders (coded F21–29) were not included in this definition of other schizophrenia. Mood disorders were defined as at least 1 discharge diagnosis coded in ICD-10 as F30–39 (ICD-10 category of "Mood [affective] disorders") with no admissions for any type of schizophrenia. The date of diagnosis was considered to be the date of first admission to a psychiatric facility, regardless of the diagnosis at that time. Diagnoses were coded as present or absent. Diagnoses in the parents were also taken from the psychiatric case registry and handled in the same way as in offspring.

*Analysis*

SAS 9.1 (SAS Institute Inc, Cary, North Carolina) was used to analyze the data. After tabulating characteristics of the 2 groups of cases, proportional hazards models were constructed to analyze and compare the effects of risk factors on their incidence. Time to event was handled as completed years since birth, ie, age, till the first hospital admission or death. Survivors were censored on December 31, 2004. Ties were handled by Efron's method. A robust sandwich estimate of the covariance matrix was used to take into account correlation between siblings.[15]

Potential risk factors were modeled as dichotomies or sets of mutually exclusive categories, coded 1 (if present) or 0 (absent). Included were male sex; maternal and paternal years of age (35+ vs <35); and parental history of schizophrenia. Other variables tested, but not included in the final models, were ethnic origin, socioeconomic status, and seasonal effects. Relative risks (RRs) and 95% CIs were estimated, both in univariate and multivariate models. To assess whether, in the adjusted models, differences in RRs for the 2 types of schizophrenia were statistically significant, we first considered whether their CIs were overlapping or not. We also constructed proportional hazards models within the 586 cases of schizophrenia; in these analyses, the outcome was catatonic schizophrenia vs other schizophrenia.

**Results**

Of the original cohort of 92 408, there were 949 (1.0%) stillbirths and 1380 (1.5%) whose ID numbers could not be traced in the Population Registry, leaving 90 079 offspring available for this study. There were 568 offspring diagnosed with schizophrenia (ICD-10 = F20), and of these, 43 had catatonia (F20.2). The additional 292 with schizophrenia spectrum disorders (ICD-10 = F21–F29 without F20) are not considered further in this article.

Table 1 shows characteristics of the 2 groups of schizophrenia patients. Those with catatonia were evenly distributed between males and females, in contrast to those with other schizophrenia who showed a preponderance of males. Those with catatonic schizophrenia were somewhat more likely to have older mothers and to be in the lowest socioeconomic class, and more had a parent with schizophrenia. Age at first admission was similar for the 2 groups.

Suicide attempts were recorded in 44% of the patients with catatonic schizophrenia compared with 25% of those with other schizophrenia (*P* = .006). We assessed the association of suicide attempts with different diagnoses, including mood disorders, among those with catatonic or other schizophrenia. Schizophrenia patients with catatonia showed less evidence of mood disorders than those with other types of schizophrenia. Of the 43 cases with catatonia, only 3 (7%) had any admission episodes coded as a mood disorder. These 3 patients had 7 recorded suicide attempts, but only one of these occurred prior to an admission for a mood disorder ("recurrent depressive disorder, current episode severe with

**Table 1.** Characteristics of Patients with Catatonic Schizophrenia and Other Schizophrenia

| | | Catatonic Schizophrenia | Other Schizophrenia |
|---|---|---|---|
| Number of cases | | 43 | 525 |
| Percentage | | 100.0 | 100.0 |
| Sex | Males | 48.8 | 64.2 |
| | Females | 51.2 | 35.8 |
| Paternal age | <35 | 58.1 | 61.9 |
| | 35+ | 41.9 | 38.1 |
| Maternal age | <35 | 72.1 | 81.3 |
| | 35+ | 27.9 | 18.7 |
| Socioeconomic status | High | 30.2 | 34.1 |
| | Medium | 27.9 | 33.3 |
| | Low | 41.9 | 32.6 |
| Parental history of admission for schizophrenia | Any | 16.3 | 9.7 |
| | None | 83.7 | 90.3 |
| Age of first admission, any diagnosis, in years | <20 | 41.9 | 33.5 |
| | 20–24 | 23.3 | 30.1 |
| | 25–29 | 25.6 | 22.9 |
| | 30+ | 9.3 | 13.5 |
| History of 1 or more suicide attempts | Present | 44.2 | 25.0 |
| | Absent | 55.8 | 75.0 |

psychotic symptoms" [ICD-10 code F33.3]). The other attempts were in conjunction with catatonic schizophrenia or other schizophrenia, except for 1 admission for an organic disorder. The 40 patients with catatonic schizophrenia but no history of admission for a mood disorder had 48 attempted suicides recorded. The suicide attempts in these 40 were in conjunction with catatonic schizophrenia or other schizophrenia, except for 1 case whose attempt was in conjunction with "Paranoid personality disorder" (F60) and another offspring who had 1 attempt with catatonic schizophrenia but the other 2 together with "Mental and behavioral disorders due to multiple drug use and use of other psychoactive substances" (F19). For the attempts recorded together with discharge for a type of schizophrenia, 11 suicide attempts coincided with admissions for catatonic schizophrenia and 34 with other types of schizophrenia.

For the 43 cases with catatonic schizophrenia, only 25 of their 386 admissions were for diagnoses other than a type of schizophrenia. The admissions were for personality disorders, for unspecified dementia, for organic mental disorders, psychoactive substance use, mood disorder, neurotic or somatoform disorders, or mental retardation. Eleven of the 43 cases had catatonic schizophrenia diagnosed in less than 20% of their total number of admissions; for all of them, as well as the others diagnosed with catatonic schizophrenia, most admissions were for some type of schizophrenia. Analyses were rerun with these 11 reclassified as having a history of schizophrenia

but not the catatonic subtype. The effects of male sex, parental history of schizophrenia, and parental age were in the same directions. Males were still less likely to have catatonic schizophrenia than other schizophrenia, but the effect was no longer statistically significant, possibly due to the smaller number of cases (data not shown). Those with catatonic schizophrenia still had a much higher percentage of suicide attempts; of those with the more conservative definition of catatonic schizophrenia, 44% had a suicide attempt, while there were 25% among those with other schizophrenia. This was a significant difference ($P = .02$).

In those with catatonic schizophrenia, the proportions with 1, 2, 3, 4, and 5+ admissions to a psychiatric hospital were 5%, 14%, 9%, 2%, and 70% while of those with other subtypes the corresponding proportions were 18%, 18%, 12%, 13%, and 39%. There were 29 cases of catatonic schizophrenia (67%) who had their first admissions for catatonic schizophrenia within their first 5 admissions to hospital; however, multiple admissions for the diagnosis were rarely consecutive. Given the limited stability of subtype diagnoses, however, those with more admissions have a greater likelihood of receiving a diagnosis of catatonic schizophrenia during any one of those admissions. Nine percent of those with catatonic schizophrenia and 6% of those with other types had court-ordered admissions, while 2% vs 3%, respectively, had at least 1 admission for an organic disorder coded "Organic, including symptomatic, mental disorders" (F00–F09) in the ICD-10. These included unspecified dementia (F03), "Other mental disorders due to brain damage and dysfunction and to physical disease" (F06), including "Organic delusional (schizophrenia-like) disorder" (F06.2).

Turning to the univariate proportional hazards models (data not shown in a table), we found that sex and mother's and father's ages were each associated with a difference in risk for the 2 types of schizophrenia, as was parental history of schizophrenia. The multivariate model is shown in table 2. While sex was not a risk factor for catatonic schizophrenia, it did markedly affect other schizophrenia, the risk of other schizophrenia being higher in males. The CIs for these RRs showed virtually no overlap; furthermore, a test of the difference, based on the model restricted to cases alone, showed them to differ significantly ($P = .03$), as reported in the right hand column of table 2.

Catatonic vs other schizophrenia did not differ significantly in relation to older age of parents in the multivariate model; however, they did show opposing trends (table 2). While older paternal age seemed unrelated to the risk of catatonic schizophrenia, it was a significant risk factor for other types of schizophrenia. In contrast, older maternal age tended to be associated with catatonic schizophrenia while it was unrelated to other types.

The psychiatric diagnoses of the parents, like those of the offspring, were determined from the national psychiatric

**Table 2.** Numbers of Cases With and Without Schizophrenia (*N*), Relative Risk (RR), and 95% CI by Type of Schizophrenia and Risk Factors for Schizophrenia

| | | | No Schizophrenia | Catatonic Schizophrenia | Other Schizophrenia | *P* (Difference Between 2 Types of Schizophrenia) |
|---|---|---|---|---|---|---|
| Total *N* | | | 89 500 | 43 | 525 | |
| Sex | Male | *N* | 46 388 | 21 | 337 | .03 |
| | | RR | | .90 | 1.70 | |
| | | CI | | 0.50, 1.64 | 1.42, 2.03 | |
| | | *P* | | .73 | <.0001 | |
| | Female | *N* | 43 680 | 22 | 188 | |
| | | RR | | 1 | 1 | |
| | | CI | | — | — | |
| | | *P* | | — | — | |
| Paternal age | 35+ | *N* | 26 285 | 18 | 200 | .59 |
| | | RR | | 1.09 | 1.27 | |
| | | CI | | 0.46, 2.58 | 1.03, 1.56 | |
| | | *P* | | .85 | .03 | |
| | <35 | *N* | 63 783 | 25 | 325 | |
| | | RR | | 1 | 1 | |
| | | CI | | — | — | |
| | | *P* | | — | — | |
| Maternal age | 35+ | *N* | 12 213 | 12 | 98 | .13 |
| | | RR | | 2.14 | 1.15 | |
| | | CI | | 0.83, 5.54 | 0.89,1.49 | |
| | | *P* | | .12 | .29 | |
| | <35 | *N* | 77 855 | 31 | 427 | |
| | | RR | | 1 | 1 | |
| | | CI | | — | — | |
| | | *P* | | — | — | |
| Parental history of schizophrenia | | | | | | |
| | Present | *N* | 1 514 | 7 | 51 | .14 |
| | | RR | | 10.88 | 6.09 | |
| | | CI | | 4.84, 24.46 | 4.56, 8.12 | |
| | | *P* | | <.0001 | <.0001 | |
| | Absent | *N* | 88 554 | 36 | 474 | |
| | | RR | | 1 | 1 | |
| | | CI | | — | — | |
| | | *P* | | — | — | |

case registry. Overall, there were 8 cases with catatonic schizophrenia and 66 with other schizophrenia who had any parental history for admission for schizophrenia or mood disorder. There were 3 catatonic patients with a mother with schizophrenia and 4 with a father, for a total of 9 parents diagnosed with the disorder. Those with other schizophrenia had 32 mothers and 19 fathers diagnosed with the disorder, making 51 overall. Parental history of admission for schizophrenia, as expected, was a strong and highly significant predictor of schizophrenia in the cohort. This relationship was somewhat stronger for catatonic schizophrenia, but the effects of parental history did not differ significantly between the 2 types of cases, as shown by their overlapping confidence limits and by the *P* value seen in the right hand column of table 2. One of the patients with catatonic schizophrenia had a mother with an admission for affective disorder, and another had a father with it. Of those with other schizophrenia, 19 had a mother and 10 had a father with affective disorder. Numbers were too small to al-

low for analysis of the effects of a parent with mood disorder or for a separate model of paternal or maternal history of schizophrenia or of mood disorder.

## Discussion

The salient findings from this study are that catatonic schizophrenia shows no difference between the sexes and no relation to paternal age, unlike other schizophrenia, for which these are strong and robust risk factors. Another finding is that those hospitalized for catatonia have been more likely to attempt suicide than those with other schizophrenia. Our results lend support to the hypothesis that catatonic schizophrenia might be biologically distinct from other types of schizophrenia, as previously suggested.[1,4–6] More tenuous is the finding that catatonic schizophrenia may have a stronger relationship to maternal ageing and/or to mental illness in the father compared with other schizophrenia.

Prior reports on catatonic schizophrenia have been limited to cross sectional and case control studies, and case series. They have assessed the patients' characteristics and have examined prognosis but could not measure effects of risk factors. For example, 1 study, in contrast to our findings, reported that for the catatonic subtype, men outnumbered women by a ratio of 6:1 ($P$ = .04)[16] but could not measure the risk conferred by male or female sex.

Regarding the prevalence of catatonic schizophrenia, Rosebush and Mazurek found that in a group of patients with catatonia, 20% had a concurrent diagnosis of schizophrenia,[17] while another study reported that among a group of inpatients, 15% had catatonia and of those 54% had schizophrenia.[18] Rosebush and Mazurek also reviewed other research of the prevalence of catatonia overall in psychiatric inpatients and reported that an estimated 9%–15% of patients admitted to a typical acute care psychiatric service meet diagnostic criteria for catatonia.[17] Other studies not included in the review, which also used standardized rating scales to report on the prevalence of catatonia in psychiatric hospitals, found prevalences within this same range.[19]

Our study found that people with catatonic schizophrenia attempted suicide more frequently than those with other types of schizophrenia, and the difference was statistically significant. This is notable because those with schizophrenia are already considered at high risk for suicide. Studies have shown that depressive disorders are important risk factors for suicide attempts and suicide deaths and may be stronger contributors than schizophrenia.[20,21] It could be considered that because catatonic symptoms appear more frequently in the context of mood disorders than psychotic ones,[2] those with catatonic schizophrenia were more likely than those with other schizophrenia to have admissions for mood disorders and that this could explain the higher rate of suicide in patients with catatonic schizophrenia in our cohort. We did not find evidence in support of this, however; although many patients with catatonic schizophrenia also had admissions for other diagnoses, only 3 had a history of mood disorder. The misdiagnosis, at times, of those with mood disorder as patients with catatonic schizophrenia would have been likely to materialize as more history of admissions for mood disorders. Thus, the link between catatonic schizophrenia and suicide in this cohort is not easily explained by the presence of mood disorder.

Our finding of an increase in suicide attempts with catatonic schizophrenia is in agreement with a cross sectional study of 31 patients hospitalized for catatonic syndrome as adolescents. The standardized mortality ratio (SMR) for suicide in these adolescents with catatonia (SMR = 54 945, 95% CI = 5189–202 066) corresponds to a 500-fold increased risk of suicide when compared with the general population of same sex and age and is clearly higher than the 9-fold increase measured in schizophrenia (SMR = 900, 95% CI = 842–962).[22] Although this suggests that adolescents diagnosed with catatonia were more likely to die from suicide than those with schizophrenia taken as a whole, a comparison of suicide in catatonic schizophrenia could not be made due to lack of reported SMR for subtypes of schizophrenia in the literature.[22] In a study of patients previously hospitalized for schizophrenia, 29% of those who eventually committed suicide had psychomotor agitation during their hospital stay compared with less than half (13%) of those who did not.[24] Psychomotor agitation is characteristic of catatonia and catatonic schizophrenia,[2,3] so that perhaps catatonia was also associated with an increased suicide risk in that study. Our finding adds to this literature, suggesting that catatonic schizophrenia confers a higher risk.

The lower proportion of mood disorders in those with catatonic schizophrenia compared with others with schizophrenia must also be considered in relation to the absence of sex differences we found. If mood disorders were diagnosed more frequently in those with catatonic schizophrenia, that could be thought to explain the finding of an equal rate in men and women as compared with higher risk in males for other schizophrenia. Because those with catatonia are less likely to have admissions for mood disorders, the findings on sex cannot be explained in that way.

This study faced some limitations. First, data are for hospitalizations for treatment; we could not ascertain the criteria for diagnosis but only that the final discharge diagnosis was made by a board-certified psychiatrist using ICD coding. These data must be interpreted with caution because notwithstanding the course of illness or any change of diagnosis during each hospitalization, the registry records only a single discharge diagnosis for each hospital episode. In addition, the reliability of the diagnosis of schizophrenia subtypes is generally considered low, and this could not be rectified in population-based data where the diagnoses were discharge diagnoses from a database. Another limitation is the low stability of subtype diagnoses in schizophrenia. In order to try to address this, we reclassified as other schizophrenia the offspring who were diagnosed with catatonic schizophrenia at less than 20% of their total number of admissions. The predictors seemed to affect the risk for catatonic schizophrenia in a similar fashion, implying that a misclassification of these cases due to low stability of subtype diagnosis does not necessarily explain our findings in this cohort.

An additional limitation is that the Jerusalem cohort's data on offspring are truncated in the late 1930s, so that differential lifetime incidence cannot be evaluated. Our study includes too few cases to speak to catatonic schizophrenia with certainty beyond ages 35+; the cohort will have to age before this question can be addressed.

There is no consensus in the literature on whether patients with catatonia in the context of schizophrenia

constitute a distinct subtype of patients with schizophrenia, whether some patients with schizophrenia are more likely to develop catatonia, or whether catatonic symptoms can appear in patients with schizophrenia but do not delineate a distinct subgroup of patients; rather, catatonia can simply co-occur with several psychiatric as well as medical diagnoses.[1,5,6,23] Both the ICD-10 and the DSM-IV list catatonic schizophrenia as a subtype of schizophrenia; DSM-IV, however, also includes catatonic symptoms in other categories and states that catatonic symptoms occur more frequently in the context of mood disorders than schizophrenia. The ICD-10 contains a category for organic catatonic disorders and also includes "stupor" as a feature of several other categories; stupor in the ICD-10 has many features in common with psychomotor disturbances seen in catatonia. Some suggest that the current classification of traditional subtypes in schizophrenia should be discarded because different subtypes can present over the course of illness with schizophrenia and because the traditional classifications do not help with prediction of treatment response or prognosis.[24] These researchers propose that schizophrenia should be described with symptom dimensions, analogous to subtypes, including a dimension for the presence of motor symptoms. A description of the severity and variation in these dimensions in a patient over time would be more accurately reflecting distinct etiopathologies and genetic effects.[24] In our data, although 67% of cases had their first admissions for catatonic schizophrenia within their first 5 admissions to hospital, multiple admissions for the diagnosis were not commonly consecutive in each patient, illustrating, as noted above, that different subtypes can present over the course of illness with schizophrenia. Perhaps, at present, the best course may be to describe phenotypes until more information emerges about the correct classification and true biological underpinnings of catatonic schizophrenia or other subtypes.

In addition to the debate about the nature of catatonic schizophrenia, there are questions about its proper treatment, and more research may be needed to determine optimal treatment protocols for catatonia in the context of chronic schizophrenia.[17,25–28] Whether it is a subtype of schizophrenia, a co-occurrence of catatonia and schizophrenia, or a symptom dimension, a better understanding of the features and etiopathology of catatonic schizophrenia would facilitate further research into the best treatments.

Certain findings in basic science experiments hint that perhaps, in some cases, catatonic schizophrenia may have a distinct underlying molecular phenotype than other types of schizophrenia. Patients with catatonic schizophrenia have been reported to have lower serum brain-derived neurotrophic factor protein levels than patients with paranoid schizophrenia and residual schizophrenia ($F = 3.27$, $df = 2,12$, $P = .04$).[29] In addition, levels of C-reactive protein in serum were reported to be increased in patients with schizophrenia and were even higher in those patients with schizophrenia and prominent catatonic features ($P = .04$), in comparison to those with schizophrenia but without prominent catatonic symptoms.[30]

Patients with catatonic schizophrenia show a different profile of risk factors and outcomes than those with other types of schizophrenia in this cohort study. This lends support to the hypothesis that their etiology differs from other cases and suggests that in future genetic and clinical studies, there may be some benefit from considering this phenotype separately. A better understanding of catatonic schizophrenia may also shed light on the etiology of schizophrenia and of catatonia presenting in other clinical contexts.

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