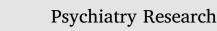
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# Gender differences in schizophrenia: A multicentric study from three Latin-America countries



Psychiatry Research

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#### ABSTRACT

This study was aimed to explore clinical differences between women and men with schizophrenia (SZ) in Latin-America. It was conducted in public mental health centers in Bolivia, Peru and Chile.

Two hundred forty-seven SZ patients participated in the study, 83 (33.6%) were women and 115 (46.6%) were Aymara. Compared to men, SZ women had slightly lower negative symptoms, reported slightly less social cognitive impairments, lower Family Relationships scores and higher Sentimental Life scores, independently of marital status, illness duration, age at illness onset and type of mental health treatment. All these differences have been replicated in the Aymara subgroup except for Sentimental Life scores. Aymara SZ women reported to be significantly less adherent into treatment compared to Aymara men. SZ women were found to have a better clinical profile and higher sentimental life scores than men. However, while SZ women reported more impaired Family Relationships compared to men, they were found to receive less psychotherapy in addition to pharma-cological treatment. SZ Aymara women were also identified as a specific subgroup that may be targeted for increased observance strategies.

#### 1. Introduction

The World Health Organization has been reporting the need for equity and justice in the distribution of resources within the mental health sector especially for vulnerable groups, such as women, indigenous and ethnic minorities (WHO, 2003). Schizophrenia (SZ) has an incidence sex ratio of 1:4, being more prevalent in men (Kraepelin, 1971; Leung and Chue, 2000; Falkenburg and Tracy, 2014). SZ women have been described to have a later age at illness onset, a lower illness severity and better global, functional and cognitive prognosis associated with a better quality of life, life satisfaction and cooperativeness (Räsänen et al., 2000; Riecher-Rossler et al., 2010; Falkenburg and Tracy, 2014; Navarro et al., 1996; Seeman, 1986; Salokangas, 1983; Goldstein, 1988). Negative symptoms have been described to be more prevalent in men while positive symptoms (paranoia or persecutory delusions) and auditory hallucinations have been found to be more prominent in women (Goldstein and Link, 1988; Goldstein, 1997; Hambrecht et al., 1992; Rector and Seeman, 1992; Tien, 1991; Abel et al., 2010; Roesch-Ely et al., 2009). From a neuropsychological point of view, SZ women have been shown to have a better verbal memory, visual recognition memory and speed processing compared to men

(Longenecker et al., 2010). Imagery studies have shown more left-lateralized abnormalities in SZ men compared to women. This has led to the hypothesis of a neurodevelopmental form of schizophrenia more frequent in men (Nopoulos et al., 1997; Jablensky, 1993; Flaum et al., 1990; Bogerts et al., 1990; Goldstein et al., 2002). However, these results have not been replicated in all studies (Fond et al., 2017).

Beyond pathophysiological/hormonal factors (Räsänen et al., 2000; Abel et al., 2010; Rietschel et al., 2017; Moriarty et al., 2001; Zhang et al., 2012; Kelly, 2006; Kelly et al., 2016; Childers and Harding, 1990; Salokangas and Stengard, 1990), SZ women have been described to have a better non-pharmacological treatment response (psychotherapy and family intervention) and a better antipsychotic adherence into treatment despite a higher rate of side-effects including tardive dyskinesia, dystonic episode, weight gain and obesity, metabolic syndrome, hyperprolactinaemia; hypotension (Usall et al., 2001; Falkenburg and Tracy, 2014; Lewis, 1992; Yassa and Jeste, 1992; Szymanski et al., 1995; Enger et al., 2004; Goff et al., 2005; Bushe et al., 2008; Seeman, 2004; Russell and Mackell, 2001).

In summary, SZ women have been described to have a global better prognosis compared to men in most of the studies carried out in Western countries. However gender differences may also be strongly

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influenced by cultural factors, which underlie the need to replicate these findings in other countries (Abel et al., 2010; Goldstein, 1997; Hambrecht et al., 1992; Harrison et al., 2001). Gender differences in schizophrenia have never been explored to date in Latin-American countries that may have strong cultural specificities and differences. For example, the Aymara ethnic group is the largest ethnic group in three Latin-America countries (Bolivia, Peru and Chile), with a population of 2 million people, and has lived in the Andes Mountains for centuries. In this type of indigenous community, the men-female relationship and in the sense of gender, refers exclusively to marriage that implies the coexistence between women and men. This conception would take into account the complementarity between genders and not equality: recognize men and women as different, valuing this difference because roles and functions are characterized by their flexibility. However, the process of "transculturation" caused by "progress, modernity and the migration of the countryside-city" has caused the conception of complementarity to be lost. Moreover, today a hierarchical position is observed where the man has greater prestige where the Aymara woman does not have the same presence as men in public spaces (Carrasco and Gavilán, 2014). Recent generations of Aymara have undertaken a massive migration from rural towns to large cities and, thus, receive healthcare services from the same clinics as Non-Aymara individuals (Köster, 1992; Van Kessel, 1996; Gundermann et al., 2007). A better characterization of their illness characteristics is needed to orientate their care in a personalized-medicine approach.

The objective of the present study was to explore clinical differences between women and men with schizophrenia (SZ) in three Latin-America countries (Bolivia, Peru and Chile) and to explore some specificity in the Aymara ethnic subgroup.

### 2. Method

#### 2.1. Study design

This study was a cross-sectional multicentric study.

#### 2.2. Study participants

Overall, 253 non-selected stabilized SZ outpatients were consecutively recruited between May 2012 and February 2013 in three public ambulatory psychiatric care centers of three areas: Arica, Northern Chile (N = 85, 33.6%), Tacna, Southern of Peru (N = 85, 33.6%), and La Paz, Central-Western of Bolivia (N = 83, 32.8%). The three centers shared similar characteristics in terms of size, type of treatment given to patients, professionals and free access of care.

Even these three Latin American countries share several cultural characteristics; however, there are some general differences between them, which should be made explicit: in Bolivia, 13.6% of the population lives with less than US\$1 per day; in Peru, this population is 5.9%; and it is, 2.0% in Chile, which shows some difference in relation to the poverty index (OMS, 2013).

Other differences are associated with psychiatric care facilities: per 100,000 inhabitants, Bolivia has 0.1 psychiatric hospitals, Peru has 0.01, and Chile has 0.003 (this country has a greater number of outpatient institutions), mental health staff (the number of psychiatrists in Bolivia is 0.1; Peru: 0.1 and Chile: 0.6 per 100,000 inhabitants); lack of day hospitals (Bolivia, 0.1; Peru, 0; and Chile, 0.5), and residential care (Bolivia, 0; Peru, without data; and Chile, 103) (Caqueo-Urízar et al., 2013; World Health Organization, 1992).

Gender was not collected in 6 patients, so the final analysis was performed on 247 patients.

#### 2.2.1. Inclusion criteria

All non-selected stabilized community-dwelling patients diagnosed with schizophrenia by a psychiatrist according to the criteria of International Classification of Diseases (ICD), 10th version (WHO, 1992) were included in this study. Non-selection was defined by offering the participation to the study to all patients fulfilling inclusion criteria to avoid any selection bias. Stabilization was defined by no acute psychotic relapse or no treatment changes during the last 8 weeks before evaluation.

#### 2.2.2. Non-inclusion criteria

Patients with a history of neurological disorders (including stroke, epilepsy and head injury) or other illnesses affecting the central nervous system (blindness, deafness) were not included in the present study.

#### 2.3. Procedures

Two psychologists, who were part of the research team, trained for scale evaluation, and supervised by the principal -investigator (AC-U), conducted A 30–40 min comprehensive evaluation of the participants under the auspices of the mental health services of each country. All information was obtained from both patients, treating psychiatrists and medical records. All patients were administered antipsychotics.

## 2.4. Data collection

#### 2.4.1. Demographic and illness characteristics variables

Sex, age, ethnicity (Aymara and Non-Aymara), educational level ( $\geq 12$  years or <12), employment status (unemployed or employed), marital status (single or in couple), family income (measure of the total salary per month for all members of the family, expressed in US dollars), illness duration, age at illness onset, age at treatment onset, the number of hospitalizations during the past 3 years and type of mental health treatment (i.e., only pharmacological treatment vs. integral treatment defined by psychotherapy, family psycho-education, and/or day care hospital in addition to pharmacological treatment) were reported. All treatments were based on shared medical-decision. The non-pharmacological treatments may vary from one medical center to another, however these treatments should have been proposed equally to men and women.

#### 2.4.2. Instruments

Positive and Negative Syndrome Scale for Schizophrenia (PANSS) (Kay et al., 1987). This 30-item, 7-point (1–7) rating scale is specifically developed to assess psychotic symptoms in individuals with schizophrenia and comprises 3 different subscores: positive, negative and general psychopathology scores (Fresán et al., 2005). The PANSS has been translated into Spanish and validated in Spain by Peralta and Cuesta (1994) and in Mexico by Fresán et al., (2005). No inter-reliability has been done for the PANSS. However the PANSS has shown good inter-rater reliability in previous studies (Kay et al., 1988).

GEOPTE Scale of Social Cognition for Psychosis (SanJuán et al., 2003). This instrument is a 15-item scale designed to measure social cognition in schizophrenia, with social cognition defined as "the part of cognition involving perception, interpretation and processing of social signals as well as the capacity to adequately respond to such signals" (Ryckmans et al., 2009). Each item is scored on a 5-point scale from (1) no, (2) a little, (3) normal, (4) enough, and (5) a lot, with higher values indicating a higher level of functional impairment. Items 1 to 7 measure neurocognitive functions. Some items on this subscale are: Do you find it hard to pay attention?; Do you find it hard to follow conversations in which several people take part?; Is it hard for you to learn new things?. Items 8-15 measure social cognitive function. Some items on this subscale are: Is it hard for you to recognize other people's emotions (for example: sadness, joy, or anger)?; When you're in a group, are you often told that you misinterpret other people's attitudes, looks, or gestures?; Do you feel very sensitive to other people's looks, words, or gestures?. For this study, each set of factors was assessed separately to compare neurocognitive deficits (GEOPTE 1-7) and social cognitive impairments

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