

# The Impact of Consanguinity on Risk of Schizophrenia

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Schizophrenia (Sz) occurs worldwide and is one of the severest mental disorders [1]. The World Health Organization documented that Sz has been recognized as a major public health problem in the fourth position among the global burden of diseases [2]. It has been generally accepted that Sz, like all other complex diseases, is caused by genetic and environmental factors. Bener et al. [3] reported that consanguinity (inbreeding) may be associated with an increased risk for a wide range of genetically complex disorders. Marriages between relatives are common worldwide and lead to human consanguinity. It was found that consanguineous marriages increase the risk for Sz in offspring [4]. Since consanguinity is widely practiced in the Eastern Mediterranean region, it was considered worthwhile to study this aspect in this population. Moreover, an elevated parental consanguinity rate of 52% was reported in the State of Qatar [3].

The aim of the study was to examine the impact of consanguinity on the risk for Sz disorders and investigate the inbreeding characteristics of the Sz patients.

## Methods

The cross-sectional study was based on the Primary Health Care Centers among Arab patients aged 18–55 years from January 2009 to December 2010. Of the sample size of 1,491 subjects, 1,184 patients agreed to participate in this study (79.4%). Institutional review board approval was obtained from the Hamad Medical Corporation for conducting this research. The subjects who did not agree to participate (20.6%) were demographically similar to those who had agreed to participate. A validated self-administered questionnaire was designed to collect the data based on face-to-face interviews by physicians and qualified nurses. Following completion of this questionnaire by the patient, the provisional diagnosis score was calculated from the responses, which was then confirmed by psychiatrists through a clinical questioning using DSM-IV criteria. The general diagnostic screening questionnaire was not designed to make a definitive diagnosis but rather to identify people at high risk. Content validity, face validity and reliability of the questionnaire were tested using 50 pa-

tients. These tests demonstrated a high level of validity and high degree of repeatability ( $\kappa = 0.84$ ) and Cronbach's  $\alpha$ -coefficient was 0.82.

Student t test, nonparametric Mann-Whitney test,  $\chi^2$  and Fisher's exact tests (two-tailed) were performed for statistical analysis. The Student t test was used to determine the mean and standard deviation of the coefficient of inbreeding of the two groups.  $p < 0.05$  was considered as the cut-off value for significance.

## Results

The data reveals the genetic factors of the studied subjects with or without Sz. Parental consanguinity was elevated among the patients with Sz (43.8%) with a higher mean coefficient of inbreeding ( $0.0198 \pm 0.29$ ) than in non-Sz subjects (38%) with a lower mean inbreeding coefficient ( $0.0151 \pm 0.24$ ). Similarly, the inbreeding coefficient was higher in schizophrenic male ( $0.01857 \pm 0.027$  vs.  $0.0145 \pm 0.024$ ) and female ( $0.0208 \pm 0.030$  vs.  $0.0158 \pm 0.024$ ) patients compared to their counterparts.

**Table 1.** Genetic factors of the studied subjects with or without Sz (n = 1,184)

Variable	Subjects		p value
	with Sz (n = 276)	without Sz (n = 908)	
<i>Parental consanguinity</i>			
None	154 (55.8)	560 (61.7)	0.015 <sup>a</sup>
First degree	74 (26.8)	180 (19.8)	
Second degree	48 (17.4)	168 (18.4)	
<i>Family history Sz</i>			
Parents			<0.001 <sup>a</sup>
Yes	72 (26.1)	140 (15.4)	
No	204 (73.9)	768 (84.6)	
Grandparents			0.007 <sup>a</sup>
Yes	45 (16.3)	92 (10.1)	
No	231 (83.7)	816 (89.9)	
Aunts			0.023 <sup>a</sup>
Yes	47 (17.0)	105 (11.6)	
No	229 (83.0)	803 (88.4)	
Uncles			0.110 <sup>a</sup>
Yes	53 (19.2)	136 (15.0)	
No	223 (80.8)	772 (85.0)	
<i>Inbreeding characteristics</i>			
All subjects			
Parent consanguinity	121 (43.8)	345 (38.0)	0.091 <sup>a</sup>
Mean coefficient of inbreeding ± SD	0.0198 ± 0.029	0.0151 ± 0.024	0.008 <sup>b</sup>
Males			
Parent consanguinity	51 (42.9)	169 (36.0)	0.170 <sup>a</sup>
Mean coefficient of inbreeding ± SD	0.01857 ± 0.027	0.0145 ± 0.024	0.122 <sup>b</sup>
Females			
Parent consanguinity	70 (44.6)	176 (40.2)	0.346 <sup>a</sup>
Mean coefficient of inbreeding ± SD	0.02084 ± 0.030	0.01580 ± 0.024	0.170 <sup>b</sup>
Results are expressed as numbers with percentages in parentheses unless indicated otherwise.			
<sup>a</sup> $\chi^2$ test performed.			
<sup>b</sup> Student t test performed.			

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## Discussion

The present study has described the association of consanguinity and Sz in the Arab population of Qatar. The most important finding was that there is an increased morbidity of Sz in the first-degree relatives of Sz patients (26.8%) compared to the controls (19.8%). Dobrusin et al. [4] reported a tenfold greater risk in first-de-

gree biological relatives of Sz patients than in the normal population. The rate of parental consanguinity (43.8 vs. 38%) and the mean coefficient of inbreeding (0.0198  $\pm$  0.29 vs. 0.015  $\pm$  0.24) was higher among Sz patients compared to subjects without Sz (table 1). Similar to our results, a significant elevated rate of consanguinity was observed among Sz patients in Egypt [5]. The present study has confirmed that con-

sanguinity contributes to a high incidence of Sz in offspring. The most striking difference in the occurrence of Sz was that familial transmission of Sz was greater among female probands (57.1%; 0.04592) with a higher mean inbreeding coefficient than in the male probands (42.9%; 0.03947) which is in line with the study results of Goldstein et al. [6]. Also, a positive family history of Sz was associated with the occurrence of Sz in parents (24.6%;  $p = 0.04$ ), grandparents (17.5%;  $p = 0.03$ ) and aunts (21.4%;  $p = 0.002$ ). Even, family studies confirmed that relatives of probands with Sz have an increased risk of developing Sz. Family members share a common culture and a common environment; hence familial environmental factors may confound genetic relationships.

In conclusion, our study revealed that the parental consanguinity and family history are the main risk factors for the development of Sz among an Arab population. The inbreeding coefficient was significantly elevated among Arab Sz patients compared to an Arab population without Sz.

## References

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