



The Psychosocial Research of the Members in a Large Von Hippel-Lindau Family in China

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Abstract

Von Hippel-Lindau (VHL) disease is a rare, autosomal inherited tumor disorder caused by mutations or deletions of the VHL gene. Most of the previous research focused on the clinical features and molecular mechanisms of the disease, few concerned about the psychosocial impact on the patients and their family. We encountered a VHL family in the clinical work and attempted to assess the possible psychological effects of the disease on the members of the family. Three questionnaires including Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS) and Revised Symptom Checklist (SCL-90-R) were used in the research. A total of 61 members participated in the investigation. The SAS and SDS tests showed that 13 members were affected by anxiety which was associated with age, and 19 members suffered from depression which was correlated with gender, marital status, age, being patients, occupation, education and close relative of the VHL patients. The SCL-90 results showed that the "total scores", "interpersonal sensitivity", "depression", "anxiety" and "panic" scored higher in our study than Chinese average level. Meanwhile, the SCL-90 data revealed that: 1) age was associated with anxiety disorder; 2) marital status was related to higher prevalence of hostility; 3) Being VHL patients was related to bigoted symptoms; and 4) closer relationship with the VHL patients was associated with depressive and hostility symptoms in the family. The study revealed that susceptibility to psychiatric symptoms was correlated with certain sociodemographic and clinical characteristics. Depression and anxiety were the most prevalent psychiatric symptoms in the VHL family. This was the first study focusing on the psychological consequences of the VHL disease. An understanding of these factors would be helpful in providing appropriate mental health services to the VHL family.

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Keywords

Von Hippel-Lindau (VHL) Syndrome, SAS, SDS, SCL-90-R, Depression, Anxiety

Subject Areas: Oncology, Psychiatry & Psychology

1. Introduction

Von Hippel-Lindau (VHL) syndrome is a rare, autosomal inherited disorder, with an approximated incidence of 1/36,000 - 1/52,000 live births. By the age of 60, 97% carriers of a VHL gene mutation will develop clinical symptoms [1] [2]. VHL is caused by deletions or mutations in a tumor suppressor gene located on the human chromosome 3p25 and is characterized by multi-organ involvement of tumors. Examples include hemangioblastomas in the central nervous system, retinal angiomas, renal clear cell carcinomas and cysts, pheochromocytomas, pancreatic lesions and so on [3]. VHL syndrome can be classified into four subtypes based on the presence of pheochromocytoma and/or RCC. Type I VHL is not associated with pheochromocytoma, and type II is associated with both haemangioblastoma and pheochromocytoma, with either a relatively low incidence (type IIA) or a high incidence (type IIB) of RCC and pancreatic tumours. In contrast, VHL IIC is characterized by a pheochromocytoma-only phenotype [1].

Tumor diagnosis always has an obvious effect on the physical and emotional conditions of the patients and their family, no matter it is benign or malignant [4] [5]. The suffering from tumor implies helplessness, uncertainty, guilt, abandonment, physical pain and death. It makes the affected patient must face new individual problems, both physical and social [6] [7]. Many studies have demonstrated the high levels of depression and anxiety symptoms in cancer patients [8] [9]. Simultaneously, the family including spouses, children, and parents also suffer from great psychological pressure [10]. Some researches indicated higher levels of anxiety and depression in the family than in general population, or even in cancer patients [11] [12]. Relatives often experience the burden and increased responsibility, which could have negative consequences such as fatigue, anxiety, agony, fear, sleep disorder, cognitive impairment, helplessness, uncertainty, family conflict, financial burdens, and speculations of the future and finality of life [13]-[15].

Since the mid-1990s there has been a growing awareness of the need to develop the palliative care service in the world that would also treat psychosocial needs of the patient and their family, which has got a rapid development in the recent years [16]. However, there were few studies documenting the psychosocial characteristics in an inherited cancer family. So we conducted the present study to evaluate the prevalence of overall psychiatric symptoms among the VHL family members, and to explore the related contributory risk factors accounting for psychiatric symptoms, which could provide relevant medical care for both the patients and family members.

2. Materials and Methods

2.1. The Object of Study

The study population consisted of 61 members in a large VHL family in the northwest of China (Age > 16). We distributed the SAS (Self-Rating Anxiety Scale), SDS (Self-Rating Depression Scale) and SCL-90-R scales to the members, and retrieved them in the prescriptive time. Data on basic demographic details included age, gender, locality, education, income and occupation. The study was approved by the research ethics committees of Xi'an Jiaotong University Medical School.

2.2. The Questionnaires

Self-Rating Depression Scale (SDS) and Self-Rating Anxiety Scale (SAS) were the primary measures. SDS had 20 items, which were divided into 4 grades according to the scoring, and the standard score equaled to the total score multiplied by 1.25. Standard score ranging from 53-62 indicated mild depression, 63 - 72 moderate, while >72 implied severe depression. SAS also contained 20 items and 4 grades. It included 5 items forward scoring and 15 reverse. The calculation method was the same as SDS. A standard score ranging from 50 - 59 indicated mild anxiety, 60 - 69 moderate, while >70 implied severe anxiety. SDS and SAS had been proved suitable

for Chinese, which were widely used in clinical and research work [17]-[19]. The Revised Symptom Checklist (SCL-90-R) was a 90-item self-report inventory developed in the 1980s by Derogatis and widely used in both normal and distressed populations. Each item was rated on a 5-point distress scale (from 0 to 4): 0 to 0.99—normal, 1 to 1.99—slight psychopathology, 2 to 2.99—moderate psychopathology, 3 to 3.99—considerable psychopathology, 4—extreme psychopathology [20] [22]. The above three questionnaires were all proved to be appropriate for the Chinese [23].

2.3. Statistical Analyses

Data was analyzed using Statistical Package for Social Sciences 18 (SPSS Inc., Chicago, IL, USA). Descriptive analyses were recorded as means and proportions. Logistic regression analysis, Chi-square test and t-test were employed to determine the association of various demographic and clinical factors with the presence of depression and anxiety in the VHL family. A p value of <0.05 was considered statistically significant.

3. Results

3.1. Characteristics of the Study Population

A total of 61 members in the VHL family completed the study, including 32 males and 29 females, of which the majority were married (75.41%). The mean (SD) age was 36.1 ± 7.8 years (range 16 - 61), and 55.74% of them were older than 30 years old. The majority of them were manual workers (90.16%), from rural areas (59.02%), with low education (65.57%, lower than high school education) and had a low household income (55.74%, lower than 500 U.S. dollar/month). There were 10 identified VHL patients, and 29 members who had the first degree relatives diagnosed (including the patients), as the direct sufferers of VHL disease. The detailed sociodemographic characteristics of the participants were shown in [Table 1](#).

3.2. The Results of the SAS and SDS Test of the VHL Family Members

The SAS test showed that 21.31% of the family members had the anxiety, which was correlated with age (≥ 30 years). Meanwhile, the SDS test showed that 31.15% of the family got the depression symptom, which were correlated with gender, age, marital status, occupation, education, being VHL patients and the relationship with the patients. [Table 2](#) showed results of the psychological evaluation of the family members using the SAS and SDS questionnaires.

3.3. The Results of the SCL-90 Scores of the VHL Family Members

Based on the results revealed by the SAS and SDS tests, we used the questionnaires to study the prevalence of psychiatric symptoms of the VHL family further. The detailed results of the SCL-90 scores were shown in [Table 3](#). Among the 10 subproject of the SCL-90 scales, the “Total scores”, “Interpersonal sensitivity”, “Depression”, “Anxiety” and “Panic” of the VHL family members were scored higher than normal Chinese level ([Table 4](#)).

3.4. Contributory Factors Associated with Psychiatric Symptoms

The results of the stepwise logistic regression analysis were summarized in [Table 5](#). Our results showed that the older age in the family was associated with anxiety ($\beta = -0.307$, $p = 0.008$). Married status was correlated with higher prevalence of hostility symptoms ($\beta = 0.271$, $p = 0.017$). Being the VHL patients was associated with bigoted symptoms ($\beta = -0.217$, $p = 0.046$). The first degree relatives of the patients (including the patients) was correlated with higher prevalence of depression symptoms ($\beta = -0.244$, $p = 0.029$) and hostility ($\beta = -0.230$, $p = 0.037$).

4. Discussion

To the best of our knowledge, the present study is the first to explore the comprehensive psychiatric symptoms experienced by the VHL family members using the SAS, SDS and SCL-90-R questionnaires. This is also the first study to try to combine the VHL patients and the relatives together as victims of the VHL disease. Overall, 61 members who came from the northwest of China, which was economic underdeveloped area, participated in

Table 1. Sociodemographic characteristics of the family members.

Characteristic	n (%)
Gender	
Male	32 (52.46)
Female	29 (47.54)
Age (yr)	
<30 Years	27 (44.26)
≥30 Years	34 (55.74)
VHL patients	
Yes	10 (16.39)
No	51 (83.61)
Relative with the VHL patients	
First degree relatives	29 (47.54)
others	32 (52.46)
Domicile	
Rural	36 (59.02)
Urban	25 (40.98)
Income per month (\$)	
<500	34 (55.74)
≥500	27 (44.26)
Occupation	
Farming	27 (44.26)
Skilled worker	28 (45.90)
Unemployed	2 (3.28)
Professional	4 (6.56)
Education	
Illiterate	1 (1.64)
Primary	7 (11.47)
Secondary	11 (18.03)
High School Certificate	21 (34.43)
Bachelor	21 (34.43)
Marital status	
Married	46 (75.41)
Unmarried	15 (24.59)

the psychosocial investigation. The main findings of this study were the high prevalence of depression and anxiety in the VHL family, which was much higher than some earlier studies conducted in cancer patients and relative groups [4] [8]. One important reason was that VHL disease is an inherited disorder characterized by multi-organ tumors, and the prevalence of tumor diagnosis was much higher than sporadic cases. A second reason for

Table 2. The results of the SAS and SDS tests of the VHL family members.

	SAS		SDS	
	Positive	Negative	Positive	Negative
Total (n, %)	13 (21.31)	48 (78.69)	19 (31.15)	42 (68.85)
Gender				
Male	9	23	5	27
Female	4	25	14	15
	$\chi^2 = 1.863$	$p = 0.172$	$\chi^2 = 7.562$	$p = 0.006^*$
Age				
<30	2	24	3	23
≥ 30	11	24	16	19
	$\chi^2 = 5.012$	$p = 0.025^*$	$\chi^2 = 8.125$	$p = 0.004^*$
Marital status				
Married	12	34	18	28
Unmarried	1	14	1	14
	$\chi^2 = 1.518$	$p = 0.218$	$\chi^2 = 4.148$	$p = 0.042^*$
Domicile				
Rural	8	28	13	23
Urban	5	20	6	19
	$\chi^2 = 20.043$	$p = 0.835$	$\chi^2 = 1.009$	$p = 0.315$
Income per month (\$)				
<500	6	28	11	23
≥ 500	7	20	8	19
	$\chi^2 = 0.615$	$p = 0.433$	$\chi^2 = 0.052$	$p = 0.820$
Occupation				
Farming	7	20	9	18
Skilled worker	4	24	7	21
Unemployed	0	2	0	2
Professional	2	2	4	0
	$\chi^2 = 3.867$	$p = 0.276$	$\chi^2 = 9.950$	$p = 0.019^*$
Education				
Illiterate	1	0	1	0
Primary	1	6	3	4
Secondary	2	9	7	4
High School Certificate	6	15	3	18
Bachelor	3	18	5	16
	$\chi^2 = 5.241$	$p = 0.263$	$\chi^2 = 11.383$	$p = 0.023^*$
VHL patients				
Yes	2	8	8	2
No	11	40	11	39
	$\chi^2 = 0.000$	$p = 1.000$	$\chi^2 = 10.413$	$p = 0.001^*$
Relative with the VHL patients				
First degree relatives	9	20	14	15
others	4	28	5	27
	$\chi^2 = 3.116$	$p = 0.078$	$\chi^2 = 7.562$	$p = 0.006^*$

Table 3. The results of the SCL-90 scores of the VHL family members.

	F1	F2	F3	F4	F5	F6	F7	F8	F9	Total
Characteristics										
Gender										
Male	1.49 ± 0.31	1.59 ± 0.16	1.76 ± 0.19	1.59 ± 0.21	1.50 ± 0.33	1.58 ± 0.43	1.54 ± 0.43	1.44 ± 0.18	1.30 ± 0.13	137.28 ± 14.20
Female	1.36 ± 0.019	1.60 ± 0.18	1.74 ± 0.16	1.64 ± 0.18	1.46 ± 0.17	1.42 ± 0.36	1.51 ± 0.25	1.44 ± 0.19	1.29 ± 0.12	135.90 ± 10.73
Age										
<30	1.44 ± 0.27	1.59 ± 0.17	1.74 ± 0.17	1.60 ± 0.22	1.58 ± 0.34	1.64 ± 0.50	1.61 ± 0.46	1.43 ± 0.17	1.31 ± 0.13	138.58 ± 15.44
≥30	1.42 ± 0.26	1.60 ± 0.17	1.75 ± 0.18	1.63 ± 0.18	1.41 ± 0.16	1.40 ± 0.30	1.46 ± 0.24	1.45 ± 0.20	1.29 ± 0.12	135.17 ± 9.95
Marital status										
Married	1.44 ± 0.25	1.55 ± 0.15	1.76 ± 0.16	1.62 ± 0.22	1.66 ± 0.41	1.77 ± 0.57	1.73 ± 0.54	1.45 ± 0.19	1.29 ± 0.12	141.87 ± 17.45
Unmarried	1.42 ± 0.27	1.61 ± 0.17	1.75 ± 0.18	1.61 ± 0.19	1.42 ± 0.16	1.42 ± 0.30	1.45 ± 0.24	1.44 ± 0.18	1.30 ± 0.13	134.91 ± 10.21
Domicile										
Rural	1.427 ± 0.25	1.622 ± 0.17	1.73 ± 0.15	1.62 ± 0.20	1.54 ± 0.31	1.54 ± 0.45	1.56 ± 0.43	1.46 ± 0.19	1.297 ± 0.13	136.03 ± 15.019
Urban	1.424 ± 0.29	1.556 ± 0.15	1.776 ± 0.20	1.609 ± 0.18	1.40 ± 0.16	1.45 ± 0.32	1.47 ± 0.21	1.42 ± 0.16	1.292 ± 0.12	134.60 ± 7.724
Income per month (\$)										
<500	1.43 ± 0.256	1.603 ± 0.35	1.734 ± 0.15	1.60 ± 0.19	1.535 ± 0.31	1.52 ± 0.44	1.52 ± 0.41	1.41 ± 0.16	1.30 ± 0.12	136.71 ± 13.639
≥500	1.42 ± 0.28	1.585 ± 0.20	1.77 ± 0.20	1.63 ± 0.20	1.42 ± 0.17	1.48 ± 0.37	1.52 ± 0.28	1.48 ± 0.20	1.289 ± 0.12	136.52 ± 12.583
Occupation										
Farming	1.44 ± 0.31	1.63 ± 0.18	1.78 ± 0.21	1.64 ± 0.19	1.43 ± 0.16	1.45 ± 0.32	1.53 ± 0.27	1.47 ± 0.20	1.29 ± 0.13	136.71 ± 10.12
Skilled worker	1.295 ± 0.18	1.65 ± 0.07	1.78 ± 0.00	1.5 ± 0.06	1.30 ± 0.14	1.335 ± 0.23	1.29 ± 0.21	1.34 ± 0.233	1.25 ± 0.07	129.0 ± 1.414
Unemployed	1.44 ± 0.24	1.58 ± 0.14	1.73 ± 0.14	1.63 ± 0.20	1.58 ± 0.33	1.60 ± 0.50	1.56 ± 0.45	1.43 ± 0.17	1.31 ± 0.13	138.67 ± 15.24
Professional	1.29 ± 0.09	1.47 ± 0.11	1.65 ± 0.11	1.42 ± 0.14	1.32 ± 0.15	1.38 ± 0.21	1.36 ± 0.08	1.42 ± 0.10	1.28 ± 0.10	126.00 ± 2.16
Education										
Illiterate	1.50	1.60	1.67	1.62	1.30	1.33	1.29	2.0	1.30	137.0
Primary	1.36 ± 0.19	1.60 ± 0.17	1.75 ± 0.17	1.61 ± 0.19	1.48 ± 0.26	1.51 ± 0.41	1.52 ± 0.35	1.44 ± 0.18	1.30 ± 0.13	136.62 ± 12.58
Secondary	1.46 ± 0.29	1.59 ± 0.20	1.73 ± 0.20	1.58 ± 0.25	1.65 ± 0.38	1.64 ± 0.57	1.59 ± 0.44	1.42 ± 0.14	1.26 ± 0.09	138.45 ± 16.67
High School Certificate	1.42 ± 0.26	1.65 ± 0.18	1.72 ± 0.11	1.66 ± 0.20	1.46 ± 0.19	1.40 ± 0.31	1.51 ± 0.34	1.46 ± 0.20	1.32 ± 0.16	137.57 ± 13.42
Bachelor	1.43 ± 0.30	1.54 ± 0.14	1.78 ± 0.21	1.60 ± 0.18	1.330 ± 0.18	1.51 ± 0.33	1.48 ± 0.23	1.41 ± 0.17	1.29 ± 0.11	134.38 ± 8.09
VHL patients										
Yes	1.44 ± 0.27	1.62 ± 0.11	1.74 ± 0.11	1.63 ± 0.14	1.56 ± 0.30	1.50 ± 0.40	1.53 ± 0.50	1.44 ± 0.20	1.27 ± 0.11	137.50 ± 13.99
No	1.34 ± 0.23	1.59 ± 0.18	1.75 ± 0.18	1.61 ± 0.20	1.47 ± 0.26	1.48 ± 0.50	1.52 ± 0.33	1.42 ± 0.14	1.30 ± 0.13	136.45 ± 12.43
Relative with the VHL patients										
First degree relatives	1.44 ± 0.30	1.63 ± 0.17	1.76 ± 0.08	1.66 ± 0.21	1.51 ± 0.31	1.47 ± 0.42	1.56 ± 0.46	1.48 ± 0.23	1.30 ± 0.14	139.21 ± 15.74
Others	1.41 ± 0.23	1.56 ± 0.15	1.74 ± 0.23	1.60 ± 0.17	1.46 ± 0.22	1.54 ± 0.39	1.49 ± 0.23	1.41 ± 0.12	1.29 ± 0.12	134.28 ± 8.42

Table 4. Compared SCL-90 scores of VHL family members to Chinese norm (Jin *et al.*, 1986).

Factors	VHL family (n = 61)	Norm (n = 1.388)	t	p
Total scores	136.62 ± 12.58	129.96 ± 38.76	4.136	<0.001*
Somatisation	1.42 ± 0.27	1.37 ± 0.48	1.606	0.114
Compulsion	1.60 ± 0.17	1.62 ± 0.58	-1.167	0.248
Interpersonal sensitivity	1.75 ± 0.17	1.65 ± 0.61	4.359	<0.001*
Depression	1.61 ± 0.19	1.50 ± 0.59	5.623	<0.001*
Anxiety	1.48 ± 0.26	1.39 ± 0.43	2.718	0.009*
Hostility	1.51 ± 0.41	1.46 ± 0.55	0.875	0.385
Panic	1.52 ± 0.35	1.23 ± 0.41	6.436	<0.001*
Bigoted	1.44 ± 0.18	1.43 ± 0.57	0.541	0.591
Psychosis	1.30 ± 0.13	1.29 ± 0.42	0.312	0.756

*A p value of < 0.05 was considered statistically significant.

Table 5. Stepwise regression analysis on the relationship between psychiatric symptoms and sociodemographic variable.

Variable	Somatization	Compulsion	Interpersonal sensitivity	Depression	Anxiety	Hostility	Panic	Bigoted	Psychosis
Gender	0.111 (0.198)	-0.028 (0.414)	0.127 (0.165)	-0.005 (0.484)	-0.065 (0.308)	-0.001 (0.496)	-0.028 (0.415)	-0.122 (0.175)	0.092 (0.138)
Age	0.135 (0.149)	0.040 (0.381)	0.001 (0.198)	-0.047 (0.360)	0.307 (0.008)*	0.174 (0.090)	0.201 (0.060)	0.084 (0.259)	0.058 (0.328)
Marital status	-0.006 (0.482)	-0.063 (0.315)	-0.132 (0.155)	0.119 (0.181)	0.201 (0.060)	0.271 (0.017)*	0.084 (0.261)	0.050 (0.352)	0.065 (0.308)
Occupation	-0.119 (0.181)	-0.147 (0.129)	-0.150 (0.124)	-0.208 (0.054)	0.020 (0.439)	0.026 (0.422)	-0.106 (0.209)	-0.160 (0.109)	-0.017 (0.447)
Education	-0.032 (0.404)	0.172 (0.093)	0.138 (0.318)	-0.022 (0.434)	0.274 (0.016)	0.108 (0.203)	0.091 (0.242)	0.162 (0.106)	-0.057 (0.331)
Being VHL patients	-0.070 (0.296)	0.208 (0.054)	-0.106 (0.209)	-0.166 (0.101)	0.099 (0.224)	-0.062 (0.318)	0.079 (0.272)	0.217 (0.046)*	0.016 (0.451)
Relative with the patients	-0.142 (0.138)	0.247 (0.028)	0.169 (0.097)	-0.244 (0.029)*	-0.110 (0.200)	-0.230 (0.037)*	0.001 (0.497)	0.149 (0.126)	0.145 (0.132)

*A p value of < 0.05 was considered statistically significant.

the difference in prevalence rates might be that the studied family was from an economic underdeveloped area in a developing country, with higher prevalence of mental health problems compared with developed countries. The third explanation was that many of the participants in our study were from rural low culture areas with low household income, which was established risk factor for psychiatric morbidity. The factors, including gender, marital status, age, being patients, occupation, education, and closer relationship with the patients, were associated with the mental illness in the VHL family.

The patient with cancer is fearful of death and full of anxiety about the future, which always indicates severer symptoms, longer recovery times, poorer outcomes and greater use of healthcare resources [24] [25]. Severe mental illness put patients at a higher risk of suicide and may produce a desire for hastened death [26] [27]. Simultaneously, when one patient is diagnosed, the family needs to take care of the patient as well as to master their own life situation during this period. As a result of this stress, they are sometimes more vulnerable to depression and anxiety, which has been proved to be associated with women, young in age, married, employed, lacking of support, poorer QOL and so on [28]-[31]. Especially in this VHL family, the diagnosed patients were suffered from the abundant payment and unknown prognosis while the other members were under great pressure to be diagnosed of the disease before gene detection. The disease afflicted every person in the family. So, when

we focused on the effect of the surgical or medical treatment on the VHL patients, we should also pay attention to the psychological status of them. To get a better therapeutic effect on them, the clinicians should get a deeper understanding the psychological status. Meanwhile, the clinicians should also investigate the psychological status of the family members and give necessary psychological therapy to offer stronger support for the VHL patients.

5. Conclusion

In conclusion, the study suggested that depression and anxiety were the most prevalent psychiatric symptoms in the VHL family. The limitations of this study must be acknowledged. Firstly, it must be admitted that the study protocol did not include any structured psychiatric diagnostic interviews, and the existence of the patients' psychiatric symptoms was based on self-administered questionnaires. Second, no information was available concerning the patients' history of psychiatric disorders, psychiatric treatment and family history of psychiatric diseases. The findings do reveal that psychiatric symptoms accompanied certain sociodemographic and clinical characteristics that were associated with susceptibility to mental disease. An understanding of these factors will be helpful in providing appropriate mental health services to a VHL family.

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Conflict of Interest

The authors have no conflicts of interest to disclose.

Human and Animal Rights, and Informed Consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all patients for being included in the study.

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Abbreviations

VHL: Von Hippel-Lindau;
SAS: Self-Anxiety Rating Scale;
SDSL: Self-Rating Depression Scale;
SCL-90-R: The Revised Symptom Checklist.