Research on quality of life and medical accessibility for patients with rare diseases: evidence from Guangdong Province

Xinyi Li

Guangzhou Foreign Language School, China

Keywords: Rare diseases, ultra-rare diseases, patients, survival status.

Abstract: Objective: To investigate the survival status of patients with rare diseases in Guangdong Province, and to provide the basis for improving the survival status of patients with rare diseases and establishing the security system for patients with rare diseases. Methods: Snowball sampling was used to investigate patients by relying on the manufacturers of drugs for rare diseases and patient organizations. Questionnaires were distributed online and on site simultaneously. Results: A total of 240 patients were investigated, among which 221 were valid questionnaires, and the effective rate was 92.08%. There were 52 patients with multiple sclerosis and 169 patients with ultra-rare diseases. The age of the patients was mainly 14 years old or below, 20.4% of the patients were treated according to the indications, and the misdiagnosis rate was 54.3%. Patients with rare diseases scored 2.33±0.94, 1.95±0.89, 9.71±2.71, 12.19±3.02, 12.11±3.59 and 10.86±2.67, respectively, in terms of their physical, psychological, social and environmental dimensions. The quality of life of patients with rare diseases was related to educational level and annual family income. Conclusion: The problems faced by patients with rare diseases mainly include heavy medical burden, poor access to drugs, high misdiagnosis rate and low quality of life. Among them, patients with ultra-rare diseases face more serious problems. In order to improve the survival status of patients with rare diseases, it is suggested to perfect the medical collaboration network for rare diseases, establish and perfect the gene screening procedure for rare diseases, and build a multi-level medical insurance model for rare diseases. Improve the management mechanism of the organization of patients with rare diseases and give play to its functions of communication and assistance.

1. Introduction

“Rare disease” is a general term for a large number of different diseases scattered throughout the disease system [1]. The definition of rare diseases varies by region and country. The standard for defining "rare disease" in the European Union is the prevalence rate less than 1/2000, and that in Taiwan is less than 1/10000. In other countries, the definition is based on the number of patients in the whole country. For example, in Japan, diseases with less than 50,000 patients are considered as "rare diseases" [2]. In May 2018, rare diseases were defined in China in the form of the First Batch of Catalogue of Rare Diseases, which provides effective reference and basis for the related work of rare diseases [3].

Compared with common diseases, rare diseases mainly have four characteristics:

1. High misdiagnosis rate; Taking rare disease patients in Hunan Province as an example, 34% of rare disease patients have experienced misdiagnosis [4]. Rare diseases are characterized by a wide variety of diseases, different clinical manifestations, a small number of patients with each disease and relatively fewer doctors. These factors lead to the wide variation and high misdiagnosis rate of rare diseases.

2. Expensive cost. Family catastrophic expenditure is defined as health expenditure exceeding 40% of family annual income [5]. As the treatment system for rare diseases is not perfect, most rare diseases are not included in medical insurance, and families of patients with rare diseases need to bear a large amount of health expenditure, and most families of patients with rare diseases are experiencing catastrophic health expenditure. A survey of 982 patients with rare diseases was conducted in 2018, and the results showed that only 1.3% of patients with rare diseases had annual treatment costs within

the range of their family annual income, and even 0.8% of patients had annual treatment costs that were more than 10,000 times of their family annual income [6].

3. Lack and low accessibility of medicines; Rare disease drugs are also known as "orphan drugs" because there are fewer rare disease patients and fewer drugs to treat them. According to the research report on medical insurance of high-value drugs for rare diseases in China, there are only 57 drugs for rare diseases in China, among which 34 drugs are used according to the indications, and only 22 drugs for rare diseases are included in the national medical insurance [7]. In China, only 5% of rare disease drugs are available [8].

4. Insufficient medical security; China's current medical security system is mainly aimed at common diseases, and the level and scope of insurance for rare diseases are low. Many rare diseases are not treatable, and those that are are expensive to treat. Until now, only some local governments of China have developed a small number of medical and social security systems for rare diseases, but they are basically in the trial stage and are not mature.

At present, some local governments have provided assistance for rare diseases, but the amount of medicine and funds is far from enough to sustain basic living needs. For example, Shaoguan Civil Affairs Bureau of Guangdong Province assisted three Gaucher disease patients in Shaoguan City in 2017, guaranteeing that each of them could receive one injection of imidase treatment every month, with a total of 276,000 yuan a year [9]. However, the treatment for gaucher disease patients is far from sufficient. The average drug dose for a Gaucher disease patient is 45U/kg ~ 60U/kg, once every two weeks [10]. Qingdao in started on January 1, 2021: Gaucher disease, Pompeii's disease, and ¥20000 to ¥400000 of the following a part to pay 80% of the ¥400000 yuan (including) above a part to pay 85% of the highest pay ¥900000 per person a medical year [11]. But Pompeii's disease treatment for global unified price 5645 yuan / 50 mg, dosage of 20 mg/kg, and need lifelong medication [12]. Adult spends two or ten thousand yuan [12]. In addition to the cost of health care, rare disease family still need to bear the cost of expensive treatment. In March 2020, Foshan City provided up to 300,000 RMB per year for 121 rare diseases in the "First Batch of Catalogue of Rare Diseases" [13]. However, on the basis of the annual treatment cost of millions of ultra-rare diseases, these policies still fail to fundamentally solve the plight of patients with rare diseases.

It can be seen that although some local governments have issued relevant laws and regulations, due to the limited funds and resources, the number of patients assisted is small, the effectiveness is low and the process is slow. Patients with rare diseases still face problems related to high treatment costs, low access to drugs and few policies, especially those with ultra-rare diseases. Tackling rare diseases is a vital step in improving people's health.

2. Method

The respondents of this study were patients with rare diseases in Guangdong Province. Due to the small number of respondents, snowball sampling was adopted in this study, and patients were investigated by relying on pharmaceutical manufacturers for rare diseases and patient organizations for rare diseases. The questionnaire was distributed online and on site at the same time. If the patients did not have the ability to answer independently, the family members of the patients would answer for them. The respondents or their guardians all gave informed consent and the survey was carried out anonymously. A total of 240 patients were investigated, among which 218 were valid questionnaires, and the effective rate was 90.83%.

The questionnaire contents include:

1. Basic information: rare disease patient's disease, onset age, education level, medical insurance, occupation, source of income, family composition, etc.;

2. Accessibility of patients' medication status: medical insurance status, dosage, purchase place, time and ability of patients with rare diseases;

3. Patients' medical information: the time of diagnosis of rare disease and the hospital, etc;

4. Medical burden of patients: annual family income, outpatient service, hospitalization, medication, medical equipment, nutrition and medical compensation expenses of patients;

5. Quality of life of patients: We used WHOQOL-BREF scale to analyze the quality of life of patients. The summary table contains at least one question of each aspect related to quality of life, and has good internal consistency, good discriminative validity and good structural validity. The score of WHOQOL-BREF scale mainly measures four fields: physiological, psychological, social relations and environmental relations, and finally includes the overall health status and quality of life of the respondents. This scale tests the quality of life of the respondents in the past two weeks, and is used to evaluate the living conditions related to their goals, expectations, standards and concerns within the scope of the culture and value system in which the respondents live. In clinical practice, the measurement of quality of life can help physicians to judge and analyze the severity of different aspects of patients' diseases and determine treatment methods [14].

The scores of each field and aspect in the WHOQOL scale are all positive, that is, the higher the score, the better the quality of life. [14]

Data input and proofreading were performed by using office software EpiData3.1 and Excel. SPSS24.0 was used for statistical analysis of the collected survey data. Data analysis was divided into three stages. (1) Descriptive analysis: the basic personal information of patients with rare diseases was statistically described, the measurement data was described in the form of "mean standard deviation", and the frequency and constituent ratio were used for classified data. (2) Statistical inference: 2 test was used to compare the drug use, medical treatment and medical burden of rare disease patients with different basic conditions; the quality of life scores of patients with rare diseases were compared by t-test or analysis of variance. All the above tests were conducted by bilateral test, and the test efficiency $\alpha=0.05$. Multiple linear regression was used to study the factors affecting the quality of life of patients with rare diseases. The variable selection method was as follows: Stepwise, the entry level α-in =0.05, the exclusion standard α-out =0.10.

3. Result

3.1 Basic situation

A total of 240 patients were investigated in this study, among which 221 were valid samples and the sample effective rate was 92.1%, including 52 patients with multiple sclerosis, 9 with Fabre disease, 19 with gaucher disease, 39 with spinal muscular atrophy and 8 with Pompeii disease. Among them, 212 (54.8%) are males and 100 (45.2%) are females. 0 ~ 14,15 ~ 24,25 ~ 34 and above 35 years old population accounted for 55.2%, 15.8%, 18.6%, 10.4% respectively. 146 persons (66.1%) were registered as urban residents and 75 persons (33.9%) were registered as rural residents. Unmarried population accounted for 81.0%, married population accounted for 16.3%, divorced or separated, widowed 6.0%. The majority of students had primary school education (56.1%), followed by junior college or bachelor's degree (10.4%), junior middle school (9.0%) and senior high school (8.6%). The majority of the people were urban workers (57.0%) and urban and rural residents (22.2%) with no health insurance (11.8%) or other conditions (9.0%). The proportion of people with annual household income less than 60,000 yuan, 60,000 ~ 120,000 yuan, 120,000 ~ 180,000 yuan and more than 180,000 yuan were 43.0%, 35.7%, 10.9% and 10.4% respectively. There were 117 persons who were unemployed or not in school (52.9%), 45 who were students (20.4%) and 59 who were employed (26.7%). The majority of people's expenditure comes from their parents' income (67.0%), followed by their own income (25.3%). Less people's expenditure comes from outside support, such as relatives and friends, government security, social assistance and so on (7.7%).

Table 1. Basic information of patients with rare diseases in GuangDong province.

Basic situation	N	%
The name of the disease		
Multiple sclerosis	23.5	23.5
Mine method disease	4.1	4.1
Gaucher disease	8.6	8.6
Spinal muscular atrophy	59.3	59.3
Glycogen accumulation disease	3.6	3.6
Mucopolysaccharide storage syndrome	0.9	0.9
gender		
female	45.2	45.2
male	54.8	54.8
age		
Age 14 and below	55.2	55.2
15 to 24 years old	15.8	15.8
25 to 34 years old	18.6	18.6
More than 35	10.4	10.4
The household registration		
Urban registered permanent residence	66.1	66.1
Rural registered permanent residence	33.9	33.9
Marital status		
unmarried	81	81
married	16.3	16.3
Divorced/separated/widowed	2.7	2.7
Level of education		
Primary school and below	56.1	56.1
Junior high school	9	9
High school/technical secondary school	8.6	8.6
College/bachelor degree or above	26.2	26.2
Health care type		
Without health insurance	11.8	11.8
For urban workers	57	57
Urban and rural residents	22.2	22.2
other	9	9
Annual household income		
Less than 60,000 Yuan	43	43
6-120000 yuan	35.7	35.7
12-180000 yuan	10.9	10.9
More than 180,000 Yuan	10.4	10.4
professional		
Unemployed/not in school	52.9	52.9
students	20.4	20.4
on-the-job	26.7	26.7
Source of overhead		
One's own income	25.3	25.3
Parental income	67	67
The outside support	7.7	7.7

3.2 Drug

Among the total number of people surveyed, 45 people were given adequate medication according to the indications (20.4%), 24 people were given adequate medication according to the indications but

not enough (10.9%), 17 people were only given symptomatic treatment (7.7%), and more than half of them were not given medication treatment (61.1%).

Table 2. Dosage treatment for the patients with rare diseases in GuangDong province.

Drug	N	%
Use adequate dosage as indicated	45	20.4
Use as indicated but not in sufficient quantities	24	10.9
Symptomatic treatment only	17	7.7
No medication.	135	61.1

3.3 Medical insurance reimbursement and drug accessibility

Among the 86 rare disease patients who were able to use drugs, only 5 patients could be reimbursed for all the drugs (5.8%), 41 patients could be reimbursed for part of the drugs (47.7%), and 40 patients could not be reimbursed for all the drugs (46.5%). The main way for patients to purchase drugs was to go to the hospital to prescribe drugs, accounting for 70.9%. The second most common is buying yourself at a pharmacy, accounting for 18.6 percent. Fewer, about 9.3 per cent, bought drugs in other ways. Only 1.2 per cent of patients received their medicines as gifts from companies or others. The duration of drug purchase is 30 minutes or less, 0.5 ~ 1 hour, 1 ~ 1.5 hours, 1. Those who spent more than 5 hours accounted for 7.0%, 10.5%, 32.6% and 50.0% respectively. More than half of them thought the affordability of drugs was very poor (69.8%), followed by 22.1% thought the affordability of drugs was poor, 7% thought the affordability of drugs was average, and only 1.2% thought the affordability of drugs was good. 22.1% of people felt that drugs were difficult to obtain, 11.6% felt that drugs were difficult to afford, 26% felt that drugs were generally difficult to obtain, 28% felt that drugs were easy to afford and only 3.5% felt that drugs were easy to afford.

Table 3. Medical insurance reimbursement and drug accessibility patients with rare diseases in GuangDong province.

Subject	N	%
Whether medicines are reimbursed or not		
It will all be reimbursed	5	5.8
Partial reimbursement only	41	47.7
Nothing can be reimbursed.	40	46.5
Buy medicine place		
Drug store	16	18.6
Hospitals	61	70.9
Presented	1	1.2
other	8	9.3
Buy medicine length		
30 minutes and less	6	7
0.5 1 hour	9	10.5
1-1.5 hours	28	32.6
Over 1.5 hours	43	50
Affordability of medicines		
Is very poor	60	69.8
poor	19	22.1
general	6	7
good	1	1.2
Availability of medicines		
It's hard to afford	19	22.1
Hard to burden	10	11.6
general	26	30.2
Better burden	28	32.6

3.4 Reasons for not using drugs in patients

For patients who did not use drugs according to their indications, the main reasons were the high price of drugs (95.4%) and the drugs were not included in the medical insurance (80.3%). The second reason was the limited therapeutic effect of drugs, which could not completely cure the disease (29.6%) and poor availability of drugs (10.5%). Not listing therapeutic drugs in China, inaccurate positioning of clinical treatment of drugs, lack of knowledge and training of doctors and other reasons accounted for 14%, 3.3%, 7.9% and 9.9%, respectively.

Table 4. Reasons for not using drugs in patients with rare diseases in GuangDong province (multiple choice).

Reasons for not using drugs	N	%
The price of medicine is too high	145	95.4
It's hard to get medicine	16	10.5
Therapeutic drugs are not on the domestic market	14	9.2
Drugs are not covered by insurance	122	80.3
The positioning of drug clinical treatment is not accurate	5	3.3
Doctors lack the knowledge and training	12	7.9
The therapeutic effect of drugs is limited and the disease cannot be completely cured	45	29.6
other	15	9.9

3.5 Treatment satisfaction

Of the total number of people surveyed, 120 were misdiagnosed prior to diagnosis (54.3%) and 101 were not misdiagnosed (45.7%). The diagnosis institutions were mainly provincial hospitals, accounting for 54.3%; 42.5% of the patients were diagnosed in municipal hospitals. Other cases accounted for 3.2%. Most of the patients were generally satisfied (31.2%) or very unsatisfied (28.1%) or unsatisfied (24.0%) with the treatment effect; 14.9% of the patients were satisfied with the treatment, while few were very satisfied with the treatment effect (1.8%).

Table 5. Misdiagnosis, treatment satisfaction for patients with rare diseases in GuangDong province.

subject	N	%
Whether the misdiagnosis		
misdiagnosis	120	54.3
There is no misdiagnosis	101	45.7
Diagnosis of institutions		
Provincial hospital	120	54.3
The municipal hospital	94	42.5
other	7	3.2
Treatment satisfaction		
Is not satisfied	62	28.1
Not satisfied with	53	24
general	69	31.2
satisfied	33	14.9
Very satisfied with	4	1.8

3.6 Misdiagnosis

Nearly half of them took less than one year (40.0%) to be misdiagnosed, while 23.3 percent took more than five years. The misdiagnosis duration of 1 to 2 years, 2 to 3 years, 3 to 4 years and 4 to 5 years accounted for 16.7%, 8.3%, 5.8% and 5.8%, respectively.

Table 6. The misdiagnosis duration for patients with rare diseases in GuangDong province.

The misdiagnosis duration	N	%
Less than 1 year	48	40
1 to 2 years	20	16.7
2 to 3 years	10	8.3
3-4 years	7	5.8
Four to five years	7	5.8
More than 5 years	28	23.3

3.7 Annual treatment cost

Of the rare disease patients surveyed as a whole, 15.8%, 22.2%, 13.6%, 30.3%, 11.3% and 6.8% of the population whose annual treatment cost was less than 20,000 yuan, 20,000 to 50,000 yuan, 50,000 to 100,000 yuan, 100,000 to 250,000 yuan, 250,000 to 500,000 yuan and more than 500,000 yuan, respectively .

Table 7. Annual treatment cost for patients with rare diseases in GuangDong province.

Annual treatment cost	N	%
≤20000	35	15.8
20000-50000	49	22.2
50000-100000	30	13.6
100000-250000	67	30.3
250000-500000	25	11.3
≥500,000	15	6.8

3.8 Quality of life score comparison

We compared the quality of life of the rare disease patients we investigated with the quality of life of the national normal disease group. The total quality of life score of patients with rare diseases was 2.33±0.94, and the total health status score was1.95±0.89.The scores of physical, psychological, social relationship and environment were9.71±2.71, 12.19±3.02, 12.11±3.59 and 10.86±2.67, respectively.

Table 8. Quality of life score for patients with rare diseases in GuangDong province.

field	Patients with rare diseases	National Model Disease Group	t	*P*
Overall quality of life (1-5)	2.33±0.94	3.38±0.69	-16.752	<0.001*
General Health (1-5)	1.95±0.89	3.27±0.80	-21.889	<0.001*
Physiology (4-20)	9.71±2.71	14.10±2.62	-24.123	<0.001*
Psychology (4-20)	12.19±3.02	13.89±1.92	-8.836	<0.001*
Social Areas (4-20)	12.11±3.59	14.18±2.00	-8.587	<0.001*
Environment (4-20)	10.86±2.67	12.51±2.28	-9.91	<0.001*

Note: * means P<0.05; # represents data from "Quality of Life and Influencing Factors Analysis of Chinese Adults".

3.9 Factors influencing the quality of life

There is a positive correlation between educational level, annual family income and the total quality of life, which is, the higher the educational level and annual family income, the higher the total quality of life. There was a negative correlation between super rare diseases and total health status, that is, the total health status score of patients with super rare diseases was lower than that of patients with multiple sclerosis. There is a positive correlation between the family annual income and the total health status, the higher the family annual income, the higher the total health status score.

The score of super rare disease was negatively correlated with physical, psychological, social and environmental fields, and the score of super rare disease patients in physical, psychological, social and environmental fields was lower than multiple sclerosis. The family annual income of patients with ultra-rare diseases is positively correlated with the physical, psychological, social and environmental fields. The higher the family annual income, the higher the scores in the physical, psychological, social and environmental fields.

Table 9. Factors influencing the quality of life for patients with rare diseases in GuangDong province.

field	factors	b	Std. e	t	*P*
Overall quality of life	Constant term	1.557	0.162	9.620	<0.001*
	Level of education	0.176	0.046	3.815	<0.001*
	Annual household income	0.174	0.062	2.815	0.005*
	Student [1]	0.393	0.150	2.617	0.009*
General health	Constant term	1.486	0.137	7.545	<0.001*
	Super rare diseases	-0.455	0.149	-3.050	0.003*
	Annual household income	0.148	0.058	2.532	0.012*
	In [1]	0.394	0.148	2.654	0.009*
	Student [1]	0.298	0.147	2.02	0.045*
Physical	Constant term	11.563	0.814	14.211	<0.001*
	Student [1]	1.901	0.391	4.856	<0.001*
	In [1]	1.943	0.394	4.931	<0.001*
	Super rare diseases	-2.112	0.396	-5.335	<0.001*
	Annual household income	0.511	0.155	3.303	0.001*
psychological	Constant term	12.468	0.895	13.933	<0.001*
	Annual household income	0.662	0.201	3.299	0.001*
	Student [1]	1.561	0.488	3.198	0.002*
	Super rare diseases	-1.045	0.46	-2.272	0.024*
social	Constant term	13.946	1.077	12.954	<0.001*
	Super rare diseases	-1.792	0.549	-3.262	0.001*
	Annual household income	0.702	0.24	2.924	0.004*
environmental	Constant term	12.877	0.755	17.047	<0.001*
	Super rare diseases	-2.037	0.388	-5.244	<0.001*
	Annual household income	0.735	0.169	4.339	<0.001*
	Student [1]	0.947	0.412	2.298	0.023*

Note: * means P<0.05; 1 refers to patients who are unemployed or not in school as a reference.

4. Discussion

According to the age group of all the patients with rare diseases investigated, it can be found that more than half of the patients are 14 years old or below, which makes most of the patients are unmarried and the education level is concentrated in primary school or below. Only a few patients can recover and survive to middle age. Therefore, it is necessary to establish a medical security system for

patients with rare diseases, so as to protect the life and health rights and interests of patients, especially children and teenagers.

Rare disease drug use rate is low, according to the indication of sufficient drug use of the population is less. Only a very small percentage of the patients surveyed who were able to take drugs for rare diseases were reimbursed for all of their drugs, while the rest were reimbursed for none or only part of their drugs. This shows that "there is no medicine to cure and no medicine to insure" is a major livelihood issue facing patients with rare diseases today. The lack of relevant drug treatment may greatly accelerate the deterioration of the disease and reduce the quality of life of patients. The national government should pay attention to the issue of medical insurance for rare diseases, increase the accessibility of medicines for patients, and solve a major problem faced by patients with rare diseases and their families. At the same time, the government should also pay attention to the introduction of drugs for rare diseases and encourage the research and development of related drugs.

Of the 221 surveyed patients diagnosed, more than half were misdiagnosed before diagnosis and more than half were diagnosed in provincial hospitals, which may be because doctors in hospitals lack the knowledge of rare diseases and cannot accurately identify the diseases of the patients. Misdiagnosis slows down the treatment process of patients, makes patients miss the best treatment period, and reduces the cure rate. The training of doctors should pay attention to the study of knowledge related to rare diseases, increase the recognition of rare diseases, and quickly diagnose patients with rare diseases.

Most patients with rare diseases spend 100,000 to 250,000 yuan a year on treatment, and there are five rare diseases that cost more than 1 million yuan a year, but nearly half of the families' annual income is less than 60,000 yuan. The high cost of rare diseases and the affordability of patients' families may influence the treatment outcome. The inability to afford treatment can prevent patients with rare diseases from receiving the most effective treatment and reduce survival rates. Therefore, the government should improve the medical security policy and reduce the cost of treatment for patients.

The quality of life analysis; The comparison of the QOL of rare disease patients and the QOL scores of the national normal disease group showed statistical significance in the total QOL, total health status, physiological, psychological, social and environmental fields. Patients with rare diseases scored well below the national norm on each measure. According to the results of multiple linear regression, the higher the family annual income of patients with rare diseases, the higher their quality of life scores. This may be related to the fact that patients with higher family income have access to more medical resources and better treatment measures. This suggests that we should encourage drug research and development and introduction, improve the quantity and quality of medical services for patients with rare diseases, so that more patients can have access to more effective treatment measures, and then improve the quality of life of patients with rare diseases.

In conclusion, the problems faced by patients with rare diseases mainly include the following aspects: 1. Heavy medical burden; 2. 2. Poor accessibility of drugs; 3. High misdiagnosis rate; 4. Low quality of life.

To solve the problem of rare diseases in China, it is necessary to start from the national top-level design, improve medical services, ensure drug supply, build a multi-payment system, and build a comprehensive social support system.

In order to solve the difficulty of diagnosis of patients with rare diseases, the state and government levels, as well as the national health authorities, should conduct standardized management of the hierarchical diagnosis and treatment system of patients with rare diseases, such as registration, diagnosis and treatment, referral and follow-up. In view of the difficulties in diagnosis and treatment and diagnosis of patients, the state should strengthen the universal education of rare diseases and standardize the training of disease diagnosis and treatment for clinicians [15].

Collaboration, the hospital is responsible for the general rare disease diagnosis and management for a long time, will be rare difficult critically ill patient referral to take the lead in the hospital in time, and according to take the lead in the hospital for follow-up treatment to do a good job in the management of patients, give full play to radiating and driving play high-quality medical resources, improve the ability of comprehensive diagnosis and rare diseases, reduce the disease, a rare disease To provide assistance for the very early diagnosis of patients with rare diseases. Therefore, the country

should strengthen the supervision and investment of gene testing institutions, and accelerate the research and development and application of gene testing institutions. The relevant government departments should establish a national unified testing standard to ensure testing standards and quality, and improve the accuracy of genetic testing for patients with rare diseases. Doctors should also participate in the genetic testing of rare diseases, so as to distinguish the genetic differences between common diseases and rare diseases and reduce the misdiagnosis rate.

At the same time, the government should also actively solve the problem of medical insurance for patients with rare diseases. Under the existing framework of basic medical security, the decision-making breakthrough of entering high-value drugs for rare diseases into the national medical insurance directory is realized, so that the basic medical security takes the lead in playing its role and driving the multi-level security. While bringing drugs for rare diseases into the scope of government guarantee as far as possible, we should integrate the market, society and other resources to share the burden, so as to build a real multi-level drug guarantee system for rare diseases, relieve the pressure on patients to pay for treatment, and improve the accessibility of drugs, especially high-value drugs.

In view of the problem of medical insurance, in recent years, the State Administration of Medical Insurance has attached great importance to the complementary role of commercial health insurance in basic medical insurance and encouraged the development of commercial security products. Commercial supplementary insurance has sprung up and played an increasingly important role in the protection of rare diseases. For example, Guangzhou introduced "Suisaikang" commercial supplementary insurance in 2021. Patients can participate in the insurance with diseases, and the maximum insurance of drugs outside the medical insurance list can reach 1 million yuan/year, which plays a very necessary supplementary guarantee role for rare diseases with small probability and high economic burden and high-value rare diseases drugs.

In addition, improving the awareness of the whole society on rare diseases and expanding the social influence of rare diseases are also of great significance to promoting the introduction of policies related to rare diseases and improving the living status of patients with rare diseases. The organization of patients with rare diseases is better able to undertake this responsibility. Rare disease patients' organizations are generally spontaneously formed by patients with rare diseases or their families, playing an important role in various links such as publicity and education, scientific research and clinical practice, drug development, and policy advocacy [16]. At present, China has established some influential public welfare patient advocacy organizations that focus on the rare disease industry in China and continue to promote the positive development of the rare disease industry in China. For example, the "Code Center for Rare Diseases" has established an organization for patients with rare diseases since 2014, and by 2020 nearly 40 communities for patients with rare diseases have hatched and established patient organizations [16]. However, the popularity of rare diseases in China is lower than that in foreign countries, and many people have never heard of or are not aware of "rare diseases".

5. Conclusion

The study mainly discussed the survival status of patients with rare diseases in Guangdong Province, and found that patients with rare diseases are mainly faced with heavy medical burden, poor drug access, high misdiagnosis rate and low quality of life, and the survival status of patients with ultra-rare diseases is more difficult. And the level of family annual income and patients' quality of life score was positively correlated.

In order to improve the survival status of patients with rare diseases, it is suggested to perfect the medical collaboration network for rare diseases, establish and perfect the gene screening procedure for rare diseases, and build a multi-level medical insurance model for rare diseases. Government and the medical institution also need to improve the management mechanism of the organization of patients with rare diseases and give play to its functions of communication and assistance.

In this study, patients with rare diseases in Guangdong Province were investigated. Due to the lack of access to all patients with rare diseases in Guangdong Province, the proportion of patients under investigation for each rare disease is different and the group age is different, which may reduce the

representativeness of patients with rare diseases under investigation and the representativeness of the sample. In addition, this survey did not carry out in-depth investigation on patients' pathological, physiological, psychological, social support and other conditions, and so the research on the influencing factors of patients' quality of life needs to be further in-depth.

Therefore, we suggest that follow-up surveys can increase the number of patients with rare diseases and ensure that each disease and population are included in the sample to increase the representativeness of the sample. At the same time, the influencing factors of patients' quality of life need to be further studied, and the improvement of patients' survival conditions before and after medical security measures need to be compared.

References

[1] Jie Ding, Ling Wang. Report of rare diseases in China. 1st. China: China Medical Publishing House, 2018.

[2] People's Daily - People's Health Network: A comprehensive report on rare diseases in China. Web Rare Diseases in China. [Online] Available from:

[3] http://www.raredisease.cn/index!index.action [Accessed 24 July 2018].

[4] Rufang Huang, Wenbin Shao: China Rare Diseases Medical Security City Report 2020. Web Rare Diseases in China. [Online] Available from: http://www.raredisease.cn/index!index.action [Accessed 31 May 2020].

[5] Rufang Huang. Health and life path and disease burden survey on rare disease patients in HUNAN province 2020. 1st. China: Chinese Organization for Rare Disorders, 2020.

[6] Ke Xu, David B Evans, Kei Kawabata, Riadh Zeramdini, Jan Klavus, Christopher J L Murray. Household catastrophic health expenditure: a multicountry analysis. Web Thelancet. 2003 [Online] Available from: www.thelancet.com.

[7] Fu M, Guan X, Wei G, et al. Medical service utilisation, economic burden and health status of patients with rare diseases in China[J]. Journal of Chinese Pharmaceutical ences, 2018, 27(5):361-369.

[8] Wenbin Shao. Research report on medical insurance of high value drugs for rare diseases in China. 1st. China: IQVIA, 2020.

[9] JX Han, Y Y Cui. Epidemiological survey of rare diseases and demand analysis of orphan drugs in 7 provinces of China -- National Science and Technology Support Project during the 12th Five-Year Plan, Seminar on Theory and Practice of Medical Social Security for Rare Diseases, 2015,12.

[10] China. People's Government of Shaoguan City. Documents of Shaoguan Municipal People's Bureau Shaoguan: People's Government of Shaoguan City Office. 2017

[11] https://www.drugs.com/mtm/imiglucerase.html Imiglucerase

[12] Ling-ling Xiao. Bandao, 2020. [Online] Available from: http://www.bandao.cn/ [Access 31 Dec 2020].

[13] Li Qingtong Fan Yong. The Pafer, 2017. [Online] Available from: https: //www.thepaper.cn/ [Accessed 12 Oct 2017].

[14] Foshan Municipal People's Government. Notice of the Office of Foshan Municipal People's Government on Printing and Distributing Medical Relief Measures of Foshan City. Foshan. Office of Foshan People's Government [2020] No.7.2020.

[15] Yuantao Hao, Jiqian Fang. Introduction to the World Health Organization Quality of Life Measurement Scale and instructions for its use. Modern Rehabilitation, August 2000, Vol.4, No. 8

[16] Mingjun Wang. Hunan has established a cooperative network for the diagnosis and treatment of rare diseases, implementing relatively centralized diagnosis and treatment and two-way referral. Journal of Hunan. 2021

[17] Chinese Organization for Rare Disorders. 2021. [Online] Available from: http: // www.c ord.org.cn/.