Original Article

DOI: 10.5582/irdr.2025.01025

Characteristics of rare diseases cases: A summary analysis of hospitalized patients at a hospital in Western China from 2015 to 2023

Qi Wang[1,§], Liang Guo[2,§], Yan Yang[3,*], Jin He[1,*]

[1] Medical Affairs Department, Gansu Provincial Hospital, Lanzhou, Gansu, China;
[2] Department of General Surgery, Ward 6, The Second Hospital of Lanzhou University, Lanzhou, Gansu, China;
[3] Quality Control Department, Gansu Provincial Hospital, Lanzhou, Gansu, China.

SUMMARY: Rare diseases, characterized by low prevalence and high heterogeneity, impose a significant burden on patients and healthcare systems globally. Utilizing clinical data from the Hospital Information System's Patient Discharge Summaries (2015–2023), we analyzed all rare disease inpatient admissions at a major tertiary hospital in Western China. We examined demographic characteristics, classification of disease systems, medical costs, and readmission rate. Among 1086 inpatient admissions identified with rare diseases (mean age: 46.89 ± 18.99 years), diseases of the nervous system (39.69%), the blood and blood-forming organs and certain disorders involving the immune mechanism (18.32%), the musculoskeletal system and connective tissue (10.50%) constituted the top three disease system categories. The number of the top15 diseases accounted for 73.66% of the total number of patients. The top 3 diseases were POEMS syndrome (11.23%), optical neuromyelitis (10.22%), and Castleman disease (7.46%). Hospitalization costs were predominantly composed of diagnostic (ranged from 6.41% to 49.75%) and medication costs (ranged from 12.97% to 46.22%). The 10 highest readmission rates ranged from 42.86% to 95.90%. The rare diseases in this hospital had a large age span, diverse disease types, high hospitalization costs and large individual differences, which was representative to a certain extent, and can provide scientific basis for the diagnosis, treatment, and prevention of rare diseases in Gansu Province and even the northwest region of China.

Keywords: rare diseases, epidemiology, in-hospital analysis, Western China

1. Introduction

Rare diseases, or orphan diseases, are a broad category of illnesses with a very low prevalence (*1*). There are an estimated 6,000–7,000 rare diseases affecting approximately 300 million individuals, with approximately 80% being genetic in origin, and 50–75% being pediatric onset, 30% of whom have a lifespan of no more than 5 years (*2*). The global prevalence is estimated to be between 3.5% and 5.9%, impacting 263–446 million people (*3*). Due to variations in medical status, social security, and economic conditions, there is no unified global definition — prevalence thresholds range from 5 to 76 cases/100,000 people across regions, with a global average of 40 cases/100,000, and definitions by the World Health Organization (WHO), the European Union (EU), and the United States (US) differing accordingly, but not exceeding (*4-8*). Globally, 90% of rare diseases lack effective treatments, leading to delayed diagnosis, high misdiagnosis rates, and heavy burdens on patients and society, especially in developing countries (*9,10*). Despite variations in incidence rates across different countries and regions, rare diseases globally demonstrate an overall upward trend year by year, posing a serious threat to public health worldwide.

China is one of the most populous countries in the world, with a population of approximately 1.4 billion. There are about 20 million rare disease patients, with over 200,000 new patients diagnosed annually (*11*). A survey conducted in 93 hospitals across seven provinces revealed that a total of 405,589 patients with 952 types of rare diseases were registered as inpatients, among which at least half were congenital diseases (*12*). Over the past few years, the Chinese Government has paid greater attention to rare diseases and it has incorporated rare diseases in national health strategy and planning (*13-15*). It released the first (2018) and second (2023) national rare disease lists covering 121 and 87 diseases respectively, which established a national diagnosis and treatment network (expanded to 394 member hospitals

by February 2024), built the National Rare Diseases Registry System (NRDRS), and set up quality control centers and multidisciplinary expert teams (*16-20*). These measures are aimed at accelerating scientific and standardized development of rare diseases diagnosis and treatment, continuously improving public awareness, and exploring Chinese solutions for the overall goal of early detection, early diagnosis, treatment, management, medicine, and affordability of rare diseases.

Despite these efforts, significant challenges persist. "Poor drug accessibility" and "heavy economic burden" remain critical issues, particularly for rural patients (*21,22*). Diagnosis is extremely difficult due to the multidisciplinary nature of rare diseases: Some patients have to consult with 5 to 10 doctors, and it may take up to 30 years to receive an accurate diagnosis. Furthermore, many doctors have limited knowledge about rare diseases, leading to frequent misdiagnoses and missed diagnoses. Currently, approximately 44% of rare diseases in China are misdiagnosed, and 75% of rare diseases are treated in a non-standardized manner. According to findings of the "2020 Comprehensive Social Survey on Rare Diseases in China" conducted by the China Alliance for Rare Disorders, among the over 20,000 patients surveyed, 15.5% required 1 to 4 years to receive a correct diagnosis, while 5% needed between 5 and 20 years. The average time to diagnosis varied from 4 to 26 years. Moreover, 42% of patients had experienced misdiagnosis. This data objectively highlights significant challenges faced in diagnosis and treatment of rare diseases in China (*23*).

Due to the extremely low incidence of such diseases, the morbidity and prevalence of the population are difficult to estimate worldwide, leading to the real assessment of the status of disease diagnosis and treatment is difficult. Current epidemiological data on rare diseases in China are remarkably limited. China's Rare Disease Diagnosis and Treatment Guide, and data on the incidence/prevalence of 76 rare diseases (62.81%) were available for 121 rare diseases in China (*12*). This data scarcity is particularly acute in the less developed regions of Western China. Although rare disease researches have received increasing attention in China over the last few years, epidemiological and health economic studies remain exceptionally scarce in the underdeveloped regions of western China. Specifically, researches focusing on clinical profiles, inpatient burden, and healthcare utilization patterns of rare disease patients in Western Chinese hospitals are virtually absent. A regional distribution analysis of rare disease research in China revealed that the western region (12 provinces) contributed only 12.3% of the national research output, significantly lower than eastern (65.7%) and central (22.0%) regions (*24*). It even affects implementation of medical insurance policies and adjustment of drug catalogs for disease relief. Although countries around the world have explored establishment of rare disease registration systems and carried out related cohort studies, existing studies mainly focus on individual characteristics of rare diseases and drug use for rare diseases. In recent years, there have also been studies on the social psychological status of rare disease patients, but few studies on distribution characteristics of rare disease patients in hospitals, and there is a lack of reliable data support.

This study focuses on characteristics of inpatients with rare diseases in a tertiary hospital of a provincial capital in western China. As well as focus on analyzing the age and gender distribution of various diseases, epidemiological characteristics of the top fifteen disease types, and composition of hospitalization costs and readmission rates, *etc*. The objective of our study is to understand the current state of diagnosis and treatment for rare diseases in western China, thereby providing a scientific foundation for the prevention and control of rare diseases, the enhancement of diagnostic and treatment capabilities, and related policy research.

2. Materials and Methods

2.1. Data source

The Hospital Information System (HIS) is a computerized information system that integrates multiple functions, aiming to improve internal workflows and management efficiency in hospitals through information technology. The HIS system typically covers common modules of daily hospital operations such as outpatient management, inpatient management, pharmacy management, and others. All data in this study were extracted from the Patient Discharge Summary in the electronic medical record system of Gansu Provincial People's Hospital. The Patient Discharge Summary is a summary of the information generated during a patient's hospital stay, including diagnosis, surgery, procedures, blood transfusions, treatment outcomes, total hospital charges, fee categories, and payment methods.

China's first rare diseases list (121 diseases) was released on May 22, 2018 (*16*), followed by the second list (86 diseases) formulated according to the "Working Procedures for Drafting the List of Rare Diseases" and announced on September 18, 2023 (*17*). In order to gain a deeper understanding of the epidemiology, clinical diagnosis, and medical insurance status of rare diseases in China, National Health Commission of the People's Republic of China launched the registration and reporting system for case diagnosis and treatment information in 2019, and retrospectively reported cases diagnosed between January 1, 2015 and October 31, 2019 (*25,26*).

Therefore, we included hospitalization cases with discharge dates between January 2015 and December 2023. Using the tenth revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) for the 207 diseases listed in the

first and second batches of the national rare disease directories as matching criteria, we mapped the discharge diagnosis codes. Ultimately, 1,086 cases were included in this study and involved 11 categories of disease classification out of 22 disease classifications according to the 10th Revision of the International Classification of Diseases and Related Health Statistics, coded as shown in Additional file 1 (*https://www.irdrjournal.com/action/getSupplementalData.php?ID=273*).

This study received an ethics exemption from the Ethics Committee of Gansu Provincial Hospital. All patient identifiers were rigorously removed or anonymized during data extraction and processing prior to analysis.

2.2. Study variables

We extracted information from the Patient Discharge Summary. The information included the basic information of patients (hospitalization number, gender, age), diagnosis and treatment information (admission route, medical insurance payment type, major diagnosis name and code. Other diagnosis names and codes, length of stay, and cost information (total hospitalization cost, drug cost, nursing cost, diagnosis fee, medical service fee, *etc.*). We double-checked questionable information and incomplete data to ensure that case information is accurate. Medical records were excluded if any of the following conditions applied: *i*) length of stay (LOS) was zero, which was excluded to ensure analytical consistency, as they represent non-actionable admissions or data anomalies inconsistent with sustained inpatient care; *ii*) some key variables were missing or unclear, including age, sex, and primary diagnosis; *iii*) other cases with obvious logical errors and unmatched information. All research information was managed and analyzed by designated personnel to ensure patient information security.

2.3. Statistical analysis

Patients' age at admission was used for analysis of age distribution. The age group included 0–14 years, 15–44 years, 45–59 years, and 60~ years. The number of these four age groups were calculated.

Readmission rate is defined as the proportion of patients readmitted for the same or related condition within a specified time window (*e.g.*, 30 days, 90 days, or 1 year) relative to the total discharged population. In this study, given the low prevalence of rare disease patients, the time window is defined as any period within the study duration. Specifically: *i*) Numerator: The total number of repeat hospitalizations for each rare disease during the study period. For a given patient with ≥ 2 hospitalizations, each admission after the first is counted as a readmission (*e.g.*, 3 hospitalizations = 2 readmissions). *ii*) Denominator: The total number of hospitalizations (including initial admissions) for the corresponding rare disease during the study period.

Data organization and cleaning were performed in Microsoft Excel 2019. Statistical analysis was conducted using IBM SPSS Statistics v23 software (IBM Corporation, USA). Graphs were performed using GraphPad Prism (version 9.0.0). Continuous variables conforming to a normal distribution were described by the mean ± standard deviation (X ± SD), while those with a non-normal distribution were presented as median (P25–P75). Categorical variables were described as frequency and proportion. Student's *t*-test or Mann–Whitney *U* test was employed to compare continuous variables (for normally and non-normally distributed data, respectively), and Chi-square test or Fisher's exact test was used for categorical variables. Bonferroni correction for multiple comparisons was applied. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Demographic and clinical characteristics

By matching ICD-10 of the rare disease catalog, a total of 1086 hospitalized cases were finally included, of which 550 were males (50.64%) and 536 were females (49.36%), with a male-to-female ratio of 1.03:1. The age distribution ranged from 0 to 89 years old, with an average age of 46.89 ± 18.99 years old, including 46.57 ± 20.69 years old for males and 47.22 ± 17.09 years old for females. There was no significant difference in the mean age between males and females ($t = 0.570$, $p = 0.571$). These cases were mainly admitted and treated through the following three routes: outpatient admission in 925 cases (85.17%), emergency admission in 149 cases (13.72%), and transfer to other medical institutions in 12 cases (1.10%). The median length of stay for all patients was 7 days (4–11 days). From the type of medical insurance payment, there were 651 cases (59.94%) of self-funded medical insurance, 223 cases (20.53%) of basic medical insurance for urban and rural residents, 188 cases (17.31%) of commercial insurance, and 24 cases (2.22%) of provincial and municipal employee medical insurance. From the perspective of time distribution, the number of cases increased year by year from 2015 to 2020, decreased slightly from 2021 to 2022 and showed a significant rebound in 2023. Table 1 showed a full demographic description of the dataset.

3.2. The disease classification of cases

According to the ICD-10, 11 of 21 disease system classifications were involved in the study, covering 96 diseases, accounting for 46.38% (96/207) of the total number of diseases in China's rare disease catalog. The distribution of 1,086 cases according to the disease classification system is shown in Table 2. The distribution

of rare cases in each disease system is uneven, in order from the highest to the lowest proportion of covered cases: diseases of the nervous system (39.69%), diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (18.32%), diseases of the musculoskeletal system and connective tissue (10.50%), Neoplasms (8.56%), endocrine, nutritional and metabolic diseases (6.63%), eye and adnexa diseases (4.24%), circulatory system diseases (3.96%), respiratory system diseases (3.87%), congenital malformations, deformations, and chromosomal abnormalities (3.78%), skin and subcutaneous tissue diseases (0.37%), digestive system diseases (0.09%). Among them, the top three disease categories covering the number of disease types are neurological diseases (27 diseases), endocrine, nutritional, and metabolic diseases (17 diseases), and congenital malformations, deformations and chromosomal abnormalities (12 diseases). The Chi-square test was used to analyze the differential distribution of male and female patients in each disease system, and the results showed that the distribution was statistically different ($\chi^2 = 31.688$, $p < 0.01$).

Based on age group categorization, the study cases were stratified by admission year and accumulated according to disease classification. The results showed that there were differences in distribution of disease types of the cases in each age group. Distribution of cases across the four age groups is as follows: 0–14 years old (77/1086), 15–44 years old (340/1086), 45–59 years old (475/1086), 60~ years old (194/1086). In the < 15 years old age group, the top three were nervous system diseases (46.75%), blood and hematopoietic organ diseases and some diseases of immune mechanism (23.38%), endocrine, nutritional and metabolic diseases (6.49%). The top three diseases in the age group of 15–44 years old were nervous system diseases (34.41%), blood and hematopoietic organ diseases and some diseases of immune mechanism (18.53%), malignant tumor/benign tumor/benign and malignant tumor (17.94%). The top three diseases in the 45–59 age group were nervous system diseases (42.95%), blood and hematopoietic organ diseases and some diseases of immune mechanism (22.32%), musculoskeletal system and connective tissue diseases (13.26%). Diseases of the nervous system (38.14%), musculoskeletal system and connective tissue (18.56%), and respiratory system (9.79%) accounted for the top three diseases in the age group 60 and above.

Table 1. Demographic and clinical characteristics of hospitalized cases with rare diseases according to subgroups

Variable	No.	%
Gender		
Male	550	50.64
Female	536	49.36
Age		
0–14	77	7.09
15–44	340	31.31
45–59	475	43.74
60~	194	17.86
Admission route		
Outpatient referral	925	85.17
Emergency	149	13.72
Referral	12	1.10
Payment type		
Self-funded healthcare	651	59.94
Urban and Rural Resident Basic Medical Insurance	223	20.53
Commercial insurance	188	17.31
Provincial and Municipal Employee Medical Insurance	24	2.22
Year		
2015	31	2.85
2016	43	3.96
2017	69	6.35
2018	90	8.29
2019	113	10.41
2020	169	15.56
2021	167	15.38
2022	136	12.52
2023	268	24.68

Table 2. Distribution of 1,086 hospitalized cases according to the disease classification system

ICD-10 Code	Disease Classification	Diseases No.	Cases No.	%	χ^2=31.688		$p < 0.01$
					Male	Female	Gender Ratio
G00-G99	Diseases of the nervous system	27	431	39.68	217	214	1.01
D50-D89	Diseases of the blood and rming organs and certain disorders involving the immune mechanism	9	199	18.32	73	126	0.58
M00-M99	Diseases of the musculoskeletal system and connective tissue	7	114	10.50	64	50	1.28
C00-D48	Neoplasms	4	93	8.56	51	42	1.21
E00-E90	Endocrine,nutritional and metabolic diseases	17	72	6.63	50	22	2.27
H00-H59	Diseases of the eye and adnexa	1	46	4.24	23	23	1.00
I00-I99	Diseases of the circulatory system	4	43	3.96	21	22	0.95
J00-J99	Diseases of the respiratory system	2	42	3.87	23	19	1.21
Q00-Q99	Congenital malformations, deformations and chromosomal abnormalities	12	41	3.78	25	16	1.56
L00-L99	Diseases of the skin and subcutaneous tissue	2	4	0.37	2	2	1.00
K00-K93	Diseases of the digestive system	1	1	0.09	1	0	/

It can be seen that neurological diseases are the main types of rare diseases in all age groups, but with age, musculoskeletal system and connective tissue diseases and respiratory diseases gradually become the main types of diseases. The results are shown in Figure 1.

3.3. Analysis of the top fifteen disease categories

The study cases were further analyzed according to the types of discharge diagnoses. The top fifteen disease categories are polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, skin changes (POEMS) syndrome (11.23%), optic neuromyelitis (10.22%), Castleman disease (7.46%), multiple system atrophy (7.09%), amyotrophic lateral sclerosis (6.54%), antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (4.24%), retinitis pigmentosa (4.24%), progressive muscular dystrophy (4.05%), systemic sclerosis (3.50%), hemophilia (3.41%), multiple sclerosis (3.31%), idiopathic pulmonary fibrosis (2.67%), idiopathic pulmonary arterial hypertension (2.30%), autoimmune encephalitis (1.75%), and Marfan syndrome (1.66%). With the exception of POEMS syndrome, optical neuromyelitis, systemic sclerosis, multiple sclerosis, and idiopathic pulmonary arterial hypertension, where the proportion of female patients exceeds that of males, the remaining ten disease categories show a higher proportion of male patients compared to females. The results are shown in Figure 2 and Figure 3.

An analysis was conducted on the age distribution of patients with the top fifteen disease categories, which are presented in Figure 4. The results showed that these patients account for 73.66% of all cases. Among them, all fifteen disease categories have patients within the 45–59 age group. Eight disease categories have patients under 15 years old, fourteen disease categories have patients within the 15–44 age group, and twelve disease categories have patients aged 60 or above. Specifically, progressive muscular dystrophy (61.36%) and hemophilia (35.14%) primarily affect individuals under 15 years old; Castleman disease (72.84%) and Marfan syndrome (72.22%) mainly occur in the 15–44 age group; ANCA-associated vasculitis (54.35%), idiopathic pulmonary fibrosis (65.52%), and idiopathic pulmonary arterial hypertension (48.00%) predominantly affect individuals aged 60 or above. For the remaining diseases, the highest proportion of cases is found in the 45–59 age group.

The results of the analysis on the composition of hospitalization costs for patients within the top fifteen disease categories are presented in Table 3. The findings revealed that for the majority of these conditions, hospitalization costs were predominantly composed of diagnostic and medication costs, with diagnostic costs accounting for between 6.41% and 49.75%, and medication costs ranging from 12.97% to 46.22%. Furthermore, for retinitis pigmentosa and Marfan syndrome, surgical costs represented the second largest component of the cost structure, accounting for 14.41% and 8.61%, respectively. For rare diseases involving neurological disorders, such as multiple system atrophy,

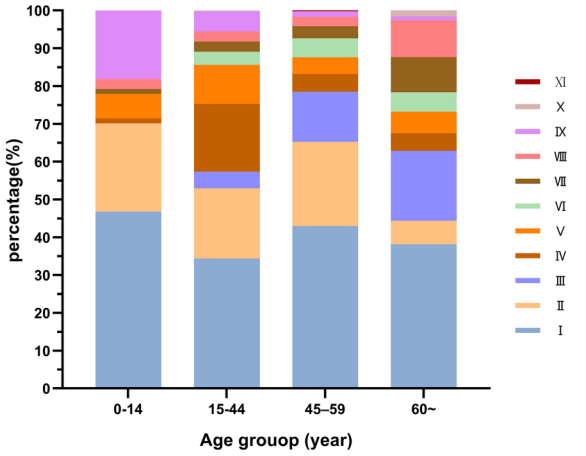

Figure 1. The distribution of cases across the four age groups.

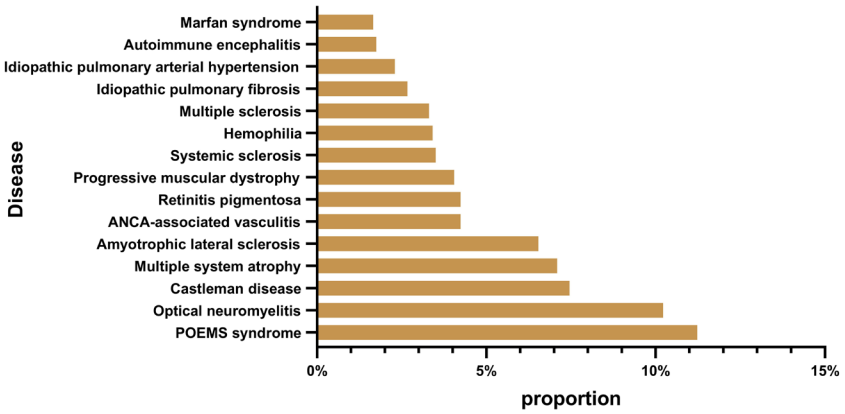

Figure 2. The proportion of the top fifteen diseases categories.

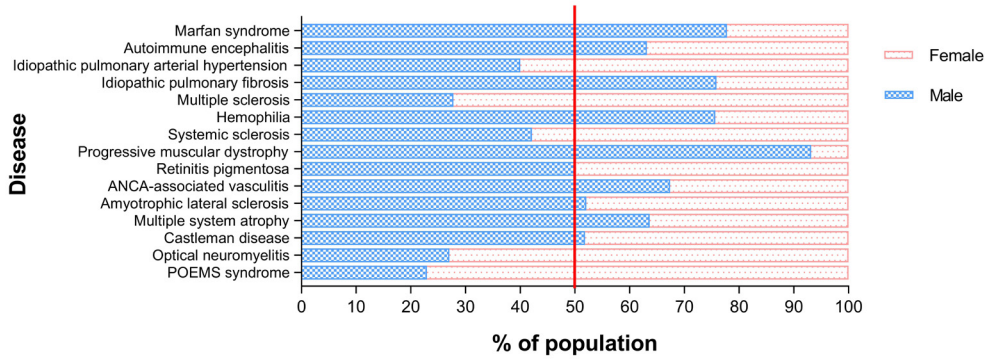

Figure 3. The gender distribution of cases in the top fifteen diseases categories.

autoimmune encephalitis, amyotrophic lateral sclerosis (ALS), and multiple sclerosis, rehabilitation treatment costs were relatively higher, at 2.23%, 1.63%, 1.12%, and 1.02%, respectively. About total hospitalization costs, the mean hospitalization costs for the top fifteen disease syndromes had the highest mean hospitalization cost at $11,559.06 ± 13,834.57, with a median cost of $3,595.89; Autoimmune encephalitis followed, with a mean hospitalization cost of $5,347.21 ± 7,175.00 and a median cost of $2,716.60; the lowest mean hospitalization cost was observed for Castleman's disease, at $863.15 ± 1,914.45, with a median cost of $373.42.

3.4. Readmission rate

Among the 96 disease categories involved in this study, 29 exhibited instances of readmission. The 10 diseases with the highest readmission rates, listed in descending order, were McCune-Albright syndrome, POEMS syndrome, Castleman disease, Langerhans cell histiocytosis, albinism, pulmonary alveolar proteinosis, ANCA-associated vasculitis, paroxysmal nocturnal hemoglobinuria, optical neuromyelitis, and Fanconi anemia. The readmission rate ranged from 95.90% to 42.86%, which is presented in Table 4.

4. Discussion

Gansu Provincial People's Hospital, a prominent tertiary A comprehensive hospital in northwest China, boasts a high patient volume, diverse patient demographics, and a broad spectrum of disease entities, with a significant proportion of complex and critically ill cases. The hospital's clinicians possess extensive and profound expertise in diagnosing and treating rare diseases, rendering the cases studied highly representative. This is also the first study conducted in Gansu on the characteristics of hospitalized patients with rare diseases, laying the foundation for research on rare diseases in northwest China and filling a gap in this field (by comprehensive literature search to confirm the

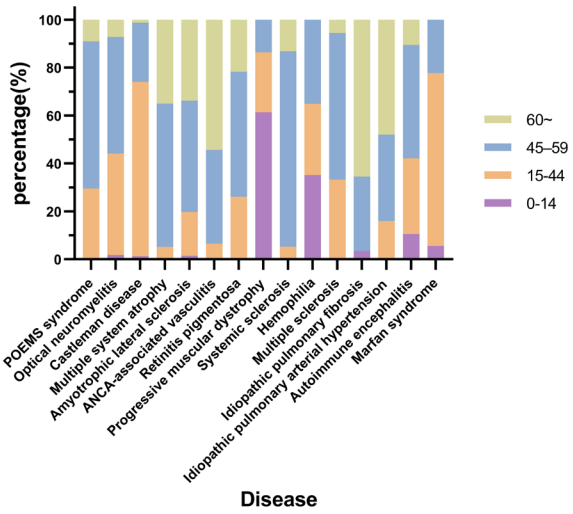

Figure 4. The age distribution of cases in the top fifteen disease categories.

novelty of our study). The results of our investigation indicated substantial heterogeneity in both composition of different rare diseases and demographic distribution of their affected populations. Consequently, our findings underscore the critical need for advancing precision of diagnosis and treatment across a wide range of medical specialties.

Our study found that neurological diseases emerged as the most common category (39.69% of cases), diseases of the blood and blood-forming organs, certain diseases involving immune mechanisms (18.32% of cases), and diseases of the musculoskeletal system and connective tissue (10.50% of cases). This is consistent with the characteristics of rare diseases, which are mostly genetic and affect multiple organs and systems, resulting in poor patient outcomes and long rehabilitation periods. In China, 106,746 hospitalizations for a rare disease were captured from 1 January 2014 to 31 December 2015, accounting for 0.69% of inpatients during the same period (*27*). The top 10 rare diseases with most cases on the TRDL 2017 were thalassemia, idiopathic pulmonary arterial hypertension, pulmonary Langerhans cell

Table 3. Analysis of the composition of hospitalization costs for patients with the top fifteen Diseases

Disease	No.	Average Hospitalization Cost per admission (USD)	Median hospitalization cost per admission (USD)	Nursing Costs (%)	Medical Service Costs (%)	Diagnostic Costs (%)	Surgical Costs (%)	Rehabilitation Costs (%)	Medication Costs (%)	Blood and Blood Products Costs (%)	Consumables Costs (%)	Other Costs (%)
POEMS syndrome	122	913.13 ± 1,569.44	363.46	1.12	12.71	37.34	1.56	0.03	25.90	1.36	0.00	1.90
Optical neuromyelitis	111	2,299.74 ± 2,021.12	1,509.58	2.75	8.08	32.68	0.27	0.56	46.22	0.12	0.00	2.69
Castleman disease	81	863.15 ± 1,914.45	373.42	0.63	9.71	49.75	1.28	0.04	23.07	3.89	0.00	0.00
Multiple system atrophy	77	2,414.77 ± 4,715.24	1,403.61	9.41	7.78	27.57	0.27	2.23	32.86	0.00	0.00	9.61
Amyotrophic lateral sclerosis	71	1,551.70 ± 1,265.60	1,332.00	2.24	6.84	37.96	0.93	1.12	22.49	0.00	0.00	14.57
ANCA-associated vasculitis	46	2,751.23 ± 6,081.99	857.46	2.49	6.99	28.24	2.56	0.34	29.36	2.17	0.00	0.97
Retinitis pigmentosa	46	1,207.94 ± 924.72	1,006.84	0.85	4.02	25.55	14.41	0.17	12.97	0.00	0.00	14.41
Progressive muscular dystrophy	44	1,235.98 ± 962.67	927.28	5.30	9.80	37.89	1.19	0.32	25.73	0.00	0.00	14.30
Systemic sclerosis	38	1,577.47 ± 2,112.03	620.41	4.20	9.72	42.00	1.03	0.07	36.57	0.59	0.00	0.00
Hemophilia	38	1,844.60 ± 1,778.23	1,378.55	1.36	8.48	30.45	3.11	0.22	22.62	10.85	0.00	5.76
Multiple sclerosis	36	2,049.26 ± 1,554.74	1,560.57	2.63	9.13	42.25	0.05	1.02	35.92	0.00	0.00	1.54
Idiopathic pulmonary fibrosis	29	2,960.66 ± 4,671.22	1,669.05	3.55	10.13	33.39	1.92	0.08	41.80	2.05	0.00	0.00
Idiopathic pulmonary arterial hypertension	26	2,062.04 ± 1,157.64	1,878.84	3.67	7.19	33.53	0.78	0.23	24.56	0.36	0.00	6.43
Autoimmune encephalitis	19	5,347.21 ± 7,175.00	2,716.60	8.95	7.70	21.03	0.23	1.63	43.71	0.44	0.00	7.77
Marfan syndrome	18	11,559.06 ± 13,834.57	3,595.89	3.16	2.41	6.41	8.61	0.51	14.64	3.37	0.00	15.94

histiocytosis, moyamoya disease, motor neuron disease, idiopathic pulmonary fibrosis, systemic sclerosis, hepatolenticular degeneration, coarctation of the aorta, and transposition of the great arteries (*28*). A study from a top-tier hospital in Shaanxi Province, which is located in the northwest region of China, found that patients with nervous system diseases, respiratory system diseases, and blood system diseases accounted for the highest proportions, at 74.12%, 7.39%, and 6.26% respectively (*29*). An analysis of characteristics of hospitalized rare disease cases in Zhejiang Province, located in the eastern region of China, found that diseases of the blood system, congenital malformations, and diseases of the nervous system ranked as the top three in terms of case numbers (*30*). In the southwestern region of China, the top three categories of rare disease inpatients were endocrine and metabolic diseases, neurological diseases, and hematological diseases (*31*). This may be related to regional differences, lifestyle habits, and the varying strengths in disease diagnosis and treatment among different hospitals. Studies have indicated that insufficient awareness of rare diseases among physicians is one of the contributing factors to delayed diagnosis and misdiagnosis of rare disease patients (*32*). Therefore, it is necessary to strengthen professional training for physicians in relevant specialties such as neurology, endocrinology, pediatrics, and hematology based on distribution of the rare disease spectrum in the region. Additionally, efforts should be made to establish expert teams for rare disease diagnosis and treatment, enhance research on clinical differential diagnosis and treatment, and optimize the multi-disciplinary diagnosis and treatment model for rare diseases, thereby improving diagnosis rate and treatment rate of rare diseases in the region.

Our study identified notable sex-based and age-related disparities in classification of rare diseases. Female patients exhibited a higher prevalence of blood and rming organs and certain disorders involving the immune mechanism, while male patients were more frequently diagnosed with musculoskeletal system and connective tissue diseases, respiratory, congenital malformations, deformations and chromosomal abnormalities, and neoplasms. These differences are consistent with previous research, which suggests that sex hormones, immune system variations, and genetic susceptibility contribute to sex-specific disease manifestations (*33,34*).

The age of diagnosis differed markedly among distinct disease groups. Although a substantial proportion of rare disorders were identified during adult years (45–59 years in our study), certain categories — particularly nervous system and congenital malformations, deformations and chromosomal abnormalities — showed a strong pediatric predominance. Distribution of the top fifteen diseases varies among different age groups. Neurological diseases are the predominant type

Table 4. Statistics on the top 10 diseases by readmission rate

Disease	No.	Readmissions No.	Readmission rate (%)
POEMS syndrome	122	117	95.90
Castleman disease	81	72	88.89
Langerhans cell histiocytosis	16	13	81.25
McCune-Albright syndrome	4	3	75.00
Pulmonary alveolar proteinosis	13	8	61.54
ANCA-associated vasculitis	46	29	63.04
Albinism	5	3	60.00
Optical neuromyelitis	111	65	58.56
Paroxysmal nocturnal hemoglobinuria	11	6	54.55
Fanconi anemia	7	3	42.86

of rare diseases across all age groups. As age increases, musculoskeletal and connective tissue diseases, as well as respiratory system diseases, gradually become the main types of diseases. This trend is consistent with progression and changes in diseases that occur with aging. It indicates that patients with rare diseases mainly affect the working-age population of young and middle-aged individuals, imposing a heavy burden on individuals, families, and social development in Gansu Province. This finding is somewhat different from conclusions reported in previous literature, which state that "the occurrence of rare diseases is closely related to genetics", "about 80% of rare diseases are caused by genetic defects", and "50% to 70% of rare diseases manifest at birth or during childhood". This discrepancy may be due to the fact that the sentinel hospitals selected for our study were general hospitals, which tend to have fewer pediatric patients compared to specialized children's hospitals. Additionally, Gansu Province, located in a less developed area of western China, faces challenges with public and primary healthcare workers' early prevention and recognition capabilities of rare diseases, which are not as advanced as those in more developed eastern regions. Consequently, many rare diseases are not identified and managed promptly at onset, leading to underdiagnosis and misdiagnosis. Therefore, we recommend sustained public health education initiatives to disseminate knowledge on the three-tiered prevention strategy for rare diseases, thereby enhancing population awareness and health literacy. This approach fosters a compassionate and socially supportive environment for affected individuals.

The severity of a disease, its treatment methods, length of hospital stay, and medication costs are all to some degree determined by type of disease. From the perspective of the global situation, treatments for rare diseases encompass medications, dietary adjustments, surgery, or rehabilitation with medical devices. Among these, pharmacological treatment is currently the primary mode of clinical diagnosis and treatment (*33*). We found that in the top fifteen diseases, inpatient costs were predominantly comprised of diagnostic fees and medication expenses, with the latter accounting for up to 46.22% of total cost. This finding is consistent with the current global situation, where rare diseases are characterized by complex etiologies, challenging diagnostic processes, extended treatment and rehabilitation periods, and a substantial economic burden on patients. Moreover, the same disease can result in significant variations in inpatient costs due to differences in patient age, disease progression, treatment methods, type of medical payment, and degree of recovery. Consequently, the standard deviation of the average inpatient cost is relatively high. On the other hand, the level of healthcare institutions, medical insurance policies, regional economic conditions, and the allocation of medical resources are also key factors that influence inpatient costs for rare diseases. A 2019 study on the economic burden of rare diseases in the United States found that inpatient medical service fees and prescription medication costs were the largest components, accounting for 32% and 18% of direct medical costs, respectively (*34*). A study on the economic burden of Epidermolysis Bullosa in Spain found that direct non-medical costs represented the largest proportion, primarily consisting of informal care costs. Among healthcare expenses, the cost of specialist visit was most significant, accounting for 5.72% of total costs, followed by nursing care, which accounted for 2.37% of total costs (*35*). In Shaanxi, China, an analysis of the top five cost components for inpatient care of rare disease patients at a tertiary hospital revealed that medication costs (ranging from 24% to 54%) and diagnostic fees (ranging from 18% to 44%) accounted for a significant proportion of total expenses (*36*). In Shanghai, China, the estimated annual average cost for inpatient care of 23 rare diseases is ¥9,846.77. Compared to the annual disposable income, the cost of inpatient treatment for rare diseases represents a significant proportion of annual disposable income for urban residents and nearly half of annual disposable income for rural residents (*22*). This also clearly indicates that medical expenses for rare diseases are heavy, especially for families from less developed rural areas.

While China’s medical security system for rare diseases has made notable progress — illustrated by 137 drugs granted priority review in Q1 2022 and an expansion of insurance coverage — high treatment costs remain insufficiently addressed (*37*). Nevertheless,

significant disparities persist when compared with the United States and European Union, particularly in drug development and approval timelines. Therefore, it is essential to increase focus on key population groups and specific disease types and to pay more attention to management of rare disease drugs and medical insurance policies. Establishing a multi-tiered medical security system and forming a co-payment mechanism involving multiple parties can effectively reduce hospitalization costs and alleviate the medical burden on patients. Additionally, less developed regions in the west of China should develop targeted medical insurance policies and drug management measures based on characteristics of rare diseases in their respective provinces. Meanwhile, efforts should be made to strengthen diagnosis and treatment training for primary care physicians at the grassroots level in the region and construction of an early referral network platform, so as to improve diagnosis rate and treatment rate of rare diseases.

As reported in our study, the number of hospital admissions was 169, 167, and 136 cases in 2020, 2021, and 2022, respectively, rising to 268 cases in 2023. This trend likely reflects delays in seeking or accessing healthcare services attributable to the COVID-19 pandemic. It is crucial to acknowledge potential impact of the pandemic on patterns of hospital admissions and disease reporting observed in our data. During peak periods of infection surges and associated public health restrictions, access to non-urgent and elective healthcare services was significantly reduced in many regions (*38-40*). Rare disease patients were further marginalised, particularly in access to regular health care, treatment (*41*). Consequently, trends observed in our data, particularly concerning admission cases or distribution of specific rare diseases diagnosed during 2020–2022, should be interpreted with caution, recognizing the exceptional circumstances that may have led to artificial depression or distortion of these metrics compared to pre or post-pandemic years.

This study had certain limitations. While the research, grounded in data from inpatients with rare diseases at a hospital in Gansu Province, offers valuable insights into the epidemiological features of a substantial portion of rare diseases within the province, it is inevitable that cases of rare diseases may be underreported, potentially leading to an underestimation of their true incidence. Firstly, this study only included information on inpatients with rare diseases, excluding outpatient records, which represent a significant proportion of the rare disease patient population. Secondly, diagnostic information utilized in this study was sourced exclusively from Patient Discharge Summary records. The accuracy of clinical diagnoses rendered by physicians and precise classification of ICD codes by medical record coders are pivotal in determining authenticity of rare disease case counts. Lastly, owing to inherent constraints of the study, we have only included Gansu Provincial People's Hospital as the sole medical institution, and were unable to obtain diagnosis and treatment data of rare diseases from all tertiary hospitals in the province. Consequently, it may inevitably exhibit a degree of selection bias and statistical bias. Despite these limitations, our findings contribute significantly to filling a data gap of rare diseases in Gansu Province. It provides important reference value for guiding medical institutions and health administrative departments in improving clinical competencies in diagnosing and treating, as well as optimizing and adjusting medical security policies for rare diseases.

5. Conclusion

Rare diseases are not only a public health problem, but also a social problem. Although national attention to rare disease communities has increased in recent years, accompanied by improved public awareness and deeper research in the field, uneven distribution of prevention and control efforts for rare diseases remains prevalent. This study focuses on the distribution characteristics of rare disease inpatients in a hospital located in western China. The demographic distribution characteristics of inpatients from 2015 to 2023, the classification of disease systems, the distribution of the top fifteen diseases, and the medical cost burden during hospitalization are described comprehensively. Our study provides important and foundational data support for development and improvement of rare disease prevention policies and medical services.

Acknowledgements

We sincerely appreciate the Gansu Province Rare Disease Quality Control Center and Gansu Provincial People's Hospital.

Funding: This work was supported by Natural Science Foundation Project of Gansu Province: Analysis and Countermeasures Research on Patients' Medical Treatment Behavior Pathways under the Normalization of Epidemic Prevention and Control (grant number: 22JR11RA57).

Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Montserrat Moliner A, Waligóra J. The European union policy in the field of rare diseases. Public Health Genomics. 2013; 16:268-277.
2. The Lancet Diabetes Endocrinology. Spotlight on rare diseases. Lancet Diabetes Endocrinol. 2019; 7:75.
3. Nguengang Wakap S, Lambert DM, Olry A, Rodwell C, Gueydan C, Lanneau V, Murphy D, Le Cam Y, Rath A. Estimating cumulative point prevalence of rare diseases:

Analysis of the Orphanet database. Eur J Hum Genet. 2020; 28:165-173.
4. Richter T, Nestler-Parr S, Babela R, Khan ZM, Tesoro T, Molsen E, Hughes DA; International Society for Pharmacoeconomics and Outcomes Research Rare Disease Special Interest Group. Rare disease terminology and definitions-a systematic global review: Report of the ISPOR rare disease special interest group. Value Health. 2015; 18:906-914.
5. Melnikova I. Rare diseases and orphan drugs. Nat Rev Drug Discov. 2012; 11:267-268.
6. European Union. Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products (2000). *https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32000R0141* (accessed October 31, 2024).
7. U.S. Food & Drug. Rare Diseases at FDA. *https://www.fda.gov/patients/rare-diseases-fda* (accessed October 31, 2024).
8. Lu Y, Han J. The definition of rare disease in China and its prospects. Intractable Rare Dis Res. 2022; 11:29-30.
9. Groft SC, Posada M, Taruscio D. Progress, challenges and global approaches to rare diseases. Acta Paediatr. 2021; 110:2711-2716.
10. Vandeborne L, van Overbeeke E, Dooms M, De Beleyr B, Huys I. Information needs of physicians regarding the diagnosis of rare diseases: A questionnaire-based study in Belgium. Orphanet J Rare Dis. 2019; 14:99.
11. Lane R. Shuyang Zhang: Pioneer in China's rare diseases programme. Lancet. 2019; 394:1134.
12. Lu Y, Gao Q, Ren X, Li J, Yang D, Zhang Z, Han J. Incidence and prevalence of 121 rare diseases in China: Current status and challenges: 2022 revision. Intractable Rare Dis Res. 2022; 11:96-104.
13. He J, Song P, Kang Q, Zhang X, Hu J, Yang Y, Tang M, Chen D, Hu S, Jin C. Overview on social security system of rare diseases in China. Biosci Trends. 2019; 13:314-323.
14. Peng A, Fan X, Zou L, Chen H, Xiang J. Trend of clinical trials of new drugs for rare diseases in China in recent 10 years. Orphanet J Rare Dis. 2023; 18:114.
15. Cui Y, Zhou X, Han J. China launched a pilot project to improve its rare disease healthcare levels. Orphanet J Rare Dis. 2014; 9:14.
16. He J, Kang Q, Hu J, Song P, Jin C. China has officially released its first national list of rare diseases. Intractable Rare Dis Res. 2018; 7:145-147.
17. Tang M, Yang Y, Ye Z, Song P, Jin C, Kang Q, He J. Release and impact of China's "second list of rare diseases". Intractable Rare Dis Res. 2023; 12:251-256.
18. Bureau of Medical Administration of the National Health Commission of the People's Republic of China. Notification on adjusting the members of the national rare disease diagnosis and treatment collaborative network hospitals and personnel in the Office. *https://www.nhc.gov.cn/yzygj/c100068/202403/e0328f505bcc47619e464148b2304dc0.shtml* (accessed October 31, 2024). (in Chinese)
19. Feng S, Liu S, Zhu C, Gong M, Zhu Y, Zhang S. National rare diseases registry system of China and related cohort studies: Vision and roadmap. Hum Gene Ther. 2018; 29:128-135.
20. Gong L, He Q. Establishing a rare diseases center: Experiences from Western China. Intractable Rare Dis Res. 2021; 10:60-61.
21. Yang Y, Kang Q, Hu J, Kong F, Tang M, He J, Jin C. Accessibility of drugs for rare diseases in China: Policies and current situation. Intractable Rare Dis Res. 2019; 8:80-88.
22. Cai X, Yang H, Genchev GZ, Lu H, Yu G. Analysis of economic burden and its associated factors of twenty-three rare diseases in Shanghai. Orphanet J Rare Dis. 2019; 14:233.
23. Shuyang Z, Xue Z. Recent polices and practice in rare diseases in China. Journal of Rare Diseases. 2022; 1:1-6. (in Chinese)
24. Report of Rare Disease in China (2018). China medical science and technology press (Jie D, Lin W, eds.). Beijing, China. 2018; PP. 142-148. (in Chinese)
25. Guo J, Liu P, Chen L, Lv H, Li J, Yu W, Xu K, Zhu Y, Wu Z, Tian Z, Jin Y, Yang R, Gu W, Zhang S; Administrative Group of National Rare Diseases Registry System of China. National Rare Diseases Registry System (NRDRS): China's first nation-wide rare diseases demographic analyses. Orphanet J Rare Dis. 2021; 16:515.
26. Bureau of Medical Administration of the National Health Commission of the People's Republic of China. Notification on launching the registration of rare disease case diagnosis and treatment information (2019). *https://www.nhc.gov.cn/yzygj/c100068/201910/1442aeb8bb5643939a83713f410bc206.shtml* (accessed October 28, 2024). (in Chinese)
27. Shi XM, Liu H, Wang L, Wang ZX, Dong CY, Wang YF, Yao C, Zhan SY, Ding J, Li Y. Study on the current situation of China's first list of rare diseases based on 15 million hospitalizations. Zhonghua Yi Xue Za Zhi. 2018; 98:3274-3278. (in Chinese)
28. Shi X, Liu H, Zhan S, Wang Z, Wang L, Dong C, Wang Y, Yao C, Ding J, Li Y. Rare diseases in China: Analysis of 2014-2015 hospitalization summary reports for 281 rare diseases from 96 tertiary hospitals. Orphanet J Rare Dis. 2019; 14:160.
29. Qian L, Jianmin G, Yiping M. Analysis of the characteristics of inpatients with rare diseases in a hospital from 2015 to 2019. Chinese Health Quality Management, 2021; 28:27-30. (in Chinese)
30. Wen X, Wang SS, Cai J, Ren JP, Gu H. Characteristics of rare diseases in Zhejiang province, 2007-2017. Zhonghua Liu Xing Bing Xue Za Zhi. 2020; 41:400-405. (in Chinese)
31. Lingyan Z, Jie H, Cheng Y, Dajin L, Jinmei L, Jie S, RuiBa L, Huabin G. Analysis of inpatient cases of rare diseases in a tertiary first-class hospital in Yunnan Province from 2015 to 2019. Chinese Medical Record. 2022; 23:79-82. (in Chinese)
32. Vandeborne L, van Overbeeke E, Dooms M, De Beleyr B, Huys I. Information needs of physicians regarding the diagnosis of rare diseases: A questionnaire-based study in Belgium. Orphanet J Rare Dis. 2019; 14:99.
33. Stolk P, Willemen MJ, Leufkens HG. Rare essentials: Drugs for rare diseases as essential medicines. Bull World Health Organ. 2006; 84:745-751.
34. Yang G, Cintina I, Pariser A, Oehrlein E, Sullivan J, Kennedy A. The national economic burden of rare disease in the United States in 2019. Orphanet J Rare Dis. 2022; 17:163.
35. Aranda-Reneo I, Oliva-Moreno J, Peña-Longobardo LM, Villar-Hernández ÁR, López-Bastida J. Economic burden and health-related quality of life in patients with epidermolysis bullosa in Spain. Orphanet J Rare Dis.

2024; 19:352.
36. Wen Z, Yue M, Qian L, Zheng C, Wenjia L, Xiaoting Y. An analysis of influencing factors on hospitalization expenses of the top five rare diseases in a tertiary general hospital. Modern Hospitals, 2023; 23:585-588. (in Chinese)
37. Liu YQ, Liu X, Zuo W, Wang SH, Zhang B, Zhang SY. Study on drug list and accessibility of rare diseases based on the China's second list of rare diseases. Journal of Rare Diseases. 2024; 3:195-201. (in Chinese)
38. Ali M, Wani SUD, Masoodi MH, Khan NA, Shivakumar HG, Osmani RMA, Khan KA. Global effect of COVID-19 pandemic on cancer patients and its treatment: A systematic review. Clin Complement Med Pharmacol. 2022; 2:100041.
39. Xiao H, Dai X, Wagenaar BH, Liu F, Augusto O, Guo Y, Unger JM. The impact of the COVID-19 pandemic on health services utilization in China: Time-series analyses for 2016-2020. Lancet Reg Health West Pac. 2021; 9:100122.
40. Xu S, Glenn S, Sy L, Qian L, Hong V, Ryan DS, Jacobsen S. Impact of the COVID-19 pandemic on health care utilization in a large integrated health care system: Retrospective Cohort Study. J Med Internet Res. 2021; 23:e26558.
41. Macaluso M, Rothenberg ME, Ferkol T, Kuhnell P, Kaminski HJ, Kimberlin DW, Benatar M, Chehade M; Principal investigators of the rare diseases clinical research network – cycle 4. Impact of the COVID-19 pandemic on people living with rare diseases and their families: Results of a national survey. JMIR Public Health Surveill. 2024; 10:e48430.

Received May 16, 2025; Revised August 14, 2025; Accepted September 10, 2025.

[§]These authors contributed equally to this work.
**Address correspondence to:*
Yan Yang and Jin He, Gansu Provincial Hospital, No. 204 Donggang West Road, Lanzhou, 730000, Gansu Province, China.
E-mail: gssyyangy@163.com (YY), hejin1978team@163.com (JH)

Released online in J-STAGE as advance publication September 26, 2025.