Current status of research on rare diseases in children in China

Abstract: Objective: In order to understand and study the diagnosis and treatment status of rare diseases in children across the country. **Method**: The data information retrieved by keywords of rare diseases in children was sorted and analyzed through the Internet, the Internet, official data and other databases. **Result** : Rare diseases are very critical, and have high disability and mortality rates, and 70% of them occur in children, rare diseases are receiving more attention. This paper briefly describes the current status of rare diseases in China in terms of their types, diagnosis, and medication.

Keywords: rare disease, children, status.

Introduction:

The term "rare disease" is derived from the English word rare disease. In contrast to common diseases, rare diseases are those with relatively low prevalence. According to the World Health Organization (WHO), rare disease is defined as a disease that affects 0.65 to 1 per 1,000 of the total population. Rare diseases usually affect multiple systems and organs and have a chronic, progressive, and exhaustive course, resulting in disability or life threatening effects.This study is to

elaborate on the current status of rare diseases in children [2,9,10].

1. Types of rare diseases in China

China is a populous country, according to the latest statistics, the total population of China is 1,411.78 million, of which 253.38 million are children, accounting for 17.95%.However, with such a large base,because rare diseases are very critical, have high disability and mortality rates, and 70% of them occur in children, rare diseasesare receiving more and more attention. At present, there are 7877 rare diseases included in the world, with data show that there are 121 types of rare diseases identified in China. The investigators investigated and analyzed the distribution of inpatients in tertiary care hospitals as a sample to explore the current status of rare diseases in China.The results showed that 19 of the known rare diseases in China were not included in the rare disease survey list of Beijing Rare Disease Society.Of these, 54,468 were 102 rare cases, accounting for 0.35% of the hospitalized patients in the same period,the number of the top 10 rarest and least rare cases was 37977, accounting for 0.25% of the hospitalized patients in the same period. The readmission rate of these top 10 rare diseases was as high as 28.42%~64.88%. In terms of age distribution, the proportion of rare diseases among children aged 25-64 years was 45.8%, and the proportion of children aged 0-14 years was 28.6%. 28.6%.These data all reveal that rare disease incidence low number of patients and high recurrence rate[1,10].Wilson's disease (WD)

is a rare autosomal recessive disease caused by mutations in the ATP7B gene mutation. The clinical features and mutational analysis of early childhood WD in China have been rarely described.One researcher retrospectively examined 114 children with WD who were on average 5.9 years old at the time of diagnosis.Eight patients developed acute liver failure at an average age of 9.7 years. 4 of them died. Of the 114 patients, 86.0% were patients were pre-symptomatic at the time of diagnosis. The double allele pathogenic ATP7B mutation was found in all patients.Of the detected of the 60 mutations detected, 10 were novel, including 7missense mutations (p.I566N, p.T704I, p.C980F, p.G1030V, p.A1096Q, p.L1327P and p.L1327P).p.G1030V, p.A1096Q, p.L1327P andp.L1373F), one nonsense mutation (p.K866X), one minor insertion (p.Y44LfsX2) and a minor deletion (p.R1118P).(p.R1118PfsX10),which affected 114 The most frequent mutations were p.R778L, p.P992L and p.I1148T, which affected 27.2%, 25.4% and 20.2%.Patients with p.R778L had a higher incidence of acute liver failure than those without p.R778 L (9.7% vs. 4.8%) .This study will help to establish early diagnosis of WD at the genetic level ,provide useful information for genetic counseling, and provide clues to the genotype/phenotype correlation of ATP7B mutations[2].Hemophilia is a group of bleeding disorders with inherited coagulation disorders.Hemophilia A, or a deficiency of factor VIII (also known as anti-hemophilic globulin, AHG); hemophilia B, a deficiency of

factor IX (also known as plasma thromboplastin component, PTC),Hemophilia C, a deficiency of factor D (also known as plasma thromboplastin precursor, PTA) .This group of diseases is not not uncommon, with an incidence of 5 to 10/100,000, with hemophilia A is more common.The common feature is a lifetime of minor injuries followed by a tendency to prolonged bleeding. There is no cure for this group of diseases treatment and the medication is expensive. There are many other rare diseases in China, such as spinal muscular atrophy, Fabray's disease, multiple sclerosis, etc.There is no specific medicine or treatment for these rare diseases, the only treatment available is symptomatic treatment to improve the quality of life.

2. Diagnosis of rare diseases

For the diagnosis of rare diseases, because of their incidence is extremely low and awareness is very limited, the high clinical misdiagnosis rate and very difficult to diagnose, which in turn to these patients are difficult to receive timely and effective treatment.And the impact of a wrong diagnosis on a child's parents the impact of an incorrect diagnosis on a parent of a child can be enormous. A study was done on the quality of life of parents caring for children with rare diseases.The results of a study on the quality of life of parents caring for children with rare diseases is severely reduced compared to parents of healthy children[3,9,10].There are studies that prove that correct and early

diagnosis of rare childhood diseases is very important , as it often has fatal consequences for young families. Even with a known disease, in many countries, the there are intolerably long delays in diagnosis.After a long time studies have found that the reason for delayed diagnosis is often not lack of expertise and other resources, but rather a lack of communication between parents, knowledgeable ineffective communication between the celebrity physician and the specialist center.It therefore proposes two promising and feasible approaches: (1) Strengthen parents' ability to have a dialogue with their physicians, which includes a written information about the diagnostic status in layman's language as an important detail,(2) Establishing binding requirements for centers that specialize in rare and unknown diseases.Many of the observations and considerations made in the field of pediatrics considerations may also be applicable to adults[4].For this phenomenon is also one of the reasons why we are desperately searching for a cure for rare diseases major reason.Recently, the International Consortium for Rare Diseases Research researchers have developed methods to enable molecular diagnosis of all rare diseases.The research provides timely molecular confirmation of rare genetic diseases in children and adults,significantly shortening their “diagnostic process”[5].Meanwhile, genome sequencing (GS) and exome sequencing (ES) have also been proven to be revolutionary in the diagnosis of rare diseases in

pediatrics.Its investigators reviewed genomic technologies associated with aspects of rare pediatric diseases associated with the use of genomic technologies, highlighting the benefits and limitations of ES and GS, the complexity of variant classification, and the importance of genetic counseling,the diagnostic potential of ES and GS in various pediatric multisystem diseases is discussed[6].A growing number of studies have also shown that GS can be used in single laboratory workflow to detect an unparalleled of pathogenic abnormalities. Its ability to deliver five inexpensive, rapid and accurate tests to patients with different clinical indications and complex presentations[7].These studies, all of which have greatly have greatly improved the diagnosis rate of rare diseases, providing a solid foundation for rapid and effective treatment of children with rare diseases worldwide.

3. Current status of drug therapy for rare diseases

For drugs for rare diseases, also known as orphan drugs.In 2018, one researcher compared orphan drugs in China by how far they have been marketed in compared with orphan drugs in international markets (e.g., the United States)to assess availability.The affordability of orphan drugs was calculated using hospital pharmacy prices and calculated under China's basic medical insurance system for analysis.As of March 16, 2016, the market share of orphan drugs approved in the U.S. reached 39.9% in China. Among them, 93 orphan drugs (54.07%) were included in the

national basic medical and work injury insurance drug catalogs, 22 Class A drugs with a high reimbursement rate and 71 Class B drugs with a low reimbursement rate; 79 orphan drugs (45.93%) are not covered by medical insurance or do not have indications for rare diseases. Orphan drugs are unaffordable for the majority of the Chinese population.t concluded that the Chinese government could can improve access and availability of orphan drugs through the establishment of incentive policies for orphan drug information sharing and public platforms[8].On the latest reports, the China is also paying more attention to the use of drugs for rare diseases. "Hemophilia disease: per capita treatment cost 80-1 million yuan/year, with about 49,000 patients in China;Spinal muscular atrophy: average treatment cost 700-1.4 million yuan/year, about 30-50,000 patients in China; Fabray's disease: per capita treatment cost 1-1.29 million yuan/year per person, with about 300 patients in China;Multiple sclerosis: per capita treatment cost 100,000-600,000 yuan/year, about 30,000 patients in China.These heavy numbers figures would often have brought down a family a decade ago, but now 67% of drugs for rare diseases in China are now covered by medical insurance, greatly reducing the burden of medication on patients. "Every small group should not be should be abandoned," is such a belief that the original price of 700,000 for Nocinasan sodium injection was reduced to 33,000 yuan.This undoubtedly shows that the country has not given up on

every small group. It gives hope to those children with rare diseases and their families.

4. Summary

For rare diseases, every successful discovery will provide potential diagnostic, preventive and therapeutic opportunities for thus providing precision medicine for that patient population. Therefore, contemporary society should pay attention to this small group of rare diseases, so that rare diseases are not rare and families with rare diseases can be happier.

References

【1】Xinmiao Shi,Hui Liu,Lin Wang,et al.A study on the status of the first rare disease list in China based on 15 million inpatients[J].Chinese Medical Journal,2018,No.40:3274-3278.

【2】Li, Xiuzhen1,Lu, Zhikun1,Lin,Yunting1,et al. Clinical features and mutational analysis in 114 young children with Wilson disease from South China[J].American Journal of Medical Genetics.Part A.2019,No8:1451-1458.

【3】Johannes Boettcher,Michael Boettcher,Silke Wiegand-Grefe,et al. Being the Pillar for Children with Rare Diseases-A Systematic Review on Parental Quality of Life[J]. International journal of environmental research and public health.2021,No.9:4993.

【4】Kohlschütter A1,van den Bussche H2.Early diagnosis of a rare disease in children through better communication between parents,

physicians and academic centers(Article)[J]. Z Evid Fortbild Qual Gesundhwes.2019, Vol.141-142:18-23.

【5】Kym M. Boycott,Ana Rath,Jessica X.Chong,et al. International Cooperation to Enable the Diagnosis of All Rare Genetic Diseases[J]. American journal of human genetics.2017,No5:695-705.

【6】Alison M,Elliott. Genetic Counseling and Genome Sequencing in Pediatric RareDisease[J]. Cold Spring Harbor perspectives in medicine.2020,No3: a036632.

【7】David Bick , Marilyn Jones , Stacie L Taylor ,et al. Case for genome sequencing in infants and children with rare, undiagnosed or genetic diseases[J]. Journal of Medical Genetics,2019,No12:783-791.

【8】Lin Ge,Cuijie Wei,Luwen Shi,et al.Study on drug use for rare diseases in China[J].Beijing Medical Science,2018,the fifth phase:432-434.

【9】Xie SM, Liu W, Xiang YY,et al.A rare disorder mimics otitis media:Langerhans cellhistiocytosis of the temporal bone in a child with interstitial pulmonary fibrosis[J].AMERICAN JOURNAL OF OTOLARYNGOLOGY – HEAD AND NECK MEDICINE AND SURGERY XX (2014),2014.06.018.

【10】Alison M. Elliott.Genetic Counseling and Genome Sequencing in Pediatric Rare Disease[J].Cold Spring Harbor Perspectives in Medicine,2020;10:a036632.