

# *Analysis of Prescription Rules of Neonatal Jaundice in 'Yibu Quanlu' Based on Data Mining*

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**Abstract: Objective:** To analyze the prescription rules for the treatment of neonatal jaundice in 'Yibu Quanlu' based on data mining technology. **Methods:** The provisions of the treatment of neonatal jaundice recorded in the 'Yibu Quanlu' were collected. Through the collation and entry of the ancient and modern medical case cloud platform, the data included in the medical case were standardized, and then the standardized prescription database was generated. Finally, the data analysis module in the platform was used to process the frequency statistics, association rule analysis, cluster analysis and complex network analysis of traditional Chinese medicine. **Results:** Included in 57 provisions (including 6 ancient medical cases), 67 prescriptions of traditional Chinese medicine, involving 112 herbs, the cumulative frequency of 751 times. The highest frequency of use of traditional Chinese medicine is licorice, followed by atracylodes, the average dose of traditional Chinese medicine is Yinchen; the taste is mainly bitter cold, followed by Ganping; most of them belong to the spleen, stomach and lung meridians. The use of moisturizing drugs is the most, followed by tonifying drugs; the Chinese herbal pair with the highest support was Poria – Atractylodes macrocephala; core Chinese medicine prescription is Yinchen Wuling Powder and Yigong Powder. **Conclusion:** A comprehensive analysis of prescription and medication rules for treating neonatal jaundice in 'Yibu Quanlu', and finds that clearing heat and removing dampness, protecting spleen and stomach, and preventing transmission become the main guiding ideology for the diagnosis and treatment of this disease. Eliminating pathogenic factors and strengthening vital energy are the main characteristics of prescription medication for ancient doctors. This study can provide new ideas for the clinical diagnosis and treatment of neonatal jaundice in modern Chinese medicine and the development of new drugs.

## 1. Introduction

Fetal jaundice is a disease characterized by yellow staining on the skin and face of infants after birth. Because the cause is related to the fetal endowment, it is called 'Taihuang' or 'Taidan'. Fetal jaundice is a modern medical neonatal hyperbilirubinemia, including physiological jaundice and pathological jaundice, about 50 % of full-term infants, 80 % of premature infants will appear visible

jaundice<sup>[1,2,3]</sup>. Modern medicine for neonatal jaundice total bilirubin concentration peak in the Bhutani nomogram between the 75 th percentile line to the 95 th percentile line or slightly higher, children generally in good condition, family members refused phototherapy, etc., to give oral western medicine treatment<sup>[1,2]</sup>. Oral western medicine in addition to oral phenobarbital tablets have a positive effect (with the exception of neonatal hemolytic disease and hypoproteinemia), there is no other positive effect of oral drugs<sup>[1,2]</sup>. Traditional Chinese medicine treatment of fetal yellow has a long history and rich experience, so Chinese medicine treatment of fetal yellow in recent years more and more attention. Based on the purpose of inheriting and developing traditional Chinese medicine prescription, the author takes literature mining as the train of thought and data mining as the method to deeply mine the traditional prescription of fetal jaundice, in order to provide reference for the clinical diagnosis and treatment of fetal jaundice in modern Chinese medicine and the development of new drugs.

## 2. Materials and Methods

### 2.1. Literature resources

‘Gujin Tushu Jicheng·Yibu Quanlu’<sup>[4]</sup> (hereinafter referred to as ‘Yibu Quanlu’) is a medical book edited by Chen Menglei in the Qing Dynasty. It contains more than 120 valuable medical works from the Spring and Autumn Period and the Warring States Period to the early Qing Dynasty. It is the largest and most authoritative traditional Chinese medicine book in China. ‘Yibu Quanlu’ to disease as the door, detailed records of the ancient famous doctor 's exposition, and its corresponding annotations, the ancient literature research and data mining provides a reliable source<sup>[5]</sup>.

### 2.2. Inclusion and exclusion criteria

Article inclusion criteria: ① Range in the ‘Yibu Quanlu’ volume 401 to 458 records of pediatric physiological and pathological provisions; ② Infants whose main feature is yellowing of the skin after birth.

Exclude the following provisions: ① Records only etiology pathogenesis; ② Use is not oral.

### 2.3. Data extraction and standardization

Two groups of people will appear in the provisions of the prescription into the Excel table and the parties involved without drug, drug name is not standardized control 'People's Republic of China Pharmacopoeia' (hereinafter referred to as 'Chinese Pharmacopoeia') [6] and 'Compendium of Materia Medica' [7] standardized treatment, Such as: 'Gualougen' standardized as 'Trichosanthis', 'Shanzhi' and 'Gardenia Seed' standardized as 'Gardenia', 'Kuxiao' and 'Mangxiao' standardized as 'Glaube's Salt', 'Pengzhu' standardized as 'Ezhu', etc., to retain the function before and after processing indications and taste differences such as: 'Liquorice Root' and 'Roasted Liquorice' and so on.

### 2.4. Establishing database and data analysis

The ancient and modern medical case cloud platform system (V 2.3.5) is a professional software for medical case data management and analysis. It combines traditional Chinese medicine with modern cloud algorithms, and has a variety of data mining related functions. It has made unique contributions to traditional Chinese medicine prescription medication and data mining.<sup>[8,9]</sup>

The input data were imported into the cloud platform system of ancient and modern medical records, and the second normalization was carried out according to the system. At the same time,

according to the 'Chinese Pharmacopoeia' and 'Compendium of Materia Medica', the data of four qi, five flavors and meridian tropism of commonly used Chinese medicines were supplemented. The fully processed database was added to the analysis pool. Through the data analysis module of the ancient and modern medical case cloud platform system, the frequency statistics, association rule analysis and cluster analysis of traditional Chinese medicine were processed.

### 3. Conclusion

#### 3.1. Statistical analysis of Chinese medicine

Using the 'Traditional Chinese Medicine Statistics' and 'Traditional Chinese Medicine Properties' section functions in the ancient and modern medical case cloud platform system, the frequency, four properties, five flavors and meridian tropism of 67 prescriptions were statistically analyzed. A total of 112 drugs were included for 751 times, of which 14 were used 15 times or more (see Table 1). The statistical analysis results of four properties, five flavors and meridian tropism are shown in Figure 1, Figure 2 and Figure 3.

Table 1: Statistical table of traditional Chinese medicine with frequency of use  $\geq 15$  times

chinese medicine	frequency of occurrence	percentage
liquorice	49	40.83%
largehead atractylodes rhizome	46	38.33%
tuckahoe	44	36.67%
cape jasmine fruit	34	28.33%
capillary wormwood herb	30	25.00%
ginseng	26	21.67%
alisma	26	21.67%
dried old orange peel	23	19.17%
agaric	19	15.83%
baked licorice	18	15.00%
chinese angelica	17	14.17%
cablin potchouli herb	16	13.33%
rhubarb	15	12.50%
chinese goldthread rhizome	15	12.50%

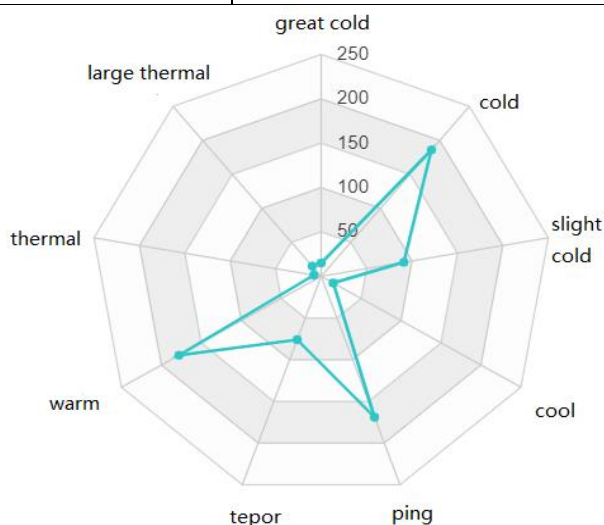


Figure 1: Four-qi statistical diagram of 112 traditional Chinese medicines

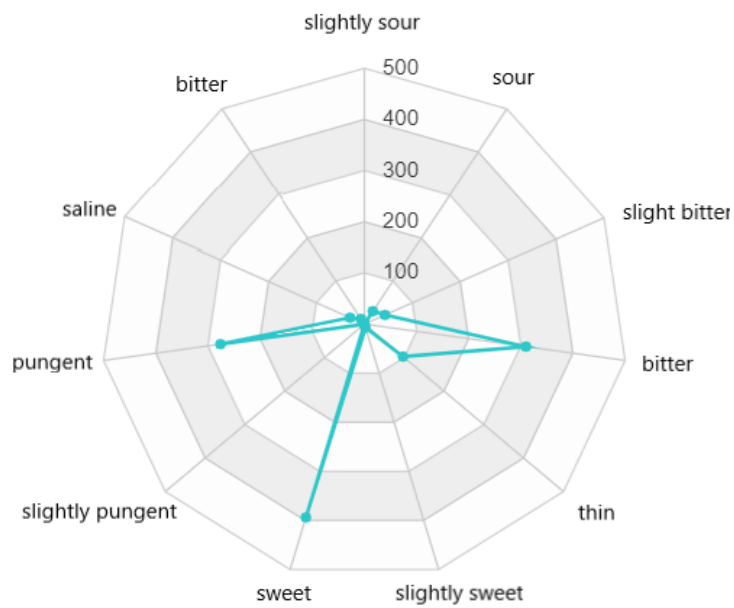


Figure 2: Statistical diagram of 112 Chinese herbs

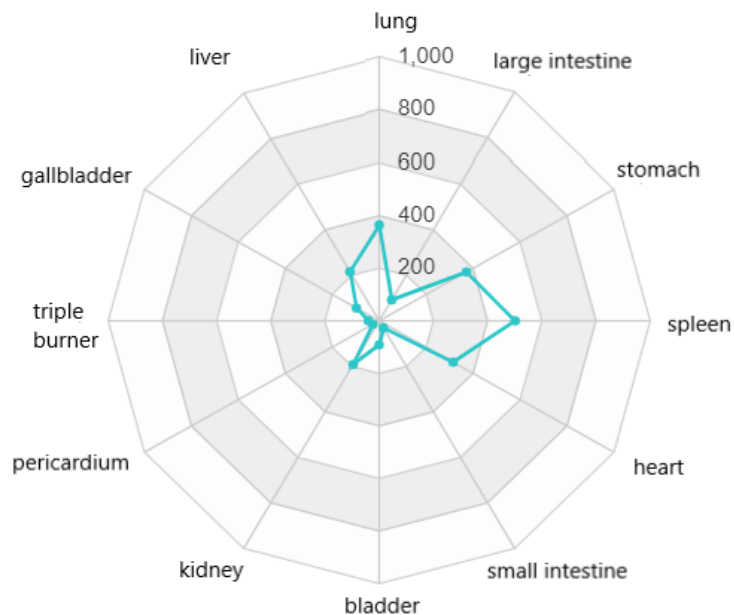


Figure 3: 112 traditional Chinese medicine meridian statistics

### 3.2. Relevance analysis

The correlation analysis of 112 traditional Chinese medicines included in the analysis was carried out. The confidence level was set to be greater than or equal to 0.5, and the support level was greater than or equal to 0.1. A total of 27 pairs of association rules were obtained (see Table 2), such as *Atractylodes macrocephala*-*Poria cocos*, *Alisma orientalis*-*Poria cocos*, *Atractylodes macrocephala*-*Glycyrrhiza uralensis*, and the degree of improvement was greater than 1.0, indicating that these related compatibility has a strong positive correlation and is statistically significant.

Table 2: Statistical table of correlation analysis of 112 Chinese medicines

chinese medicine	chinese medicine	support	Degree of confidence	upgrading degree	co-occurrence
largehead atractylodes rhizome	tuckahoe	0.28	0.72	1.96	33
tuckahoe	largehead atractylodes rhizome	0.28	0.75	1.96	33
alisma	tuckahoe	0.2	0.92	2.51	24
tuckahoe	alisma	0.2	0.55	2.54	24
largehead atractylodes rhizome	liquorice	0.19	0.5	1.22	23
ginseng	largehead atractylodes rhizome	0.18	0.81	2.11	21
alisma	largehead atractylodes rhizome	0.17	0.77	2.01	20
alisma	agaric	0.16	0.73	4.61	19
agaric	alisma	0.16	1.0	4.62	19
agaric	largehead atractylodes rhizome	0.16	1.0	2.61	19
common gardenia fruit	capillary wormwood herb	0.15	0.53	2.12	18
capillary wormwood herb	common gardenia fruit	0.15	0.6	2.12	18
agaric	tuckahoe	0.15	0.95	2.59	18
capillary wormwood herb	tuckahoe	0.13	0.53	1.45	16
cablin potchouli herb	liquorice	0.13	0.94	2.3	15
dried old orange peel	largehead atractylodes rhizome	0.13	0.65	1.7	15
alisma	capillary wormwood herb	0.13	0.58	2.32	15
capillary wormwood herb	alisma	0.13	0.5	2.31	15
ginseng	tuckahoe	0.11	0.5	1.36	13
ginseng	liquorice	0.11	0.5	1.22	13
dried old orange peel	liquorice	0.11	0.57	1.4	13
rhubarb	capillary wormwood herb	0.11	0.87	3.48	13
chinese angelica root	szechwan lovage rhizome	0.1	0.71	7.1	12
szechwan lovage rhizome	chinese angelica root	0.1	1.0	7.06	12
rhubarb	common gardenia fruit	0.1	0.8	2.82	12
cinnamon	tuckahoe	0.1	1.0	2.73	12
agaric	capillary wormwood herb	0.1	0.63	2.52	12

### 3.3. Cluster analysis

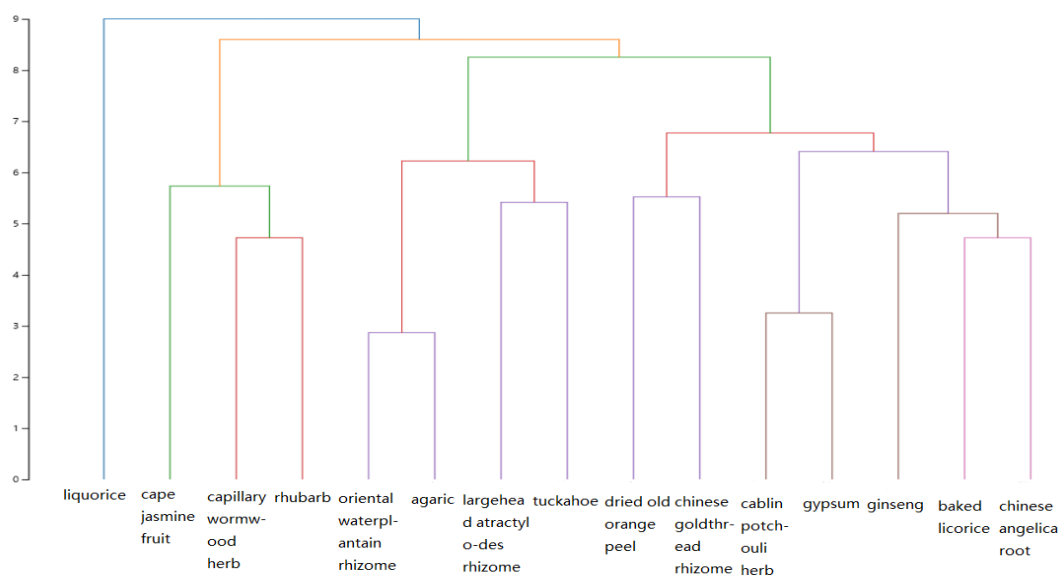


Figure 4: Cluster analysis of 112 Chinese medicines

Cluster analysis was performed on 112 traditional Chinese medicines included in the analysis. Set the frequency  $\geq 13$ , the distance type selects the Euclidean distance, the clustering method is the longest distance method, and the cluster analysis diagram (see Figure 4 for details) is obtained. With the longest distance  $\geq 8$  as the boundary, a total of Class III was obtained, and Class I was licorice; the second category is gardenia, wormwood, rhubarb; class III Alisma, Polyporus, Atractylodes, Poria, Coptis, Pogostemon cablin, Gypsum, Ginseng, Radix Glycyrrhizae, Angelica.

## 4. Discuss

According to traditional Chinese medicine, the cause of fetal jaundice is mainly due to the feeling of damp-heat or cold-damp evil at the time of production and after birth, or the formation of damp-heat or yang deficiency and cold-damp constitution. The viscera of the disease are liver, gallbladder, spleen and stomach. The key pathogenesis is the accumulation of dampness in the fetus, while the primary spleen and stomach of children are weak. Therefore, in the course of treatment, it is necessary to take care of the acquired spleen and stomach qi, not to use bitter and cold drugs, so as to prevent bitter and cold from failing the stomach and cutting down the healthy qi<sup>[3]</sup>. In the Sui Dynasty, there was a record of 'yellow fetus' in the 'theory of various diseases of children's miscellaneous diseases 'in the Sui Dynasty, which was called: 'Children are in the fetus, and their mother's viscera are hot, fumigated in the fetus, until birth. Children are yellow, called fetal jaundice also'<sup>[3]</sup>. Qian Yi in the 'children to the certificate' pointed out that 'if 100 days or half a year not due to illness and yellow, stomach fever and jaundice; if pale yellow and white, stomach timid also'<sup>[4]</sup>. The Ming Dynasty Fang Xian in the 'Qi Xiao Liang Fang · fetal heat' pointed out that 'all children with fetal heat, but see the newborn under the red and white skin, two months later, all over the yellow swelling, ..., this is due to fetal heat, or due to mother caused by hot medicine, also known as blood jaundice'<sup>[4]</sup>. Lu Bosi 'baby asked' pointed out that 'fetal yellow, then the child was born, all the face is yellow, like gold, ..., are transmitted to the fetus because the mother is heated'<sup>[4]</sup>. Xue Jia pointed out in the 'Bao Ying Cuo Yao', 'yellow fetus, with yellow eyes, ..., this in the fetal mother over eating spicy, hot and humid'<sup>[4]</sup>.

### 4.1. Common Drug Analysis

According to the results of the four qi analysis of traditional Chinese medicine, the top four are cold (186 times, accounting for 24.77 %), warm (178 times, accounting for 23.70 %), flat (169 times, accounting for 22.50 %), slightly cold (91 times, accounting for 12.12 %); according to the analysis results of the five flavors of traditional Chinese medicine, the top four are sweet (394 times, accounting for 52.46 %), bitter (310 times, accounting for 41.28 %), pungent (276 times, accounting for 36.75 %), light (97 times, accounting for 12.92 %); according to the analysis results of meridian tropism of Chinese medicine, the top four are spleen meridian (502 times, accounting for 66.84 %), stomach meridian (372 times, accounting for 49.53 %), lung meridian (365 times, accounting for 48.60 %) and heart meridian (315 times, accounting for 41.94 %). Commonly used drug categories for tonic medicine and diuretic moistening medicine is given priority to, commonly used drugs taste for sweet and warm medicine and bitter cold medicine is given priority to, commonly used drugs meridian tropism attribute for lung, spleen, kidney three meridian is given priority to.

'Medical orthodoxy ·pediatric general' pointed out that 'when the news pediatric pulse, the ancients called the mute department, the most costly treatment, ..., and the viscera crisp tender, and Menglang agent, and husband Jun cold steep heat of the medicine, can not be used lightly'<sup>[4]</sup>.

Drug analysis results in line with traditional Chinese medicine in the cognitive, indicating that the treatment of fetal yellow selection of traditional Chinese medicine should be clearing heat and removing dampness, protect the spleen and stomach, and to avoid the use of cold and heat, the

function of the fierce. Feng Jianrui et al.<sup>[10]</sup> studied the results of modern jaundice oral Chinese medicine. The results showed that the most frequently used Chinese medicines were Yinchen, Gancao, Zhizi, Fuling, Dahuang, etc. The medicinal properties are mostly cold, and the medicinal flavors are mainly bitter, sweet and pungent. The meridians are mostly spleen and stomach meridians. The results of this study are different from their results. It may be that the research object is modern medical records, the research object is ancient literature, and the oral prescription is completely selected in this study.

## 4.2. Analysis of prescription compatibility

According to the results of cluster analysis and community analysis, the commonly used drug pairs were Atractylodes-Poria, Alisma-Poria, Atractylodes-Glycyrrhiza, Ginseng-Atractylodes, Alisma-Atractylodes, Alisma-Poria; commonly used horn medicine is Yinchen, Zexie, Zhuling; rhubarb, mirabilite, gardenia; atractylodes, Poria, tangerine peel; atractylodes, Poria, Ginseng; according to this result, the ancient and modern medical case cloud platform was uploaded, and the identified prescriptions were Yigong Powder, Zexie Decoction, and Yinchen Wuling Powder.

'Herbal play' pointed out that 'spleen evil wet, Gan first into the spleen. Poria, Atractylodes of the sweet to benefit the spleen, water'<sup>[11]</sup>. Prescriptions of Poria-Atractylodes in traditional medicine are Sijunzi decoction, Yigong powder, Zhenwu decoction, Fuzi decoction, Qiweibaizhu powder, Xiaoyao powder, etc. Prescriptions with Alismatis Rhizoma-Poria Cocos drug pairs include Zhuling Decoction, Liuwei Dihuang Pill, Alismatis Rhizoma Decoction, Duqi Pill, Shengyang Yiwei Decoction, etc. Atractylodes - licorice prescriptions are four gentleman soup, Lizhong Decoction, Juyuanjian, Yigongsan, Guizhi Renshen Decoction.

The compatibility results of the prescription are consistent with the commonly used prescriptions for the treatment of fetal jaundice and post-mortem care in traditional Chinese medicine, indicating that the selection of prescriptions for the treatment and care of fetal jaundice should be based on diuretics and tonics. Feng Jianrui et al.<sup>[10]</sup> study of modern jaundice oral Chinese medicine results, the use of high-frequency drugs with licorice - Yinchen, Gardenia - Yinchen, rhubarb - Yinchen. The results of this study are quite different from their results. It may be that the research object is modern medical records, the research object is ancient literature, and the oral prescription is completely selected in this study.

## 4.3. Modern Pharmacological Analysis

Liu Cheng et al.<sup>[12]</sup> confirmed by animal experiments in poria cocos polysaccharide on jaundice has a significant intervention. Kim et al.<sup>[13]</sup> confirmed that Yinchen has a significant anti-inflammatory effect by activating Nrf2 / HO-1 signaling. Shi et al.<sup>[14]</sup> confirmed that chlorogenic acid in Artemisia capillaris can reduce liver inflammation. Zhu et al.<sup>[15]</sup> confirmed that the active ingredients in licorice have significant hepatoprotective effects through animal experiments. Huo et al.<sup>[16]</sup> confirmed that Alismatis Rhizoma has a significant effect on eliminating cholestasis through animal experiments. Zhang Xiaoxia et al.<sup>[17]</sup> confirmed that Polyporus umbellatus has significant antioxidant activity through drug experiments. Du Jinliang et al.<sup>[18]</sup> confirmed that Polyporus umbellatus has liver protection and anti-oxidation effects through animal experiments. Tae-Kyung et al.<sup>[19]</sup> confirmed that the water extract of Atractylodes macrocephala has anti-inflammatory effect through animal experiments. Christian et al.<sup>[20]</sup> confirmed that Atractylodes has anti-inflammatory and antioxidant effects. Wu Xianhao et al.<sup>[21]</sup> confirmed that the water extract of Gardenia jasminoides Ellis could increase the level of bilirubin in bile and enhance bilirubin excretion through animal experiments.

Modern studies have shown that neonatal jaundice is closely related to the abundance of neonatal

intestinal flora, and the abundance of lactic acid bacteria has a negative correlation with the incidence of neonatal jaundice<sup>[22]</sup>. Liang et al.<sup>[23]</sup> confirmed through animal experiments that Yigong Powder has a significant positive regulatory effect on the abundance of neonatal intestinal flora, and has a positive stimulating effect on the abundance of lactic acid bacteria. Fan Yaohua et al.<sup>[24]</sup> found that Yinchen Wuling Powder has the effects of liver protection, gallbladder, anti-inflammatory and analgesia through network pharmacology, and quercetin,  $\beta$ -sitosterol, isorhamnetin, hederagenin, and artemisia flavonoids can match more targets. ZENG H et al.<sup>[25]</sup> proved that quercetin can reduce liver damage and restore liver function through animal experiments. Yin et al.<sup>[26]</sup> proved that  $\beta$ -sitosterol can reduce liver inflammation through animal experiments.

Combined with modern pharmacological research, it is proved that the single Chinese medicine and prescription in this analysis have rich intervention mechanisms and good prevention and treatment effects on neonatal jaundice.

#### 4.4. Clinical application guidance

Through the study of the 'medical records', we found that the ancients in the diagnosis and treatment of fetal yellow characteristics are as follows: ① mainly dampness. The disease is mainly caused by dampness and heat, and the treatment should be mainly based on clearing heat and removing dampness. Through this analysis, it can be seen that the ancient prescription is not mainly based on clearing heat and removing dampness, but mainly based on invigorating spleen and drying dampness, promoting diuresis and oozing dampness. Because of the physiology of children 's' yang is often more than enough, yin is often insufficient ' and ' spleen is often insufficient ', if a large number of heat-clearing and dampness-eliminating products are put in, it is likely to hurt children 's healthy qi, which is easy to cause children 's evil to be eliminated and healthy qi to be injured. ② reuse of benefits. This disease is mainly caused by dampness and heat, and the treatment should be mainly based on clearing heat and removing dampness. Through research, we found that the most frequently used is not the product of bitter cold and clearing heat, but the licorice that supplements the spleen and qi, and reconciles the various drugs. And there are a large number of qi-tonifying drugs in the three drug groups obtained by cluster analysis. Description of ancient medicine and its emphasis on children 's 'immature Yin and Yang' physiological characteristics. ③ heavy spleen and stomach and light liver. The disease is located in the three zang-organs of liver, gallbladder and spleen. In this analysis, the meridian tropism of drugs is mostly in the spleen and stomach, less in the liver and gallbladder. The drug nature of the drugs for clearing liver and gallbladder is fierce, while the children 's zang-fu organs are delicate, and the drugs with severe drug nature cannot be lightly cast. ④ Multi-purpose powder. In the collation of the provisions, it can be seen that many doctors mostly give powder rather than decoction. First, Chinese traditional medicine believes that the powder is light and scattered, and it has the effect of evacuation. Both children with less dosage, decoction and pills is not easy to control the dosage and taking, and the principle of external washing and neonatal attention to keep warm back, and external washing is difficult to make the drug directly to the disease, so more use of powder.

#### 5. Complimentary close

This study comprehensively analyzed the rules of prescription and medication in the treatment of fetal jaundice in the ' ancient and modern book integration · medical department full record'. It was found that clearing heat and removing dampness and protecting the spleen and stomach were the main guiding ideology for the diagnosis and treatment of the disease. Eliminating pathogenic factors and strengthening the body resistance are the main characteristics of ancient doctors' prescription and



medication. This study can provide important reference value for the clinical diagnosis and treatment of fetal jaundice in modern Chinese medicine and the development of new drugs. Some of the conclusions are inconsistent with modern medicine clinical medication<sup>[3, 10]</sup>, clinical practice needs further study.

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