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Study on the Correlation between Diabetes Nephropathy and TCM Constitution

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Abstract: Diabetes nephropathy is one of the common and serious chronic micro vascular complications of diabetes. The degree and development speed of kidney damage are more serious than other types of nephropathy, and the negative impact on the physical and mental health of patients cannot be underestimated. A number of studies have shown that the occurrence and development of DKD is closely related to TCM constitution. This paper discusses the relationship between TCM constitution and the occurrence and development of DKD, summarizes the research contents of DKD, TCM constitution characteristics, etiology and pathogenesis, syndrome, clinical indicators and clinical application of constitution, hoping to provide some reference value for the prevention and treatment of DKD.

As one of the main causes of chronic kidney disease and end-stage renal disease, diabetes nephropathy accounts for an increasing proportion of secondary kidney disease and has become one of the main causes of death of diabetes patients. It is very likely to become the primary cause of end-stage renal disease (ESRD) in China in the near future, posing a serious threat to the life and health of patients. At present, the etiology and pathogenesis of DKD are not completely clear, and in terms of treatment, modern medicine is still a lack of specific therapy, which mainly focuses on

Blood sugar control and symptomatic support, and the treatment effect is not ideal [1, 2]. TCM constitution is an important part of the basic theory of TCM. The "constitution" of traditional Chinese medicine is reflected in the human morphological structure, psychological state, and physiological function, which is a relatively stable characteristic adapted to the external environment formed under the combination of innate endowment and acquired various complex factors[3]. Many experts point out that constitution and TCM syndrome are closely related and influence each other, and the syndrome distribution of different physical groups has its characteristics. Physical factors are the internal cause of disease occurrence. Although it does not deny the role of evil qi, whether the disease occurs and the transmission after the disease depends on people's constitution to a large extent, which is consistent with the argument of "physical disease related" proposed by Professor Wang Qi [4]. Now starting from the TCM constitution theory, we explore the relationship between constitution and the occurrence and development of DKD;

summarize the physical characteristics and prevention and application of the disease, aiming to provide reference for the clinical diagnosis and treatment of DKD.

1. Ancient Doctors' Knowledge of DKD

Traditional Chinese medicine believes that DKD can be classified into the category of "kidney elimination", which belongs to the syndrome of "Xiao Ke". Therefore, the etiology and pathogenesis of DKD in traditional Chinese medicine should be similar to "Xiao Ke and Xiao Dan".The name of eliminating thirst disease first appeared in "Su Wen Theory of Strange Disease", which pointed out that one of the causes of "Xiao Ke" is a Long-term food fat and sweet taste, endogenous hot and humid, long-term depression, body fluid wasting injury, then turned to Xiao Ke."Sheng Ji Zong Lu Xiao Ke Men" pointed out that Xiao Ke "for a long time, can be the disease of edema and ulcer", and summarized as "kidney qi deficiency" and "spleen wet", emphasizing that the onset of DKD is related to spleen and kidney deficiency. Zhang Lei et al. [5] conducted an exploratory study on the origin and flow of DKD TCM disease names, thus believing that "Shen Xiao" and "Xia Xiao" had a high agreement with DKD. From the Qin and Han dynasties to the Ming and Qing dynasties, ancient physicians summed up the clinical manifestations of Shenxiao, such as annoyance and thirst, hunger, turbid urine, emaciation and so on. Among them, "Taiping Shenghui prescription" recorded that the small and medium stool tastes sweet and white turbid, which is consistent with the clinical symptoms of proteinuria produced by DKD. Cataract, night blindness, sores, and other symptoms will appear in the late stage of Xiaoke, which are also complications in the late stage of modern DKD, which are recorded in ancient books such as “Xuan Ming Lunfang ·XiaoKe” and “Zhu Bing Yuan Hou Lun ·Xiao Ke”.

2. Overview of TCM Constitution

“Neijing” describes the differences of human physique through "shape" and "quality", while in Treatises on febrile Diseases, words such as "person" and "family" are used to refer to physique, such as "balance people", "win people" and so on.

From the point of view of practice, it is applied in many clinical aspects, such as guiding the treatment of the disease, predicting the therapeutic effect, and judging

The prognosis of the disease at the same time, it also points out the drug taboos of different physique, which reflects the embryonic form of separable physique, adjustable physique and adapting measures to personal conditions. Subsequently, many doctors discussed the constitution from different aspects on the basis of the “Huangdi Neijing”, which gradually enriched the content of the constitution theory. For example, Yu Chang's "Medical Law" cloud: "Men's disease in gas, women's disease in blood." It indicates gender differences in physique; Wu Jutong's "warm disease strip discrimination" contained: " childish Yang is not full, childish Yin does not grow also." Emphasize that age is an important factor affecting physical fitness. For example, Chao yuan Fang described the characteristics of allergic constitution for the first time in the “Zhu bing yuan hou lun”,Wang Shuhe described the relationship between pulse image and constitution in the Book of thr ” pulse meridian”, and in the book of the “Qianjin Fang”, Sun Simiao applied it to observation, treatment, health preservation and other aspects. Doctors in all dynasties have constantly improved their understanding of the constitution of traditional Chinese medicine, which has laid a good foundation for the study of modern constitution theory. In the 1970s, Wang Qi and other researchers constructed a clear concept of TCM constitution, that is, that is, constitution is a comprehensive and relatively stable trait [6] in morphological structure, physiological function and psychological state on the basis of innate heredity and acquired and through the epidemiological investigation, put forward the nine kinds of physical conditions of the Chinese population classification and their

characteristics, according to the clinical characteristics, is recognized by the majority of scholars(see fig.1).Influenced by Zhang Zhongjing's theory of Yin and Yang, Zhao Jinxi [7] put forward the physical classification of "three Yin and three Yang", pointing out that physical factors are the important reasons for different patients showing different symptoms, symptoms and condition changes, that is, "Conghua" of constitution(see fig.2).Although all doctors have their own views on TCM constitution, they all adhere to the principle of people-oriented and attach importance to the relationship between TCM constitution and disease, which provides new ideas for a more comprehensive understanding of diseases.

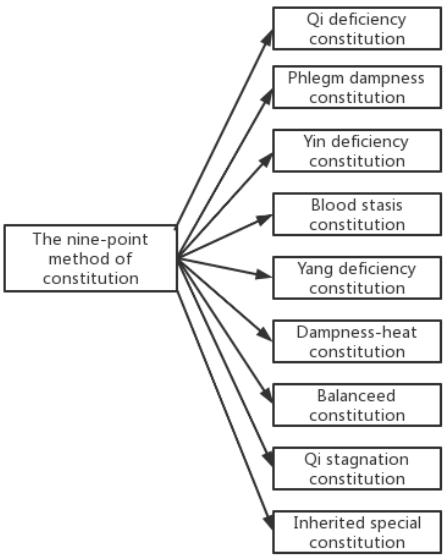

Figure 1: The nine-point method of constitution.

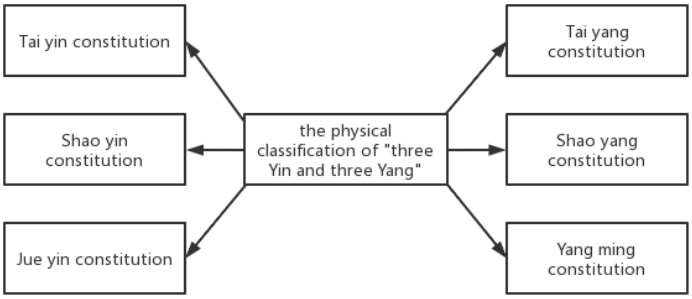

Figure 2: The constitution of “three Yin and Three Yang”

3. Correlation between DKD and TCM Physiology

Many modern scholars have carried out various and multilevel studies on DKD TCM constitution, including physical distribution characteristics, syndrome and laboratory indicators of different physical groups, clinical application of constitution, etc. Through the systematic summary of TCM constitution theory, combined with the analysis of DKD etiology and pathogenesis, it is conducive to a more comprehensive understanding of DKD and provides new ideas for DKD prevention and treatment.

3.1. Distribution Characteristics of TCM Physique in DKD

In recent years, many TCM scholars have studied the physical distribution characteristics of DKD. Although the results are not the same, the coincidence degree of high-risk physical fitness types is relatively high. Yu Jun et al. [8] studied 300 cases of early DKD patients in Wenzhou and found that qi deficiency was the most common constitution type, while Yin deficiency and blood stasis were also more common, while peace and quality was relatively rare, and blood stasis was also a risk factor for early DKD. Zhou Jianyang et al. [9] compared the constitution of early DKD and healthy people in Ningbo and found that the most common constitution types of early DKD patients in their area were blood stasis and qi deficiency. Tan Yanyun [10]

Questionnaire survey on 150 DKD patients found that the single constitution of DKD patients had the highest proportion of qi deficiency, while the two part-clamp constitutions had the highest proportion of qi deficiency and phlegm dampness, and the three part-clamp constitutions had the highest proportion of qi deficiency, phlegm dampness and Yin deficiency. The overlap rate of the above results is quite high. Zhang Rongdong et al. [11] studied the TCM constitution distribution characteristics of 236 patients with DKD and found that qi deficiency, phlegm dampness, yin deficiency, blood stasis, yang deficiency and dampness heat were high-frequency constitution. Ningde city is located in the southeast coast, with high humidity and temperature, and people like to eat "fat ", which is an important reason for the formation of partial constitution such as phlegm dampness and dampness heat. Wang Tong [12] investigated the population of DKD in northern China and found that the main types of DKD in stage III were yin deficiency, qi deficiency and blood stasis, while phlegm-dampness and dampness heat accounted for relatively low. It can be seen that the differences of region, climate, and eating habits have a certain impact on the physical distribution of DKD patients, this with "SuWen" about the geographical environment, living conditions of the description of different physical differences. In addition, Wang Tong also pointed out the relationship between age and DKD physique, that is, young and middle-aged people are dominated by yin deficiency, while old people are dominated by qi deficiency. Therefore, the elderly are the key population for the prevention and treatment of DKD, and the reason may be related to the senility and lack of source qi .The results of the above investigation on the physique distribution of DKD are not the same, and the reasons may be related to the samples, geographical limitations and other factors(see fig.3), but according to the current research, there is an obvious relationship between DKD and physique, and the high-frequency physique overlap rate of DKD in various studies is quite high, and its physique classification is basically in line with the characteristics of etiology and pathogenesis of DKD.

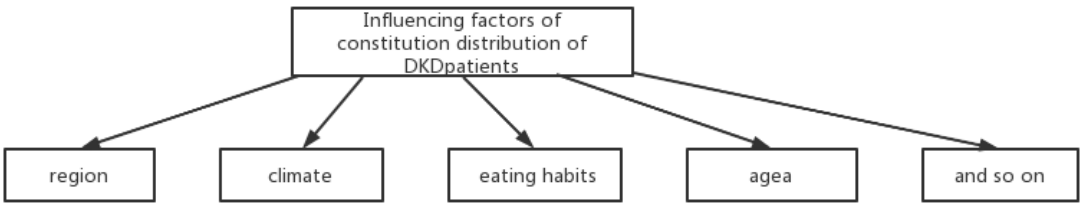

Figure 3: The factors of constitution distribution.

3.2. Discussion on Susceptible Physique of DKD based on Etiology and Pathogenesis

Different constitutions have a special susceptibility to certain diseases and causes, and DKD patients are no exception. Past Chinese doctors have attributed the incidence of DKD to insufficient

endowment, dietary irregularities, emotional disorders; excessive activity, external contraction, six excesses, mistreatment, and so on. Sun Jie et al. [13] studied 201 patients with DKD. The results showed that in the early stage of DKD, deficiency of both qi and yin was the pathogenic factor, and

Long-term disease resulted in deficiency of both yin and yang, which resulted in deficiency of both yin and yang and syndrome of dampness, dampness and heat during the disease. In the study, it is found that the proportion of qi deficiency constitution is the highest, so it is considered that qi deficiency is closely related to the occurrence and development of the disease. The spleen is mainly transporting biochemical qi and blood, so the loss of health of the spleen can easily lead to accumulation of dampness into phlegm, deficiency of qi and blood, and finally involve kidney qi. The main disease position of DKD is in the kidney, and the kidney is the congenital foundation. There is a saying in "Suwen Liujie Zangxiang Theory": "the kidney, the root of the seal, the essence is also." It shows that the function of the kidney is to seal the subtle substances in the body, and if the sealing function of the kidney is impaired, it is easy to make the subtle substances leak out; if the kidney yang is insufficient, cannot warm, Yang does not change qi, it is easy to make water and dampness stop gathering, cause edema and other manifestations, clinical manifestations are the appearance of proteinuria, the increase of biochemical products such as urea nitrogen and creatinine. Some doctors believe that DKD is secondary to diabetes, which belongs to the category of “Xiao Ke” in traditional Chinese medicine, and its basic pathogenesis is "yin deficiency and dryness heat". With the progress of diabetes, its pathogenesis evolution roughly follows the basic law of yin deficiency, qi and yin deficiency, yin and yang deficiency (see Fig.4), so there can be high-frequency constitution of qi deficiency, yin deficiency and yang deficiency. Secondly, with the development of DKD, pathological products such as blood stasis and damp turbidity accumulate. Along the southeast coast, dampness and heat are exuberant, people like to eat "fat", take medicine for a long time, and other factors can damage the spleen and stomach, resulting in damp heat, thus leading to the emergence of blood stasis, damp-heat and high-frequency physique. Modern medical research points out that glomerular endothelial cell injury, podocyte apoptosis, mesangial cell proliferation and hypertrophy, and a series of pathological changes such as glomerulosclerosis and renal interstitial fibrosis are consistent with the TCM pathogenesis of diabetes nephropathy with blood stasis and obstruction of renal collaterals during the development of the disease [14]. In other words, "blood stasis" is the pathological basis of diabetic glomerulosclerosis.

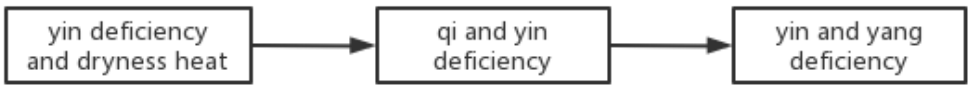

Figure 4: Pathogenesis evolution of “Xiao Ke”

3.3. Correlation between DKD Physique and Clinical Indexes

Different physical DKD has a certain correlation with some clinical indicators. Tian Zhigang's study found that in [15], the increased level of HbA 1 C will cause the hypoxia response of tissue cells, damage the vascular endothelial cells, increase the glomerular permeability, and thus accelerate the development of DKD. HbA 1 c varied among constituconstitution, indicating that HbA 1 c levels were significantly higher in DKD patients with Yin deficiency DKD than those with Yang deficiency DKD. Urinary microalbumin / creatinine have been widely recognized in the clinic as a new and reliable indicator for detecting urinary protein excretion and as one of the diagnostic criteria for DKD staging. Some studies have confirmed [16] that there are significant differences in

urinary Microalbumin / creatinine among different physiques. It is concluded that the level of urinary microalbumin / creatinine in patients with yang deficiency DKD is significantly higher than that in patients with phlegm dampness and mild DKD. The study found that the level of serum creatinine in patients with blood stasis diabetic nephropathy was higher, suggesting that the renal function damage of such patients was more serious [17].Another study showed that patients with blood stasis have high levels of hemoglobin, which may be associated with blood viscosity [18].The study of Hangzhou Honghui Hospital showed that the frequency of TGF-β1 (T869C) gene polymorphism in diabetic nephropathy group was higher than that in type 2 diabetes mellitus without diabetic nephropathy group, and there were more CC/CT genotypes in diabetic nephropathy group than in type 2 diabetes mellitus without diabetic nephropathy group. Phlegm-dampness, dampness heat and blood stasis were associated with TGF-β1 (T869C) gene polymorphism. Therefore, it is considered that physique may help to predict the occurrence of diabetic nephropathy in patients with type 2 diabetes [19].The main types of DKD, proteinuria are yang deficiency, qi deficiency and phlegm dampness. Traditional Chinese medicine believes that DKD involves the spleen, kidney, and other viscera. Deficiency of kidney qi, dereliction of duty or deficiency of middle qi, depression of qi deficiency or yang, deficiency of spleen and kidney, retention of no right or phlegm, and dampness, and stagnation of Sanjiao can lead to subtle leakage and albuminuria. From the above studies, it can be found that there are differences in the distribution of TCM constitution in different patients with diabetic nephropathy, and the physique is related to the test index and genotype.

3.4. Correlation between DKD Physique and Syndrome

The constitution and syndrome of traditional Chinese medicine are established on the basis of traditional Chinese medicine theories, which reflect the different life states of the human body. For example, some doctors believe that the emergence of a syndrome is based on constitution; therefore, the exploration of disease evidence should also be based on constitution. After the pathogenic in the human body, the different conversion is also due to the different constitution leading to the change of syndrome.Jiang Zhaozhao et al. [20] found that the constitution of patients with chronic kidney disease is mainly deficiency constitution, and there is a clear correlation between constitution and syndrome. They believed that doctors should pay attention to the influence of constitution on syndrome in clinical syndrome differentiation, and body differentiation is an important basis for syndrome differentiation.Zhang Rongdong et al. in the analysis of the correlation between TCM constitution and syndrome types of 236 patients with DKD, it was found that the clinical manifestations of patients with qi deficiency were spleen and kidney qi deficiency syndrome, qi-yin deficiency syndrome, dampness-heat trapping spleen.

Syndrome and blood stasis collateral syndrome. The most common types of patients with blood stasis are qi deficiency of spleen and kidney, deficiency of qi and yin, dampness-heat trapping spleen and blood stasis and collaterals. Most of the patients with yin deficiency were yin deficiency and heat syndrome, qi-yin deficiency syndrome, and dampness-heat syndrome; yang-deficiency patients were mainly spleen-kidney qi deficiency syndrome, qi-yin deficiency syndrome and blood stasis vein syndrome; most of the damp-heat patients were yin deficiency heat syndrome, spleen-kidney qi deficiency syndrome, qi-yin deficiency syndrome, damp-heat syndrome and blood stasis collateral syndrome. Yu Jun et al. [21] in the study of the correlation between TCM syndrome and TCM constitution of 300 patients with early DKD, it was found that qi deficiency, yin deficiency and blood stasis were mostly manifested as qi deficiency syndrome, yin deficiency syndrome and blood stasis syndrome. There was an obvious correlation between these TCM constitution types and TCM syndrome. Through the role of "Conghua", TCM, physical factors will

make patients show different types of TCM syndromes. Zhao Xiaoyan [22] studied the correlation between main physique and syndrome in 290 patients with DKD IV and found that there was an obvious correlation between physique type and syndrome in DKD patients. The syndrome types of qi deficiency were mostly spleen-kidney qi deficiency syndrome and qi-yin deficiency syndrome; the syndrome types of yin deficiency were mostly yin deficiency, dryness-heat syndrome and yin-yang deficiency syndrome, while the main syndrome types of yang deficiency were yin-yang deficiency syndrome(see Fig.5).From this, we can judge that there is a clear correlation between TCM syndromes and TCM constitution, and different physiques may determine the onset and syndrome characteristics of DKD patients.

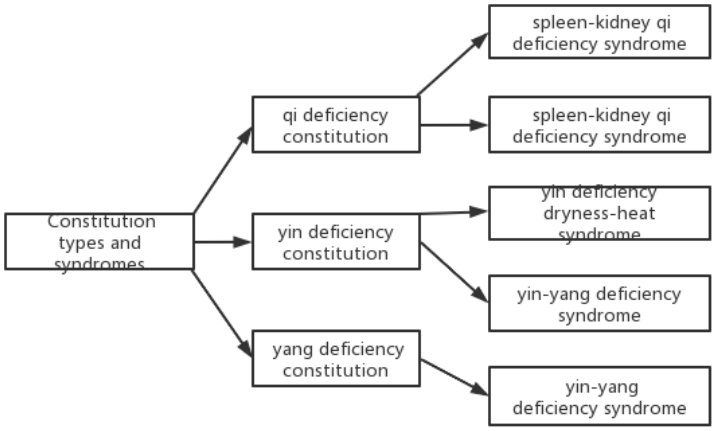

Figure 5: Correlation between DKD physique and syndrome.

3.5. Application of DKD Physique in the Prevention and Treatment of Diseases

Physique determines individual susceptibility to disease. In clinic, strengthening the attention to physique and using physique theory to guide the prevention and treatment of diseases is the main purpose of physique research, and it is also the embodiment of the thought preventive treatment of diseases and seeking the root causes of diseases in traditional Chinese medicine. Wang Qianfei [23] believes that the establishment of the principle of treatment should not only include "disease" and "syndrome", but also take people as the background, grasp the nature of the human body, and understand the emergence and evolution of diseases as a whole. It is discussed in detail from "seeking the Root of the disease", "three Reasons for treatment" and “preventive treatment of diseases". Zhao Jinxi [24] puts forward the idea of diagnosis and treatment of "constitution differentiation, disease differentiation and syndrome differentiation". He thinks that DKD is the result of the complex interweaving of various causes. The inducement of DKD can be understood by physique differentiation, and the main components of pathological factors in each stage of DKD can be grasped. Syndrome differentiation can distinguish deficiency, excess, cold, and heat according to the characteristics of patients' syndromes. Yan Xiaohua et al. [25] identified the physique of 208patients with DKD and randomly divided them into two groups. The treatment group was treated with traditional Chinese medicine according to the physical characteristics. The results showed that the improvement of symptoms and biochemical indexes in the treatment group was significantly better than that in the control group. Liu Jitao [26] used the "traditional Chinese Medicine characteristic Health Security Service Model (KY3H Model)" to treat the early DKD patients in Guiyang area. This model is guided by the thought of treating non-disease with traditional Chinese medicine, and adjusts the patients' biased constitution through diet, mental and

emotional intervention, and other non-drug intervention measures. The results show that the return rate of patients' biased physique has been improved, and the relevant experimental indicators. In particular, the level of urinary microalbumin decreased significantly. Moxibustion is a major feature of traditional Chinese medicine to treat diseases. Guan Yuanyuan [27] uses aconite, cassia bark, and astragalus to treat Yang deficiency DKD patients, which has good results in clinical symptoms, physical and chemical indicators and physical transformation, and has the advantages of safety and simplicity. Jana [28] based on the four-image medical theory, patients with DKD were divided into Greater yang people, Lesser yang people, Lesser yin people, and Greater yin people, and were treated with different traditional Chinese medicine enemata according to their physical characteristics, which finally improved the therapeutic effect of DKD.

4. Summary

In recent years, the incidence of DKD remains high, and the degree and development speed of renal injury are more serious than other types of nephropathy. The negative impact on the physical and mental health of patients cannot be underestimated. The physique of traditional Chinese medicine, as a discipline with a long history, has been well promoted and developed with the unremitting efforts of modern people. Researchers use modern medicine and advanced technology to make an in-depth study of the physiology of traditional Chinese medicine, so that the discipline has a certain scientific theoretical basis. This paper expounds the correlation between DKD and physiology from many aspects, discusses the susceptible constitution of DKD, and finds that Yin deficiency, qi deficiency, yang deficiency, blood stasis and phlegm dampness are the susceptible constitution of the disease. In the research progress of the relationship between DKD and TCM constitution, it is found that the overlap rate of DKD high-frequency constitution is quite high, and its constitution classification is basically in line with the above-mentioned susceptible constitution. There is a significant correlation between different physique DKD and some clinical indexes, so in the syndrome differentiation treatment of DKD, we should pay attention to the relationship between physique and syndrome differentiation, combined with physique differentiation and syndrome differentiation treatment, in order to improve the overall curative effect level of traditional Chinese medicine in the treatment of DKD.

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