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Research Progress on IgA Nephropathy based on Traditional Chinese Medicine Theory

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Abstract: ***This article systematically reviews the research progress on the application of Traditional Chinese Medicine (TCM) theories in the treatment of IgA Nephropathy (IgAN), focusing on the guiding value and practical application of the Collateral Disease Theory, Xuanfu Theory, and Nutrient-Qi and Defense-Qi Theory. As a common primary glomerular disease, the pathogenesis and progression of IgAN are closely related to the dysfunction of qi and blood and the impairment of zang-fu organs. The Collateral Disease Theory elucidates the core pathogenesis of renal collateral damage and blood stasis obstructing the collaterals from the perspective of "prolonged illness entering the collaterals," providing a basis for the use of the method of promoting blood circulation to remove collateral obstructions. The Xuanfu Theory focuses on the abnormal opening and closing of qi and fluid pathways, offering a new perspective for regulating water metabolism and the distribution of essence-qi at a micro-level. The Nutrient-Qi and Defense-Qi Theory, from the aspects of harmonizing qi and blood and strengthening the defensive exterior, reveals the intrinsic link between immune dysregulation and pathological damage. Studies have shown that TCM syndrome differentiation and treatment guided by these theories demonstrate unique advantages in reducing proteinuria, protecting renal function, and modulating immunity. This article aims to provide theoretical reference and conceptual insights for the integrated prevention and treatment of IgAN using both Chinese and Western medicine.***

Keywords: IgA Nephropathy, Traditional Chinese Medicine Theory, Collateral Disease Theory, Xuanfu Theory, Nutrient-Qi and Defense-Qi Theory, Research Progress**.**

1. Introduction

IgA nephropathy (IgAN) is the most common primary glomerulonephritis in China [1]. It is diagnosed based on renal biopsy pathology, characterized by the deposition of immunoglobulin A (IgA)-dominant immune complexes in the glomerular mesangial area. Its clinical manifestations vary widely in severity, making it a clinico-pathological syndrome that is fundamentally an immune complex-mediated glomerular disease [2]. It predominantly affects young and middle-aged adults, with most patients exhibiting an insidious onset. Notably, 30% to 40% of patients progress to end-stage renal disease (ESRD) within 10 to 20 years after diagnosis, becoming dependent on dialysis or kidney transplantation to sustain life, which poses a serious threat to health.

The precise pathogenesis of IgAN remains incompletely elucidated; however, the currently accepted model is the "multiple-hit hypothesis" [3]. Against a genetic background, the mucosal immune system produces galactose-deficient IgA1 (Gd-IgA1). The body then generates corresponding autoantibodies against these glycans. The subsequent binding of Gd-IgA1 and antibodies forms circulating immune complexes, which deposit in the renal mesangial area. This deposition activates the complement system, triggering an inflammatory response that ultimately leads to kidney injury and fibrosis.

In recent years, the treatment landscape for IgAN has evolved from traditional broad-spectrum immunosuppressants to a more precise and targeted era of "specific therapy." Examples include budesonide enteric-coated capsules, which act locally on the gut mucosal immune system; telitacicept, which dually inhibits B cell proliferation and plasma cell antibody production; and eculizumab, which targets the complement system. These targeted agents have more specific mechanisms of action and more manageable side effect profiles. Nevertheless, challenges such as limited efficacy and high recurrence rates persist, necessitating further in-depth research into clinical specific therapeutics. Currently, extensive clinical and basic research has confirmed that Traditional Chinese Medicine (TCM) holds certain advantages in alleviating clinical symptoms and improving the disease course for patients with IgAN.

2. Understanding of IgA Nephropathy in Traditional Chinese Medicine

The term "IgA Nephropathy" (IgAN) is not recorded in ancient TCM texts. Instead, based on its clinical manifestations, TCM categorizes it under disease entities such as "Turbid Urine" (Niao Zhuo), "Bloody Urine" (Niao Xue), "Edema" (Shui Zhong), "Kidney Water Disease" (Shen Shui Bing), and "Kidney Wind" (Shen Feng) [4].

Most scholars believe that the acute stage of IgAN is primarily characterized by Wind-Heat invading the Lung, intense Internal Fire-Heat, or Damp-Heat accumulation, leading to Blood Stasis obstructing the Collaterals, collateral damage, and blood extravasation. This phase is considered an excess pattern with pathogenic factors at its core. If the disease becomes chronic and unhealed, it typically transforms into a deficiency pattern, notably Qi Deficiency of the Spleen and Kidney. Deficiency may also lead to stasis, causing damage to the Yin Collaterals and resulting in external bleeding of blood. The fundamental pathogenesis is a deficiency-root (Ben Xu) and excess-manifestation (Biao Shi) pattern, characterized by a complex intermingling of deficiency and excess. The disease location is associated with the Lung, Spleen, Kidney, and San Jiao (Triple Energizer). The root deficiency primarily involves Qi and Yin Deficiency, Lung-Spleen Qi Deficiency, or Spleen-Kidney Deficiency. The manifestations are

primarily Wind, Dampness, Heat, and Blood Stasis.

Deng Yueyi [5] posits that this disease is based on innate constitutional insufficiency and a weakened defensive exterior. This allows Wind-Heat toxins to invade the Lung-Defense system, become retained in the Lung, and force blood to move recklessly, resulting in hematuria. Alternatively, due to habitual Spleen deficiency, Damp-Heat accumulates in the intestines and damages the kidney collaterals. Kidney Yin Deficiency may scorch the blood collaterals, also leading to hematuria. A prolonged disease course or recurrent episodes consume Qi and injure Yin. Prolonged Qi deficiency leads to the Spleen's failure to control blood, and Kidney Qi deficiency results in the leakage of essential nutrients (Jing Wei) through urine, thus forming proteinuria. Chen Yiping [6] considers IgAN a deficiency-root (Ben Xu) and excess-manifestation (Biao Shi) pattern. The root deficiency involves dysfunction of the San Jiao (Triple Energizer) and multi-organ dysfunction, while the manifestations are Blood Stasis and Damp-Heat. External to the disease, pathogenic Damp-Heat is often present. Internal retention of water-dampness leads to Damp-Heat pervading the San Jiao, causing the Kidney to lose its storage capacity and resulting in disease. Ye Chuanhui [7] attributes the root deficiency to impairment of the Lung, Spleen, and Kidney. If this root deficiency is not treated, the body becomes susceptible to external pathogens and experiences repeated attacks. The interplay between the root deficiency and Dampness, Stasis, and Heat leads to clinical manifestations such as gross hematuria and hypertension.

3. Collateral Disease Theory and IgA Nephropathy

The Collateral Disease Theory is a significant theoretical system in Traditional Chinese Medicine (TCM), focusing on the concept of the collaterals (Luo) and the transmission and evolution of diseases within the body. The term "collateral vessels" (Luomai) first appeared in Huangdi Neijing (The Yellow Emperor's Inner Canon), which states: "The main channels are the interior; those that branch transversely are the collaterals, and the branches of the collaterals are the minute collaterals". Lingshu·Yongju (The Spiritual Pivot, Chapter on Carbuncles and Abscesses) further elaborates: "When the blood is harmonious, the minute collaterals first fill and overflow, then pour into the collateral vessels; when these are all full, they pour into the main channels" [8]. The collateral vessels, branching hierarchically from the main channels (Jingmai), form a pervasive, reticulated, and arborizing network throughout the body. They interconnect vertically and horizontally, link the exterior and interior, and communicate among the zang-fu organs, serving as the pathways for the movement of qi and blood in the human body. Zhang Zhongjing, in Jinkui Yaolüe (Synopsis of the Golden Chamber), noted: "The five overstrains cause extreme deficiency, emaciation, abdominal fullness, and inability to eat… resulting from damage by food, worry, drink, sexual indulgence, hunger, and overexertion, which injure the qi of the channels, collaterals, nutrient, and defense" [9], thereby enriching the understanding of the connotation, etiology, and pathogenesis of collateral diseases.

Ye Tianshi, in Linzheng Zhinan Yi'an (Case Records as a Guide to Clinical Practice), wrote: "In the initial stage of disease, qi stagnation is in the channels; prolonged illness then leads to blood damage entering the collaterals" and "Generally, the channels govern qi and the collaterals govern blood; prolonged disease leads to blood stasis." His work extended the understanding of collateral disease from the channels and collaterals to the blood collaterals, proposing that disease initially involves qi and blood, and its progression leads to collateral damage and the formation of static blood (stasis). He was also the first to explicitly propose the term "kidney collaterals" (Shen Luo), stating in a case of a "middle-aged man with long-term deficiency of the lower origin… the disease is in the kidney collaterals." He pioneered the concept of using pungent (Xin) herbs to drain (Xie) the collaterals, establishing the therapeutic method of "unblocking the collaterals with pungent ingredients." Wang Qingren differentiated the relationship between collateral disease and blood stasis, creating famous formulas such as Xuefu Zhuyu Decoction (Drive Out Stasis in the Mansion of Blood Decoction) and Shaofu Zhuyu Decoction (Drive Out Stasis in the Lower Abdomen Decoction). Scholar Wu Yiling conceptualized the collateral system as a "three-dimensional network system," distributed according to external, middle, and internal layers, which performs physiological functions vital for maintaining human life activities at specific speeds and rhythms [10].

The extensive distribution, fine structure, and role in transporting qi and blood allow the collateral network to maintain normal physiological activities. Damage or obstruction to this network leads to stagnation of qi and blood. Collateral disease, therefore, emphasizes the invasion and impairment of these reticulated pathways during the course of prolonged illness. The foundation of the theory lies in the patency of the collateral pathways; pathological changes in collateral disease first manifest in the collaterals themselves before affecting the solid organs. Collateral disease is often closely associated with chronic conditions, reflecting the progression of illness from superficial to deeper levels. The Collateral Disease Theory encompasses two key concepts: "prolonged illness entering the collaterals" (Jiu Bing Ru Luo) and "prolonged deficiency entering the collaterals" (Jiu Xu Ru Luo). "Prolonged illness entering the collaterals" refers to the process where a progressing disease not only damages the main channels and zang-fu organs but also disrupts the flow of qi and blood within the collaterals. This disruption leads to the formation of pathological products like static blood (blood stasis) and phlegm-turbidity, which further exacerbate disease development, creating a vicious cycle. This is clinically manifested as local pain, swelling, ecchymosis, etc. "Prolonged deficiency entering the collaterals" emphasizes how chronic illness consumes the body's qi and blood. The collaterals, lacking proper nourishment, become susceptible to obstruction or invasion by pathogenic factors. This is commonly seen in clinical practice in cases of consumptive disease (Xu Lao) and general debilitation.

The kidney collaterals (Shen Luo) store essential qi (Jing Qi) densely without leakage, and promote diuresis and toxin excretion by draining without retention. They maintain a balanced state of storage and discharge, opening and closing appropriately. The kidney meridian is full, which helps to produce sperm and marrow, and the blood formed by the liver

nourishes the whole body [11]. During glomerular filtration, the entire organizational structure and functional unit are formed through the layered differentiation of larger vessels into a capillary network structure. This bears similarity to the structure of the kidney collaterals, suggesting that pathological changes of the kidney collaterals serve as the primary pathological basis for kidney diseases. Glomerular diseases are thus closely linked to collateral disease. Patent kidney collaterals ensure the orderly movement of qi, blood, and body fluids, allowing the zang-fu organs to be nourished [12]. Conversely, if the kidney collaterals are deficient, obstructed, or damaged, the "kidney gate" (Shen Guan) malfunctions, leading to dysfunction in separating the clear from the turbid. This results in malnourishment of the five zang and six fu organs, formation of pathological products, extravasation of qi and blood, and the consequent emergence of various diseases. Due to their fine and delicate structure, the flow of essential substances within the collaterals is easily obstructed. They are characterized by a pathogenic tendency towards easy stagnation and stasis, easy penetration by pathogens but difficult expulsion, and easy accumulation leading to form tangible masses [13]. Local impeded flow of qi and blood within the kidney collaterals affects nutrient supply and waste excretion, ultimately damaging renal function. Stagnation in the kidney collaterals forms static blood (stasis), increasing intraglomerular pressure and leading to pathological changes such as renal fibrosis.

In IgAN, exposure to external Wind-Heat or internal accumulation of Damp-Heat injures the blood collaterals, forcing blood to move recklessly and manifesting as hematuria. Prolonged illness inevitably leads to deficiency (Xu). Deficiency fails to move blood, resulting in blood stasis. Static blood obstructs the collaterals, preventing blood from following its proper pathways, leading to persistent hematuria. Dysfunction of the zang-fu organs, particularly weakness of the spleen and kidney, leads to the spleen's failure to contain and the kidney's failure to store. Alternatively, blood stasis obstructing the kidney collaterals can cause the leakage of essential substances, manifesting as proteinuria and hematuria. The recurrent and protracted nature of IgAN eventually causes deficiency and impairment of the lung, spleen, and kidney. This leads to failure of qi transformation, internal accumulation of turbid-dampness transforming into toxin, flooding of water-dampness, obstruction of qi dynamics, impaired water passage function, slowed blood flow forming stasis. Turbid-toxin entering the collaterals can also cause stasis, as the toxin contends with the blood, stagnating and congealing it due to the pathogenic toxin. This ultimately results in qi stagnation and blood stasis within the collaterals, internal accumulation of turbid-toxin, and the formation of accumulations within the collaterals (Luo Xi Cheng Ji).

In summary, blood stasis obstructing the kidney collaterals permeates the entire course of IgAN. This disease belongs to the category of collateral disease. Given the structural characteristic of collaterals being "easy for pathogens to enter but difficult to exit," IgAN often follows a chronic course. The kidney collaterals play an extremely important role in the occurrence and development of the disease. Its pathogenesis can be summarized as obstruction of the kidney collaterals, deficiency and impairment of the kidney collaterals, and disturbance of the kidney collaterals. The general treatment principle is "The Collaterals Function by Being Free-Flowing" (Luo Yi Tong Wei Yong).

Gao Yanbin [14], in treating IgAN, emphasizes the principle "The Collaterals Function by Being Free-Flowing." He posits that "unblocking the collaterals" (Tong Luo) means repairing the structure and restoring the function of the kidney collaterals. This involves tonifying deficiency, eliminating pathogens, dissipating bindings, attacking retained pathogens, and promoting movement of stagnancy—it is not solely referring to promoting blood circulation and resolving stasis. Wang Shirong [15] believes that dysfunction of the kidney collaterals is the core pathogenesis of IgAN. He advocates for treatment strategies based on the disease condition and stage: during the acute phase, where pathogenic excess is prominent and excess patterns dominate amidst underlying deficiency, the focus should be on expelling pathogens and unblocking collaterals. During the prolonged/migratory phase, where healthy qi gradually declines and pathogenic qi moderates, presenting as deficiency with lingering pathogens, the focus should shift to supporting the healthy qi and unblocking collaterals. The overarching method is to regulate and smooth the kidney collaterals, ensuring harmonious flow of qi and blood within them, allowing the recovery of healthy qi and stabilization of the disease.

4. The Xuanfu Theory and IgA Nephropathy

The term "Xuanfu" (Mysterious Offices or Subtle Portals) was first introduced in Huangdi Neijing (The Yellow Emperor's Inner Canon). It is recorded: "The so-called Xuanfu refers to the sweat pores" (Su Wen). Furthermore, in Su Wen·Tiao Jing Lun (Basic Questions, Chapter on Regulating the Channels), it states: "When the striae and interstices (Couli) are blocked, and the Xuanfu are obstructed, the defensive qi (Wei Qi) cannot be discharged." The Neijing integrates the functions of "sweat pores" and "Couli," proposing that the Xuanfu reside at the body's superficial level, possessing the functions of discharging sweat, regulating the harmonious flow of nutrient and defensive qi (Yingqi and Weiqi), and resisting external pathogens.

Liu Wansu extended the understanding of Xuanfu from the Huangdi Neijing [16], breaking through its spatial and functional limitations. In Suwen Xuanji Yuanbing Shi (The Etiology and Mechanism of Diseases from the Suwen), he stated: "Xuanfu means subtle and minute offices. However, Xuanfu exist in all things. They are present in human viscera and bowels, skin and hair, muscles, membranes, bones and marrow, nails and teeth, and even in all things under heaven. They are the pathways and portals for the entry, exit, ascent, and descent of qi." He theorized that Xuanfu are distributed extensively throughout the human body and all things in the world, representing an extremely refined and minute structure [17].

Scholar Chang Fuye et al. [18] consider Xuanfu to be the body's smallest structural and functional units, serving as pathways for the movement of qi dynamics (Qiji), the distribution of body fluids (Jinye), the perfusion of blood and qi, and the circulation of the spirit mechanism (Shenji). Scholar Wang Mingjie, from the perspective of the life view encompassing "form, qi, and spirit" (Xing, Qi, Shen),

proposes that Xuanfu are a continuation of the minute collaterals (Sun Luo) and are the portals for the entry, exit, ascent, and descent of nutrient and defensive qi, blood and qi, body fluids, and the spirit mechanism [19]. The Xuanfu theory represents a refinement of TCM histology and physiology, expanding the visceral manifestation (Zangxiang) theory from a microscopic perspective [20]. The essence of Xuanfu is a "pathway" system from the TCM viewpoint.

Xuanfu maintain the connection between all parts of the body, both superficial and deep. Superficially, they are the "external Xuanfu," such as sweat pores and Couli, which communicate with nature and the environment. Internally, they are the "internal Xuanfu," such as kidney Xuanfu or lung Xuanfu, facilitating material exchange and information communication [19]. As pathways, Xuanfu not only nourish the whole body but also serve as the route for the struggle between healthy qi and pathogens and the advancement and retreat of pathogenic factors. When Xuanfu are open, qi and blood flow freely; once they become closed, yang qi becomes depressed and constrained, leading to the development of various diseases [21].

The basic pathogenesis of Xuanfu theory is excessive opening or excessive closing, both of which can lead to Xuanfu blockage (Xuan Bi). The corresponding therapeutic principle is primarily to open and unblock the Xuanfu [22]. Xuanfu has the characteristics of universality, microscopism, circulation and openness. Traditional medicine has no record of kidney Xuanfu, but many scholars have connected kidney and Xuanfu through the "method of taking images and comparing categories".

Scholar Han Shisheng et al. [23] compared the slit diaphragm formed between podocyte foot processes in the glomerulus to the kidney's Xuanfu. The slit diaphragm is a pore-like structure, morphologically similar to the conceptual Xuanfu. The kidney stores essence and regulates the body's fluids and blood. The normal movement, distribution, and perfusion of fluids and blood rely on the proper opening, closing, and free flow of Xuanfu. The kidney possesses mechanical and charge barriers that maintain normal filtration function, allowing for the selective filtration of substances, which is analogous to the free-flowing and opening-closing characteristics of Xuanfu. The pathology of IgAN can manifest as podocyte foot process effacement (fusion), representing a dysfunction in the opening and closing of Xuanfu, clinically presenting as proteinuria and edema.

Yang Jiamin et al. [24] consider the podocyte slit diaphragm to be the ultrastructural equivalent of Xuanfu. Through experiments, they found that the Guben Tongluo Formula could reduce proteinuria in IgAN model rats, regulate the mRNA expression of podocyte proteins Podocin and α-actinin-4, and repair the filtration barrier. Zhu Qin et al. [25] analogized the glomerular filtration barrier to the Xuanfu (subtle portals) of the kidney, proposing that its blockage, atrophy/closure, or excessive opening and leakage leads to disease pathogenesis. Zhang Tiane et al. [26] suggested that aquaporins (AQPs), which facilitate water molecule transport across membranes and influence extracellular fluid, share functional similarities with the Xuanfu's role in promoting the movement of qi and fluids. They proposed that aquaporins might be the modern correlate of Xuanfu. Li Miao et al. [27] found through research that Ephedra (Mahuang), with its acrid-warm properties to unblock the Xuan, increased 24-hour urine volume and decreased 24-hour urine protein in rats via its decoction and active components. The mechanism may be related to the downregulation of renal aquaporin AQP1 and AQP2 expression.

Ren Xuelei et al. [28] posit that IgAN is based on qi deficiency of the lung or kidney. Dysfunctional opening and closing of the external Xuanfu allow invasion of external wind-heat toxins, leading to internal accumulation of heat-toxin. The internal Xuanfu become blocked due to this stagnation, finally resulting in the congealment of phlegm and stasis. "Dysfunctional opening and closing of the Xuanfu" permeates the entire disease course. The treatment principle is to dredge the Xuanfu, heavily using acrid (Xin) herbs to open and unblock, using tonification to achieve free flow (Yi Bu Wei Tong), and resolving phlegm and expelling stasis, thereby reviving the spirit mechanism and regulating qi and blood.

Zheng Yu et al. [29] believe that "Xuanfu stagnation and blockage" (Xuan Fu Yu Bi) in the lung, spleen, and kidney is the core pathogenesis of IgAN. Deficiency and impairment of the zang-fu organs lead to unconsolidated Xuanfu, allowing wind pathogens to take advantage of the deficiency to invade. Damp-heat and static blood form, leading to Xuanfu stagnation and blockage. Ba Yuanming [30] considers "prolonged illness entering the collaterals" (Jiu Bing Ru Luo) key in IgAN, with the pathological characteristics being root deficiency and manifestation excess. The disease arises from external contraction of wind pathogens, which lodge in the kidney collaterals. The root is deficiency, often yin deficiency, progressing to qi and yin deficiency over time. Damp-heat congestes the collaterals, ultimately leading to deficiency of both yin and yang, with turbid-toxin and stasis obstructing the kidney collaterals. He emphasizes the treatment principle of "The Collaterals Function by Being Free-Flowing," focusing on fortifying the spleen and supplementing the kidney, boosting qi and nourishing yin to support the right qi. Concurrently, he stresses dispelling wind and clearing heat, expelling dampness and resolving turbidity, and activating blood to resolve stasis and unblock the collaterals. Lu Peng et al. [31] integrate the Xuanfu theory with the Collateral theory, proposing that the microscopic structures of Xuanfu and collaterals pervade the kidney system, with Xuanfu being the portals to the retiform pathways of the collaterals.

5. The Nutrient-Qi and Defense-Qi Theory and IgA Nephropathy

The concepts of Nutrient-Qi (Yingqi) and Defense-Qi (Weiqi) were first documented in Huangdi Neijing (The Yellow Emperor's Inner Canon). Lingshu Jing·Ying Wei Sheng Hui (The Spiritual Pivot, Chapter on the Generation and Convergence of Nutrient and Defense) states: "Humans receive qi from food grains. The grains enter the stomach and are transmitted to the lung. The five zang and six fu organs all thereby receive qi. The clear portion becomes the Nutrient-Qi; the turbid portion becomes the Defense-Qi." Under physiological conditions, Defense-Qi resides exteriorly, providing warmth and defense, while internally harmonizing

with Nutrient-Qi to aid its movement and distribution. Nutrient-Qi resides interiorly, transforming to produce blood and nourish the body, while externally harmonizing with Defense-Qi. This state is known as the harmonious regulation of Nutrient and Defense (Ying Wei He Xie), where yin is calm and yang is firm, preventing the occurrence of disease.

Modern research suggests that Nutrient-Qi is analogous to nutrients such as carbohydrates, fats, and proteins, serving cellular nutritional metabolism and influencing immune function [32]. The level of cellular nutritional metabolism determines the strength of the body's immune efficacy [33]. Nutrient and Defense are the functional manifestations of Qi and Blood, while Qi and Blood constitute the substantive basis of Nutrient and Defense. Thus, the Nutrient and Defense system represents one of the functional expressions of Qi and Blood.

Zhang Ke [34] posits that the functions of Defensive Qi (Wei Qi) are analogous to the immune defense and clearance of foreign pathogens performed by immune cells such as T cells, B cells, and leukocytes. Liu Xiao et al. [35] suggest that Defensive Qi (Wei Qi) is materially represented by lymph and tissue fluid, while Nutrient Qi and Blood (Ying Blood) correspond to peripheral blood cells. They propose that the immune cells and immunologically active substances within the lymphatic system constitute the material basis of Defensive Qi. The pathways (Meridians/Jing Luo) through which Defensive Qi circulates coincide with the trafficking routes of immune cells and also demonstrate convergence in terms of temporal rhythms [36]. Thus, it is evident that Nutrient and Defensive Qi (Ying Wei) serve as the body's barrier and form the material foundation of the immune system. The occurrence of Immunoglobulin A Nephropathy (IgAN) is primarily attributed to an imbalance (disharmony) of Nutrient and Defensive Qi (Ying Wei Shi He). When the Ying and Wei are harmonized, the circulation is regulated, the qi and blood are full, the pores and tissues are dense, and the strength of the Wei to protect against evil is strong, which can eliminate immune complexes in time to avoid the occurrence of diseases.

Patients with IgAN often present with an underlying deficiency of Kidney Qi (Shen Qi Xu). As stated in the Lingshu Jing (Spiritual Pivot), Chapter 18 (Ying Wei Sheng Hui): "Defensive Qi originates from the Lower Jiao." Since Defensive Qi is rooted in the Kidneys, its deficiency leads to impaired warming and securing functions. This compromised external defense allows for the invasion of pathogenic factors, which then lodge latently within the body. The interaction and conflict between the Nutrient-Defensive systems and the lurking pathogen cause Defensive Qi to stagnate and become replete and stagnant. Its inherently swift and smooth nature becomes intensified, leading to emptiness in the meridians and dissociation between Qi and Blood. Consequently, Nutrient and Defensive Qi cannot follow their normal pathways or perform their functions, exacerbating their separation. This process consumes and injures the Nutritive Yin (Ying Yin), which can no longer moisten the tissues or restrain the Defensive Qi. The Defensive Qi, failing in its guardian role, turns inward and damages the body itself, manifesting as the autoimmune dysfunction characteristic of IgAN.

The hyperactivity and accelerated movement of Defensive Qi are analogous to the vascular dilation, increased blood flow, aggregation of inflammatory factors, and release of chemokines to inflammatory cells that occur during an immune response. This leads to the recruitment and accumulation of neutrophils and monocyte-macrophages at the site of lesion, triggering inflammatory reactions. Persistently, the constant engagement of Defensive Qi in combating pathogens leads to its consumption, while Nutrient Blood becomes stagnant, and its production source becomes depleted. With Nutrient and Defensive Qi failing to circulate normally, pathological products such as Blood Stasis (Yu Xue) and Phlegm-Turbidity (Tan Zhuo) form within the kidneys. These pathological changes correspond consistently with the observed histological manifestations in IgAN, including mesangial cell proliferation, increased intracapillary cellularity, segmental glomerulosclerosis or adhesion, interstitial fibrosis, and crescent formation [37].

Du Jieli [38] proposed that the pathogenesis of Immunoglobulin A Nephropathy (IgAN) involves an external component characterized by disharmony between Nutritive and Defensive Qi (Ying-Wei disharmony) with pathogenic factors invading the superficial muscles and interstices, and an internal component of deficiency of the Spleen and Kidneys, resulting in insufficient generation of Qi and Blood. The interaction of these internal and external factors leads to the accumulation of pathological products in the renal collaterals, thereby initiating the disease. The fundamental treatment principle is to harmonize Nutritive and Defensive Qi. During the acute phase, the focus is primarily on expelling wind and eliminating pathogenic factors. In the chronic phase, the main strategy shifts to warming the Kidneys and strengthening the Spleen. Li Wenwen [39] adopted the principle of harmonizing Nutritive and Defensive Qi as the therapeutic approach. She developed a self-formulated prescription called "Yiqi Guben Tiao Mian Decoction" (Benefit Qi, Consolidate the Root, and Regulate Immunity Decoction) for the treatment of IgAN, which has demonstrated favorable clinical efficacy.

6. Discussion

As the most prevalent primary glomerular disease worldwide, Immunoglobulin A Nephropathy (IgAN) presents with a complex pathogenesis and diverse clinical manifestations. This article reviews the research progress on the application of traditional Chinese medicine (TCM) theory in the treatment of IgAN, focusing on the guiding value and practical application of the Collateral Disease Theory, the Xuanfu Theory, and the Nutrient-Defensive (Ying-Wei) Theory.

The Collateral Disease Theory elucidates the essence of IgAN from a micropathological perspective, characterizing it as "obstruction of the collateral vessels". It identifies the interplay of dampness-heat, blood stasis, and toxins, leading to renal collateral injury, as the key pathogenesis. The therapeutic principle emphasizes "dredging the collaterals" through methods such as promoting blood circulation and resolving stasis, clearing heat, resolving dampness, and detoxifying to unblock the collaterals. Formulas like Tongxinluo or preparations containing Panax notoginseng (Sanqi) can effectively improve renal microcirculation and

delay disease progression.

The dysfunction in the opening and closing of the renal Xuanfu (subtle portals) is a critical aspect in the development and progression of IgAN. Blockage of the Xuanfu impedes the flow of qi and fluids, resulting in the internal accumulation of turbid toxins and the leakage of essential nutrients (e.g., proteinuria). Treatment focuses on “unblocking the Xuanfu” as the core strategy. This involves using wind-medicinals (such as Ephedra [Mahuang], Saposhnikovia root [Fangfeng], and Cicada molting [Chantui]) for their acrid and dispersing properties to open and unblock, combined with therapies to drain dampness and activate blood circulation. This approach aims to disperse stagnation, restore the normal flow of qi and fluids, and thereby control proteinuria and hematuria.

The Nutrient-Defensive (Ying-Wei) Theory addresses systemic functional regulation. It proposes that weakness of the defensive qi failing to secure the exterior and disharmony between the nutrient and defensive systems are significant factors contributing to the protracted course of IgAN. Harmonizing Nutrient and Defensive Qi (e.g., with formulas like Cinnamon Twig Decoction [Guizhi Tang] and its variants) helps stabilize the internal environment, regulate immune dysfunction, and reduce relapse triggered by infections.

In summary, while these theories emphasize different aspects, they are interconnected: the Collateral Disease Theory focuses on structural pathological damage, the Xuanfu Theory emphasizes the patency of pathways for qi and fluids, and the Ying-Wei Theory highlights systemic functional homeostasis. Together, they form an integrated TCM diagnostic and therapeutic framework based on the unity of “Disease - Mechanism - Pattern”.

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