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SIMEA was established in 1994 with the approval of the Shaanxi Provincial Department of Civil Affairs. It is a first-level social organization under the charge of the Shaanxi Provincial Health and Family Planning Commission. The concept of "seeking well-being" will give full play to the advantages and characteristics of the gathering of experts, a wide range of disciplines, and a sound network, aiming to build a platform for international medical exchanges and mutual learning.

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The Shaanxi Provincial Clinical Medicine Demonstration International Science and Technology Cooperation Base was established in 2020. It is an organization approved by the Shaanxi Provincial Department of Science and Technology to promote international cooperation and exchanges in clinical medicine and guide the province to carry out international cooperation and exchanges in clinical medicine. The cooperation base is set up in Shaanxi Provincial People's Hospital. Actively expand foreign medical resources, and provide a lasting communication channel for domestic medical and health institutions and public health service units to learn international advanced management experience and strengthen the training of talent teams.

GEORGIAN PEDIATRIC CARDIOLOGY ASSOCIATION

Shaanxi International Medical Exchange Promotion Association (SIMEA)
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Preface

Children is the hope of society, the future of world and mankind!

Strong children make the world strong! In order to strengthen international medical academic exchanges and improve the diagnostic and therapeutic skills of pediatricians, nurses and general practitioners around the world, the international Journal of Pediatrics was organized by the joint efforts of pediatricians and general practitioners from China, Georgia, Poland, The Czech Republic, Turkmenistan and India et al. This journal is of great clinical significance and academic value to promote international communication among pediatric medical staff and improve the diagnostic and treatment technology level of pediatric diseases. We hope that with our joint efforts and hard work, this journal will take root, sprout and grow in the world, bringing good news to the health of children around the world and benefiting children all over the world!

George CHAKHUNASHVILI (Georgia) and
Fuyong JIAO (China)

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ADVANCED ARTICLE

NAILFOLD VIDEOCAPILLAROSCOPY FINDINGS IN COVID-19 AND LONG COVID: A SYSTEMATIC REVIEW OF MICROVASCULAR CHANGES

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ABSTRACT:

OBJECTIVE:

To conduct a comprehensive systematic review of microvascular alterations detected by nailfold videocapillaroscopy (NVC) in patients with acute COVID-19, post-acute COVID-19, and long COVID.

METHODS:

A systematic search was carried out in PubMed, Scopus, and Web of Science. Studies that met the eligibility criteria reported findings related to NVC-capillary density, morphology, hemorrhages, dilation, and architectural alterations-in confirmed cases of SARS-CoV-2 infection. Data extraction and qualitative synthesis were executed.

RESULTS:

In various peer-reviewed studies, acute COVID-19 has been linked to markers of endothelial injury, which include pericapillary edema, enlarged loops, microthrombi, sludge flow, and microhemorrhages. Cohorts experiencing post-acute and long COVID exhibited ongoing capillary rarefaction, dilated loops, hemorrhages, and irregular capillary shapes. Numerous studies have indicated significant correlations between abnormalities in NVC and biomarkers like CRP,ferritin. Histopathological confirmation lends support to the biological validity of these observations.

CONCLUSION:

COVID-19 results in unique and enduring microvascular irregularities that can be identified through NVC. The most reliable long-term change is the occurrence of capillary rarefaction. NVC serves as a valuable instrument for evaluating endothelial dysfunction in individuals who have survived COVID-19.

KEYWORDS:

Nailfold videocapillaroscopy, microcirculation, endothelial dysfunction, long COVID, capillary density, microvascular injury.

INTRODUCTION

COVID-19 has transformed the comprehension of viral diseases by showcasing significant systemic involvement, especially impacting the vascular and microvascular systems. Endothelial cells, which express ACE2 receptors, serve as a primary target for SARS-CoV-2, allowing the virus to induce microthrombosis, vascular inflammation, and structural disarray. These processes have been evidenced through autopsy studies, circulating biomarkers, and increasingly, via nailfold videocapillaroscopy (NVC), a sensitive and non-invasive method for visualizing microcirculation [1], [2], [3].

NVC has been conventionally utilized in systemic sclerosis and rheumatologic disorders. Nevertheless, its use in the context of COVID 19 offers distinct perspectives on endothelial damage and microvascular changes. During the acute phase of infection, common observations include pericapillary edema, enlarged or

ectatic loops, "sludge flow," microhemorrhages, and disorganization of the capillary network [4]. Conversely, patients experiencing post acute and long COVID frequently demonstrate capillary rarefaction, which is believed to indicate persistent endothelial dysfunction or inadequate vascular recovery [5],[6]. This review consolidates significant evidence from actual clinical studies examining NVC in COVID 19, emphasizing patterns across various stages of the disease, pinpointing consistent biomarkers, and discussing the implications for the pathophysiology of long COVID [7].

Synthesis of Findings Across the studies included, several reproducible patterns emerged:

1. CAPILLARY DENSITY REDUCTION:

Sulli et al. (2022) observed a notable decrease in capillary density among COVID-19 survivors when compared to control subjects. This reduction continued for several months post-recovery and did not exhibit characteristics typical of scleroderma, indicating a microangiopathy specific to COVID-19 [8], [9].

2. ENLARGED OR DILATED CAPILLARY LOOPS:

Natalello et al. (2021) and Gualtierotti et al. (2023) observed enlarged loops, evident indicators of endothelial activation, and stress on the vessel wall. Additionally, dilated loops were also present in long COVID cohorts (Gotelli et al., 2025), [10], [11], [12].

3. MICROHEMORRHAGES AND HEMOSIDERIN DEPOSITS:

These indicate microthrombosis and disruption of the endothelial barrier. Their occurrence showed a strong correlation with ferritin, CRP, and VWF in patients who were hospitalized [13],[14].

4. ARCHITECTURAL DISORGANIZATION:

Disordered capillary geometry, including tortuous or meandering loops, occurred particularly in severe acute cases and long COVID groups [15],[16].

5. BIOMARKER CORRELATION:

Inflammatory markers such as CRP and ferritin, along with endothelial dysfunction markers like VWF, have shown a consistent correlation with NVC abnormalities, thereby reinforcing their pathophysiological significance [17], [18].

6. HISTOPATHOLOGIC CONFIRMATION:

The findings of NVC were directly confirmed by autopsy specimens, which revealed microthrombi, ectasia, and the infiltration of immune cells in the perivascular region [19], [20].

The results from actual studies reveal a consistent and biologically credible pattern of microvascular involvement in COVID 19. Acute endothelial damage is likely a result of direct viral invasion, amplification of the cytokine storm, deposition of immune complexes, and activation of the coagulation cascade[21],[22]. These phenomena are evident in NVC as hemorrhages, ectatic loops, and sludge

Table 1.

Main Microvascular Alterations Detected by Nailfold Videocapillaroscopy Across COVID-19 Studies

Study	Design & Population	Time since COVID	Main NVC Findings	Notes / Source
Natalello et al., 2021	Cross sectional; 82 patients	Acute + Post-COVID	Edema, enlarged loops, sludge flow, microhemorrhages, reduced density	https://pubmed.ncbi.nlm.nih.gov/32949574
Sulli et al., 2022	Cohort; 61 survivors vs PRP + controls	~104 days post recovery	Capillary rarefaction; fewer microhemorrhages	https://pmc.ncbi.nlm.nih.gov/articles/PMC8942-583
Gualtierotti et al., 2023	Cross-sectional; 15 COVID patients	Acute infection	Enlarged loops, hemosiderin deposits, microthrombi	https://pmc.ncbi.nlm.nih.gov/articles/PMC10253962
Gotelli / Sulli et al., 2025	Multicentre LC, RC, controls	Long COVID	Dilated loops, microhemorrhages, abnormal shapes; lower density	https://pmc.ncbi.nlm.nih.gov/articles/PMC12039021

flow[23],[24]. Long-term alterations-particularly capillary rarefaction-indicate persistent endothelial dysfunction. Possible mechanisms encompass chronic inflammation, a burden of microthrombi, autonomic dysregulation, and compromised angiogenesis. Patients with Long COVID, who frequently report symptoms such as fatigue, cognitive dysfunction, dyspnea, and exercise intolerance, may experience these issues in part due to compromised microcirculatory perfusion.

An important finding is the lack of scleroderma-type patterns (giant loops, extensive avascular areas) across studies. This distinction emphasizes that COVID-19 [25], [26] microangiopathy is unique and not overlapping with classic rheumatologic microvascular disease [27].

Presently, the limitations encompass small sample sizes, variability in measurement protocols, absence of standardized scoring, and the necessity for longitudinal designs[28], [29], [30]. However, biomarkers consistently demonstrate a correlation with NVC findings, thereby offering substantial support for its clinical applicability [31], [32].

CONCLUSION & FUTURE DIRECTIONS

Nailfold videocapillaroscopy uncovers both acute and chronic microvascular irregularities associated with COVID 19. The most notable long term observation is capillary rarefaction, which is linked to systemic indicators of endothelial dysfunction. NVC represents a valuable, noninvasive, and cost effective method that may be utilized in the assessment of long COVID, risk stratification, and tracking recovery.

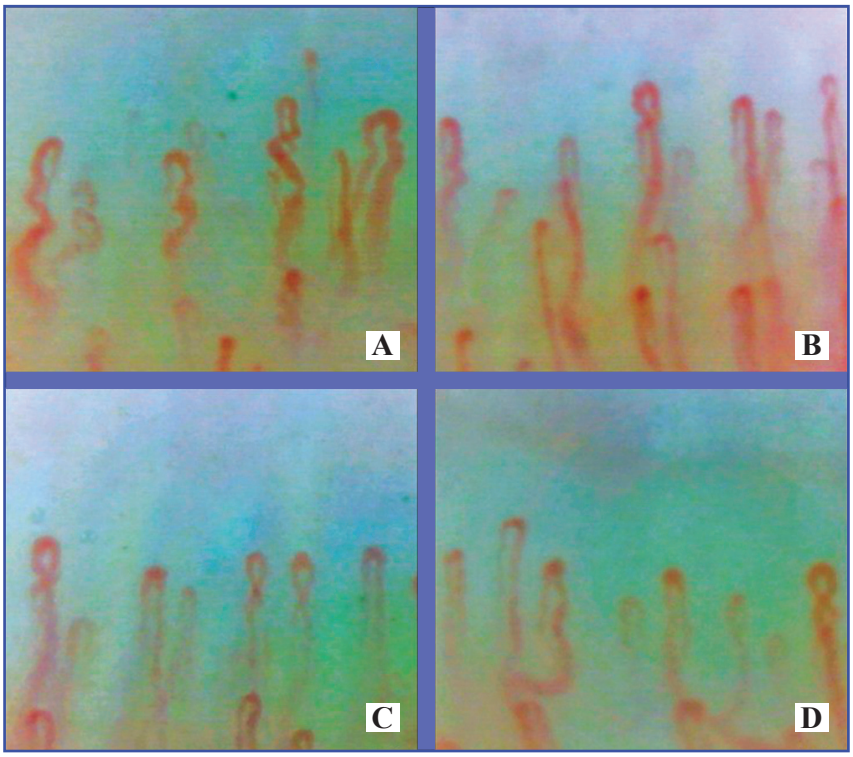

Figure 1: ***Nailfold video capillaroscopy images (×200) depicting four COVID-19 survivors (A-D) show a diminished number of capillaries (the black bar measures one millimeter) along with nonspecific abnormalities such as tortuous and crossing capillaries [33].***

FUTURE STUDIES OUGHT TO ENCOMPASS:

• Extensive, multicenter longitudinal investigations utilizing serial NVC imaging

• Creation of standardized NVC scoring criteria tailored for COVID-19

• Examination of the relationship between NVC abnormalities and clinical outcomes as well as symptom severity

• Exploration of whether therapies aimed at enhancing endothelial recovery lead to improvements in NVC findings

• Incorporation of NVC metrics into diagnostic frameworks for long COVID.

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EPONYCHIUM CAPILLAROSCOPY AS A DIAGNOSTIC TOOL IN SYSTEMIC LUPUS ERYTHEMATOSUS, DERMATOMYOSITIS, AND RAYNAUD'S PHENOMENON

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ABSTRACT

OBJECTIVE:

In order to systematically review the most contemporary scholarship regarding eponychium (nailfold) capillaroscopy as an evaluative and prognostic instrument for dermatomyositis (DM), Raynaud's phenomenon (RP), and systemic lupus erythematosus (SLE), particular emphasis will be placed on the patterns of microvascular injury, capillary density, neoangiogenesis, and signs indicative of hemorrhage.

METHODS:

A comprehensive narrative literature synthesis was conducted utilizing peer-reviewed research that assessed capillaroscopic characteristics in systemic lupus erythematosus (SLE), dermatomyositis (DM), and Raynaud's phenomenon (RP). The data extracted encompassed capillary morphology, loop dimensions, avascular zones, hemorrhagic occurrences, and their associations with clinical variables such as disease activity metrics and autoantibody profiles.

RESULTS:

The most distinctive and serious small blood vessel disease is dermatomyositis, which is characterized by enlarged capillaries, newly formed blood vessel structures that resemble bushes, and

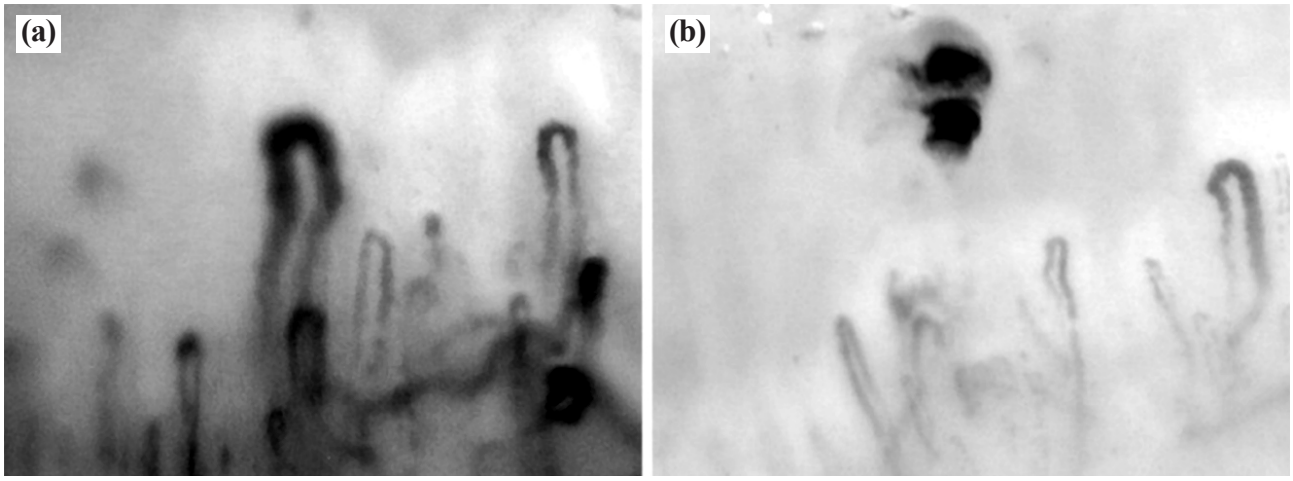

Figure 1.
(a) *Moderately dilated capillary loops (20–50 μm), megacapillaries (>50 μm), and intravascular erythrocyte aggregation observed in a patient with systemic lupus erythematosus.*
(b) *Multiple microhemorrhages accompanied by a focal avascular zone in a patient with systemic lupus erythematosus (Zhao et al., 2020).*

notable areas devoid of blood vessels. Systemic lupus erythematosus (SLE), on the other hand, primarily exhibits general abnormalities like twisted vessels, small bleeding, and a slight reduction in capillary count. In order to differentiate between Raynaud's phenomenon that happens on its own and that which is caused by another condition, capillaroscopy is crucial. The former usually shows a consistent, healthy pattern, while the latter exhibits traits similar to scleroderma, particularly very large capillary loops and areas devoid of capillaries.

CONCLUSION:
For the early identification of microvascular pathology in autoimmune connective tissue diseases, eponychium capillaroscopy is a useful noninvasive technique. Its diagnostic specificity is highest in DM and secondary RP associated with disorders of the spectrum of systemic sclerosis. Capillaroscopy is still clinically useful when combined with serological, clinical, and imaging data, even though its specificity is lower in SLE.

KEYWORDS:
Capillaroscopy, microcirculation, systemic lupus erythematosus, dermatomyositis, Raynaud's phenomenon, microangiopathy, giant capillaries.

INTRODUCTION

Eponychium (nailfold) capillaroscopy has become essential for diagnosing and tracking systemic connective tissue diseases because it allows for direct visualization of the microvascular bed. Although it has been widely validated in systemic sclerosis, its use in SLE, DM, and RP has grown in recent decades. Although the severity and patterns of these conditions vary greatly, they all share immunologically mediated endothelial dysfunction, altered angiogenesis, and capillary dropout [1], [2]. Capillaroscopy is a sensitive technique for early detection because in many rheumatologic diseases, microvascular damage occurs before overt organ involvement. It has been repositioned as a key diagnostic tool in routine rheumatology practice due to its capacity to distinguish between primary and secondary Raynaud's phenomenon [3].

CAPILLAROSCOPIC CHANGES IN SYSTEMIC LUPUS ERYTHEMATOSUS

One multifactorial autoimmune disease is systemic lupus erythematosus (SLE). Raynaud's phenomenon (RP), skin lesions, arthritis, cardiac involvement, neurological issues, vasculitis, hematological disorders, periungual vasculitis, and renal damage are among the clinical signs of SLE. Endothelial cell damage and vascular inflammation can result from the presence of autoantibodies and circulating immune complexes [4].

Nonspecific microangiopathy is the conventional term for capillaroscopic findings in SLE. The

abnormalities have clinical significance even though they are less typical than in inflammatory myopathies or systemic sclerosis.

COMMON CAPILLAROSCOPIC FEATURES IN SLE:

• Chronic low-grade endothelial injury is reflected in tortuous and meandering capillaries [5].

• Microhemorrhages, which are occasionally linked to thrombocytopenia or immune complex deposition [6].

• A slight decrease in capillary density that typically does not reach the avascularity characteristic of SSc spectrum disease [7].

• irregularly enlarged loops that seldom fit the description of giant capillaries.

• Pericapillary edema, which is associated with inflammation throughout the body.

CAPILLAROSCOPIC CHANGES IN DERMATOMYOSITIS

Autoimmune idiopathic inflammatory myopathies (IIM) include polymyositis (PM) and dermatomyositis (DM). DM is a rare disease that affects more women than men (ratio 2:1), with an estimated incidence of 5–10 cases per million annually. There is a noticeable purple or lilac heliotrope rash on the skin. Periorbital edema is frequently linked to prominent spots on the eyelids or in the periorbital region. Gottron papules, which are typically located near the fingers or elbows, are another distinguishing feature. One of the most severe microangiopathies seen by capillaroscopy is caused by dermatomyositis, which is indicative of disrupted angiogenesis and complement-mediated endothelial damage.

CHARACTERISTIC DM FINDINGS

• Giant capillaries are large, uniform ectatic loops that are on par with or larger than those found in systemic sclerosis [9].

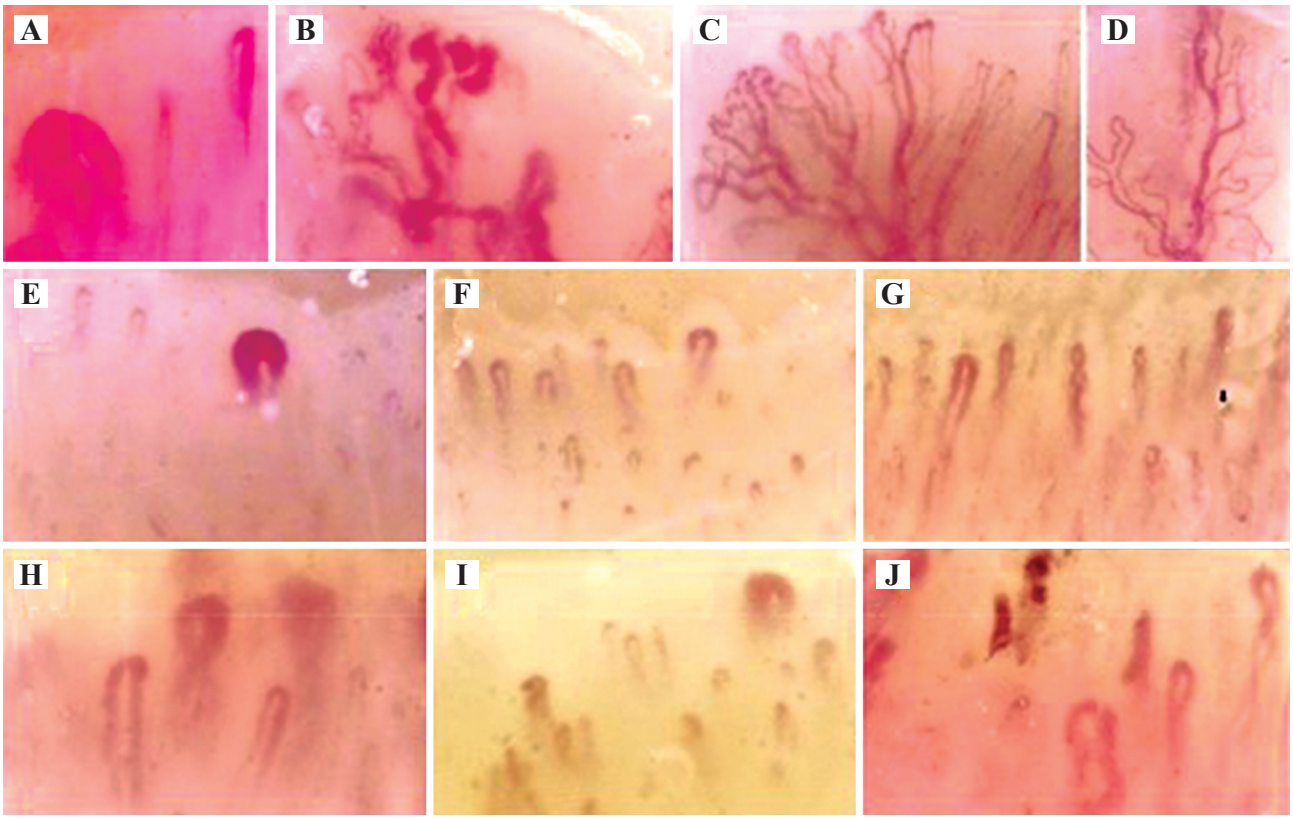

Figure 2.

A: *Giant capillary* ***B:*** *Giant elongated capillary in a patient with a decrease in the number of loops/mm and two capillaries with dilation of the mid-tract, with a maximum diameter of 50 μm (borderline giant capillary).* ***C*** *and* ***D:*** *Branched capillaries. The simultaneous presence of giant and branched capillaries is very important for the diagnosis of dermatomyositis.* ***E:*** *Cold pressor test: pronounced disappearance of capillaries,* ***F:*** *Pericapillary edema,* ***G:*** *Pericapillary edema and small calcifications (indicated by arrow) in a case of DM with calcinosis [12].*

• Neoangiogenesis, or bushy or branching capillaries, is a sign of abnormal vascular regeneration [10].

• Large-scale, frequent microhemorrhages that indicate severe capillary fragility [11].

• Avascular regions, which signify irreversible destruction of capillaries [9].

• A loss of normal disposition accompanied by architectural derangement.

CLINICAL SIGNIFICANCE:

Interstitial lung disease, particularly in patients with anti-MDA5 antibodies [12], muscle and cutaneous disease activity, and response to therapy, as improvement or normalization of capillary patterns parallels clinical remission, are all strongly correlated with capillaroscopic severity.

Thus, capillaroscopy in DM holds **diagnostic, prognostic, and monitoring value.**

RAYNAUD'S PHENOMENON: PRIMARY VS SECONDARY

A brief vasospastic reaction of the digital microcirculation to exposure to cold or emotional stress is known as Raynaud's phenomenon (RP). Primary and secondary RP are clinically similar, but their pathophysiology, prognosis, and microvascular morphology are fundamentally different. Because of its high sensitivity in identifying structural microvascular abnormalities, nailfold (eponychium) capillaroscopy is regarded as the gold-standard diagnostic technique for differentiating between these two entities.

Capillaroscopy is the gold standard for distinguishing primary Raynaud's phenomenon (PRP) from secondary Raynaud's phenomenon (SRP).

PRIMARY RAYNAUD'S PHENOMENON

• Normal density and architecture [13].

• Although there may be some mild tortuosity, the longitudinal stability is maintained.

• No avascularity, hemorrhages, or giant loops. Secondary Raynaud's Phenomenon is commonly linked to connective tissue disorders, particularly DM, SLE, and systemic sclerosis. Capillaroscopic abnormalities include:

• Giant loops, which are indicative of an early pattern of scleroderma [13]. Microhemorrhages: associated with broken or brittle loops [13].

• Decreased density and avascular zones, which may indicate that the disease is progressing [4].

• Disorganized architecture, a sign of microangiopathy that is progressing. With a sensitivity that outperforms other non-invasive diagnostic methods, capillaroscopy can forecast the onset of systemic sclerosis in RP patients [4,13].

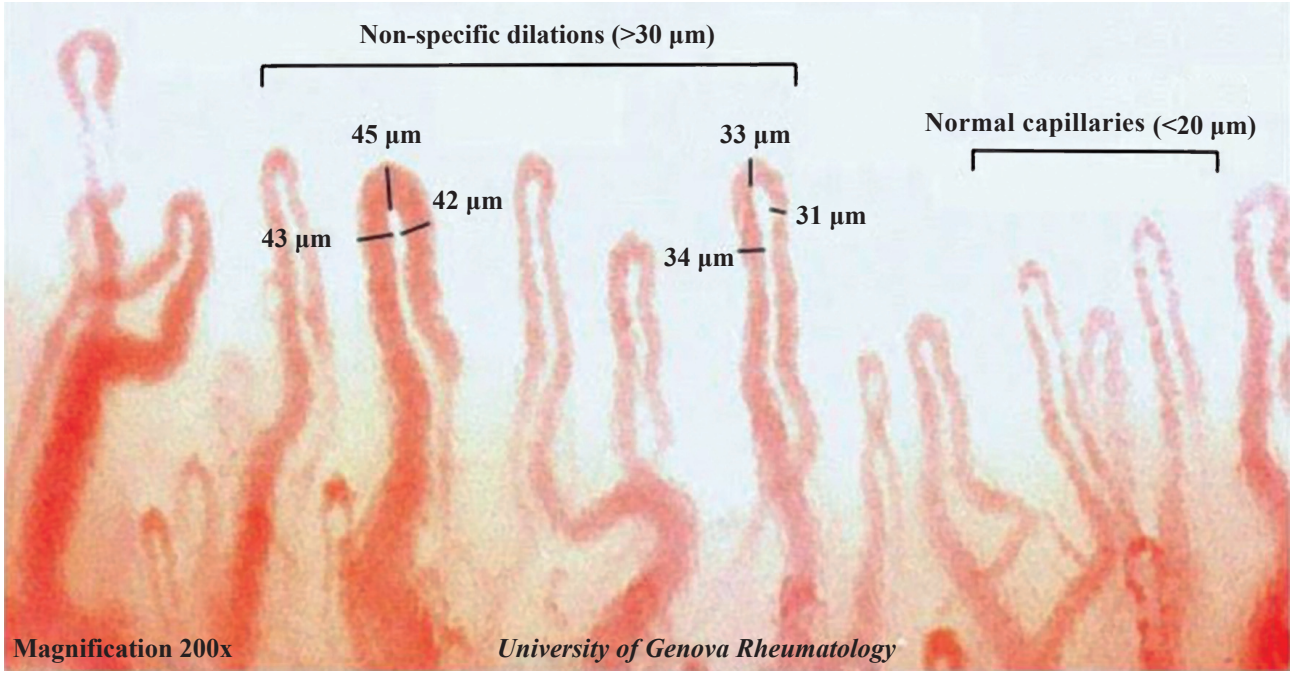

Figure 3.

Nailfold capillaroscopy Raynaud's phenomenon patient.Image demonstrates normal capillary loops (<20 µm in diameter) alongside mildly enlarged, nonspecific dilated capillaries (>30 µm in diameter) [14].

Table 1.

Pathophysiologic Mechanisms and Capillaroscopic Correlates in SLE, Dermatomyositis, and Raynaud's Phenomenon

Disease	Dominant Pathophysiology	Resulting Microvascular Injury	Capillaroscopic Expression	Clinical Implication	Diagnostic Utility
Systemic Lupus Erythematosus (SLE)	Immune-complex deposition; complement activation; endothelial dysfunction	Mild endothelial swelling;capillary fragility; subtle dropout	Tortuous loops, nonspecific dilations, microhemorrhages, mild density reduction	Identifies microangiopathy in active SLE; supports suspicion of secondary RP	Supportive but not specific
Dermatomyositis (DM)	Complement-mediated endothelial necrosis (MAC deposition); type I interferon–driven angiopathy	Marked capillary destruction; aberrant repair; hypovascularity	Giant capillaries, bushy-/branching loops, extensive hemorrhages, avascular areas	Reflects disease activity; correlates with ILD and anti-MDA5; guides monitoring	High specificity; strong diagnostic marker
Primary Raynaud's Phenomenon	Functional vasospasm without structural damage	No endothelial injury; preserved microarchitecture	Completely normal capillaroscopic pattern	Indicates benign prognosis with minimal risk of CTD	Confirms non-pathologic RP
Secondary Raynaud's Phenomenon	Autoimmune-driven structural vasculopathy (SSc, SLE, DM, MCTD)	Endothelial loss; capillary dropout; neoangiogenesis	Giant loops, microhemorrhages, reduced density, avascular zones	Predicts progression to CTD; early marker of systemic sclerosis-spectrum	Highly sensitive in detecting early CTD

DISCUSSION

Important information about autoimmune microvascular pathology can be obtained through eponychium capillaroscopy. The presence of SLE-related abnormalities aids in the identification of patients with secondary Raynaud's disease and active microangiopathy, despite their lack of specificity. Dermatomyositis exhibits a distinctive destructive pattern that corresponds with the severity and systemic involvement of the disease.

The approach is essential for assessing Raynaud's phenomenon because it makes it possible to distinguish between primary and secondary forms and makes it easier to identify connective tissue disorders early on. The noninvasiveness, affordability, and early detection of microvascular injury are among the technique's advantages. The lack of standardized, disease-specific scoring outside of systemic sclerosis and operator dependence are two drawbacks.

CONCLUSION

An effective method for identifying and describing microvascular damage in SLE, DM, and RP is eponychium capillaroscopy. While it continues to be a crucial supplement to clinical and serological evaluation in SLE, its greatest diagnostic value is observed in dermatomyositis and secondary Raynaud's. Future studies should focus on correlations with molecular markers of endothelial dysfunction, longitudinal studies evaluating vascular evolution, and standardized scoring systems for non-scleroderma diseases.

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Table 2.

Autoantibody Profiles and Associated Capillaroscopic Patterns in SLE, Dermatomyositis, and Raynaud's Phenomenon

Autoantibody	Associated Disease	Pathophysiologic Mechanism	Expected Capillaroscopic Pattern	Clinical Implication
ANA (antinuclear antibodies)	SLE, DM, SRP	Generalized autoimmune activation	Mild nonspecific abnormalities (tortuosity, rare hemorrhages)	Supports autoimmune background; low specificity for microangiopathy
Anti-dsDNA	SLE	Immune-complex vasculopathy	Microhemorrhages, mild rarefaction	Possible correlation with vasculitic flares and renal involvement
Anti-Sm/Anti-RNP	SLE, MCTD	Endothelial dysfunction, immune complexes	Tortuosity, dilations; possible mild hemorrhages	Higher risk of secondary Raynaud's; useful for CTD differentiation
Anti-MDA5	Dermatomyositis (clinically amyopathic)	Complement-mediated endothelial necrosis	Severe hemorrhages, giant loops, extensive avascular zones	Strong predictor of rapidly progressive ILD; severe microangiopathy on NVC
Anti-Mi-2	Dermatomyositis	Muscle/skin involvement, but milder vasculopathy	Moderate dilations; limited hemorrhages; fewer avascular zones	Associated with better prognosis; less destructive microangiopathy
Anti-Scl-70 (Topo I)	Systemic sclerosis → Secondary RP	Fibrotic microangiopathy	Giant capillaries, avascular areas, late SSc pattern	High risk of progressive vasculopathy and ILD
Anti-centromere	Limited cutaneous SSc → SRP	Indolent microangiopathy	Early SSc pattern: giant loops, moderate hemorrhages	Slow disease progression; milder microvascular loss
Antiphospholipid antibodies (aPL)	SLE, APS	Microthrombosis, endothelial activation	Microhemorrhages, sluggish flow, occasional thrombotic loops	Increased thrombosis risk; microcirculatory stasis detectable on NVC

Table 3.

Comparative Overview of Capillary Alterations

Disease	Density	Morphology	Hemorrhages	Avascular Areas	Specificity
SLE	Mildly ↓	Tortuous, mildly enlarged	Mild-moderate	Rare	Low–Moderate
DM	Markedly ↓	Giant, bushy loops	Extensive	Common	High
PRP	Normal	Normal	None	None	Very High (normal pattern)
SRP	↓	Giant/ectatic loops	Frequent	Possible	High

ORIGINAL ARTICLES AND SCIENTIFIC ACTIVITIES IN PEDIATRICS

CLINICAL ADVANCES IN PHARMACOTHERAPY FOR ACUTE KAWASAKI DISEASE

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ABSTRACT:

Kawasaki disease (KD) is an acute, self-limiting vasculitis that predominantly affects children under 5 years old. The precise etiology and pathogenesis of KD remain incompletely understood. This multisystem disorder represents the most common cause of acquired heart disease in children and may lead to coronary artery lesions (CALs), with severe complications including myocardial infarction and sudden cardiac death. Consequently, standardized treatment during the acute phase is of paramount importance to reduce coronary complications. This article focuses on recent advances in pharmacotherapy for acute-phase KD, aiming to inform clinical management strategies.

Keywords: Kawasaki disease; Pharmacotherapy; Clinical Advances; Heart disease; Children; Heart disease; Coronary artery lesions.

INTRODUCTION

Since its initial description in 1967, Kawasaki disease (KD) has been studied for over five decades, yet its precise etiology and pathogenesis remain incompletely elucidated. Current evidence suggests that KD arises from complex interactions among genetic, environmental, and immunological factors. The incidence rate of KD in East Asian children is far higher than that in European and American children, and the report also shows with surveillance data indicating a rising trend in China [1]. Untreated acute-phase KD can lead to serious complications, most notably coronary artery abnormalities including coronary artery aneurysms (CAAs), thrombosis, stenosis, and even sudden cardiac death. KD has become the leading cause of acquired heart disease in chil-

dren across developed countries and regions [2], with approximately 25% of untreated patients developing coronary artery lesions (CALs) [3]. The main goal of acute phase treatment is to alleviate or terminate inflammatory reactions, neutralize antibodies and toxins, and prevent the occurrence and development of CAL. Consequently, acute-phase management is critically important in KD. Multiple international guidelines have been established to standardize diagnosis and treatment., including the Scientific Committee of the Japanese Society of Pediatric Cardiology and Cardiac Surgery (JSCCCS) jointly published the "Medical (Drug) Treatment Guidelines for Acute Kawasaki Disease (Revised 2020 Edition)" in 2021, and China also published the "Evidence based Guidelines for the Diagnosis and Treatment of Kawasaki Disease in Children (2023)" in 2023. These consensus documents aim to: Optimize diagnostic and therapeutic protocols, standardize pharmacotherapy, reduce acute KD complications, decrease hospitalization costs. This article synthesizes contemporary global research to provide a comprehensive review of acute KD management, especially in terms of clinical medication selection, dosing optimization, and medical cost-effectiveness.

1. ACUTE PHASE TREATMENT EVALUATION OF KD

KD is a self-limiting systemic vasculitis predominantly affecting children under 5 years of age. Its exact pathogenesis and etiology remain elusive, and the absence of specific diagnostic tests necessitates clinical diagnosis based on characteristic features combined with manifestations of multisystem vasculitis, supported by laboratory investigations and echocardiography. Diagnosis mainly relies on clinical features combined with the manifestations of systemic vasculitis and auxiliary examinations such as laboratory and echocardiography for clinical diagnosis [4]. For patients diagnosed with KD, early intervention is imperative to mitigate acute-phase inflammation and prevent coronary artery lesions (CALs). Japanese guidelines [5] recommend that IVIG treatment should be given no later than the 7th day before the onset of extensive arteritis. Even in IVIG-nonresponsive patients and has persistent or recurrent fever, treatment should strive to start on the 9th day of the disease, before coronary artery dilation, to reduce fever and inflammatory markers that cause vasculitis as early as possible, such as C-reactive protein (CRP). Current primary treatments for acute KD includes standard therapy, initial combination therapy, additional therapy, and complementary therapy. High-dose IVIG plus aspirin remains the standard initial regimen. However, approximately 10-20% of patients exhibit IVIG resistance. With the continuous deepening of research, second-line and third line treatment drugs have also achieved good therapeutic effects. So far, drugs used for acute KD treatment include immunoglobulin, steroids, immunosuppressants, biologics, etc. Notably, Kawasaki disease shock syndrome (KDSS) is a critical variant of KD, presents with hypotensive shock, impaired left ventricular systolic function, consumptive coagulopathy, multiorgan dysfunction [5]. Due to its stronger inflammatory response and high proportion of incomplete KD, it is easy to miss diagnosis, resulting in an increased incidence of CAL and requiring intensive treatment. Since the outbreak of COVID-19, a disease similar to Kawasaki disease like children's multiple system inflammatory syndrome (MIS-C) has been more and more reported. MIS-C is a serious high inflammatory reaction state that occurs 2-6 weeks after the infection of COVID-19 in children, mainly manifested as damage to digestive tract, skin mucous membrane and cardiovascular system [6]. With the normalization of the COVID-19, we also need to pay attention to the identification of two diseases in clinical practice to prevent some children with Kawasaki disease from being misdiagnosed as MIS-C. At present, there is still no consensus on the treatment of MIS-C, which mainly includes pathogenic microorganism therapy, supportive therapy, and immune regulation therapy, while IVIG and steroid hormones are still used as first-line treatments.

2. ACUTE PHASE MEDICATION FOR KD

2.1 INTRAVENOUS IMMUNOGLOBULIN (IVIG)

Since Furusho et al. first reported the use of IVIG for Kawasaki disease (KD) treatment in 1984 [7], IVIG remains the safest and most reliable treatment method for KD. The most de-

pendable anti-inflammatory therapy for acute KD is the early administration of high-dose intravenous immunoglobulin. IVIG therapy is also the most effective method for reducing the risk of coronary artery abnormalities (CAA) development [8]. IVIG is indicated in virtually all patients with typical febrile acute KD meeting diagnostic guidelines who are at risk for CAA complications. Guidelines also recommend initiating high-dose IVIG treatment as soon as possible after KD diagnosis to maximally reduce the risk of CAA occurrence [4]. Historically IVIG dosing regimens included a single-dose protocol (2 g/kg/day) and a divided-dose protocol (200–400 mg/kg/day for 3–5 days). Extensive clinical research has been conducted regarding IVIG dosage and administration methods. Current clinical findings demonstrate that the single-dose regimen significantly reduces CAA incidence, shortens fever duration, and decreases the need for additional treatments [9]. Consequently, high-dose IVIG therapy is now universally recommended for KD patients. Although high medical costs have prevented a consensus on the maximum therapeutic dose for larger and more severely affected children, a single 2 g/kg dose is recommended. Infusion rates vary among different IVIG preparations. In Japan and China, a single dose of IVIG (2 g/kg) is typically administered intravenously over 12–24 hours, while in the US, it is given over 10–12 hours. The recommended initial infusion rate is 0.01 mL/kg/min [equivalent to 30 mg/kg/h for 5% IVIG], maintained for 15–30 minutes. The rate can then be increased to 0.02 mL/k/min. If well tolerated, it may be adjusted to 0.04 mL/kg/min, and finally to a maximum rate of 0.08 mL/kg/min. During IVIG administration, physicians should closely monitor for the development or worsening of heart failure due to rapid volume load and ensure the infusion is not administered too quickly. For patients who are non-responsive to initial IVIG therapy defined as those with persistent or recurrent fever of any degree occurring between 36 hours and 2 weeks after starting initial IVIG treatment early retreatment with IVIG (again at 2 g/kg) is still recommended. Alternatively, infliximab may be combined with this second IVIG dose. Studies have shown that combination therapy with infliximab is more beneficial for IVIG-resistant KD patients [10]. However, as IVIG is a blood product, although complications are infrequent, potential side effects include chills, shock (cyanosis, hypotension), allergic reactions, aseptic meningitis, hemolytic anemia, jaundice, acute renal failure, thrombocytopenia, and pulmonary edema. It is particularly crucial to monitor immediately after starting the intravenous infusion for symptoms such as chills, shivering, coma, restlessness, tremor, cyanosis, hypotension, or shock [11]. To be aware of potential myocardial damage and heart failure during the acute phase, close attention should be paid to the rapid increase in circulating blood volume and changes in vital signs during intravenous infusion [12].

2.2 ANTIPLATELET AGENTS

2.2.1 Aspirin (ASA)

The combination of IVIG and ASA currently serves as the standard treatment for KD. ASA is a non-selective cyclooxygenase (COX) inhibitor. Its primary mechanism involves the irreversible acetylation of the serine residue at position 529 of COX-1, thereby inactivating COX-1. This inhibits arachidonic acid metabolism, leading to reduced production of its metabolite thromboxane A2 (TXA2), and consequently suppresses platelet aggregation [13]. There is debate regarding the optimal ASA dose during the acute phase of KD, as high-dose ASA exerts non-specific anti-inflammatory effects, while low-dose ASA primarily exhibits antiplatelet activity.

Current Chinese guidelines recommend:

Acute phase: 30–50 mg/(kg·d), divided into 2–3 oral doses. After fever subsides for 48–72 hours or by day 14 of illness: Reduce to 3–5 mg/(kg·d), administered as a single daily dose (SID).

Duration: Maintain low-dose ASA for 6–8 weeks. Children who develop coronary artery lesions (CAL) require continued ASA until coronary arteries normalize.

Potential complications of ASA include hepatic impairment, shock, allergic reactions, gastrointestinal ulcers, recurrent epistaxis (nosebleeds), and melena (black, tarry stools). If these complications occur, dose reduction or discontinuation of ASA is necessary. ASA can be routinely used in patients presenting with abnormal liver function on admission, **but requires close monitoring** of liver

enzymes. If significant liver dysfunction develops during ASA therapy**, dose reduction or discontinuation should be considered. Crucially, KD patients concurrently infected with influenza or varicella (chickenpox) are at risk of developing Reye's syndrome when treated with high-dose ASA. Therefore, IVIG alone is recommended for initial treatment in these cases. Subsequent antiplatelet therapy should utilize dipyridamole or clopidogrel instead of ASA. For children on long-term low-dose ASA if they develop symptoms of influenza or varicella, or have close contact exposure to these infections, it is advisable to discontinue ASA for 2 weeks and substitute with clopidogrel during this period. Children receiving long-term low-dose ASA are advised to receive prophylactic influenza vaccination, and close monitoring for relevant clinical symptoms is essential [14].

2.2.2 Other Antiplatelet Agents

Anti-platelet agents with different mechanisms include clopidogrel and dipyridamole. Clopidogrel, an adenosine diphosphate (ADP) receptor P2Y12 antagonist, is converted to its active metabolite by the cytochrome P450 enzyme system in hepatocytes. The active metabolite irreversibly binds to the platelet surface ADP receptor P2Y12, inhibiting ADP-mediated activation of the glycoprotein IIb/IIIa complex, thereby suppressing platelet activation and aggregation. It also possesses fibrinolytic and thrombolytic effects with minimal adverse reactions [15]. The recommended dosage is 0.2 mg/kg once daily for children under 2 years old and 1 mg/kg once daily for children aged 2 years and above. Adverse effects of clopidogrel may include fatigue, dizziness, gastrointestinal reactions, and bleeding, though hepatic impairment is rare.

Dipyridamole primarily inhibits platelet adhesion and aggregation through multiple mechanisms. However, due to its vasodilatory effect, it may reduce blood flow in distal aneurysms, leading to a steal phenomenon. Thus, it is not recommended for children with severe coronary obstruction or for long-term use. Adverse reactions such as chest pain, angina, and headache may occur. If adverse reactions develop, the dose may be reduced or discontinued as appropriate. The recommended dosage is 3-5 mg/(kg·d), administered orally in three divided doses.

2.3 OTHER ANTICOAGULANT AND THROMBOLYTIC AGENTS

2.3.1 Anticoagulants

Anticoagulants primarily include warfarin and heparin. Warfarin exerts its anticoagulant effect by inhibiting the synthesis of coagulation factors II, VII, IX, and X, thereby preventing thrombus formation in coronary artery aneurysms (CAAs) [16]. The dosage is 0.16 mg/kg/d once daily for children under 12 months of age, and 0.04–0.10 mg/kg/d once daily for children aged 1 to 15 years. According to guidelines [17], patients with coronary artery lesion (CAL) risk classification grade IV or higher require combined therapy with low-dose aspirin and warfarin. The dosage should be adjusted based on PT-INR, with a target range of 1.5–2.5. During the acute phase, warfarin is less effective in controlling inflammatory responses, and time is needed for disease stabilization. Low molecular weight heparin (LMWH) is preferred in the acute phase due to its rapid onset and anti-inflammatory effects. Once the condition stabilizes and coronary aneurysm expansion ceases, LMWH may be switched to oral warfarin. Since warfarin takes 3-7 days to take effect, the two agents should overlap for 3-7 days. The most significant side effect of warfarin is bleeding (e.g., nasal, gingival, intracranial, or intra-abdominal hemorrhage). Warfarin is also considered teratogenic; administration 6-9 weeks before pregnancy may cause skeletal malformations, cartilaginous deformities, and microcephaly [18]. Heparin is indicated for giant CAAs, myocardial infarction, and thrombosis within CAAs. For thrombolysis, heparin is administered as a continuous infusion at 10-20 U/kg/h, with close monitoring of coagulation parameters and bleeding. Physicians should monitor for heparin-induced thrombocytopenia (HIT), bleeding, hepatic dysfunction, alopecia, rash, and diarrhea during use [19]. Generally, anticoagulants are unnecessary for patients without CAAs, but combined aspirin (ASA) and anticoagulant therapy in patients with giant CAAs can prevent long-term cardiac complications.

2.3.2 Direct Oral Anticoagulants (DOACs)

This class of drugs directly inhibits thrombin and factor Xa

to exert anticoagulant effects, primarily used for preventing thrombosis in atrial fibrillation and venous thromboembolism [20]. In adults, they are indicated for preventing hemorrhagic stroke and systemic embolism in non-valvular atrial fibrillation, as well as for treating and preventing recurrent deep vein thrombosis and pulmonary embolism. Adult dosages include: dabigatran ester 150 mg twice daily, rivaroxaban 15 mg once daily, apixaban 5 mg twice daily, and edoxaban 60 mg once daily (30 mg for patients weighing <60 kg). Pediatric dosages have not yet been established. In the future, DOACs may serve as alternatives to warfarin and heparin.

2.3.4 Thrombolytic Agents

Myocardial infarction frequently occurs within 2 years after Kawasaki disease (KD) onset, primarily due to acute coronary obstruction caused by intraluminal thrombosis in aneurysms. The Japan Pediatric Society guidelines recommend thrombolytic therapy as more suitable for children due to their smaller body size and lower risk of bleeding complications. Thrombolysis is indicated for acute coronary obstruction in KD and should ideally be initiated within 12 hours of acute myocardial infarction onset; efficacy diminishes significantly beyond this timeframe. The most commonly used thrombolytic agents in pediatrics include:

Tissue plasminogen activator (tPA): 0.5 mg/(kg·h) for 6 hours.

Urokinase: Single bolus of 4,400 U/kg over 10 minutes, or 1,000–4,000 U/kg over 30 minutes (less effective than tPA).

Concomitant aspirin and low-dose heparin (10 U/kg/h) should be administered during thrombolysis. Coagulation parameters and bleeding must be monitored, with fibrinogen maintained >1.0 g/L and platelets $>50\times10^9$/L. Clinical experience with thrombolytic agents in pediatrics remains limited. Potential complications include intracranial hemorrhage, hemorrhagic infarction, gastrointestinal bleeding, pulmonary hemorrhage, allergic reactions, and shock [21].

2.4 GLUCOCORTICOIDS

The role of glucocorticoids in Kawasaki disease (KD) treatment has evolved significantly in recent years. Initially used cautiously due to concerns about increased coronary aneurysm risk, they are now increasingly recommended in guidelines for refractory KD as part of combination therapy. Monotherapy with glucocorticoids is not advised as first-line treatment for KD.

Glucocorticoids exert potent anti-inflammatory and immunosuppressive effects, rapidly and effectively controlling KD vasculitis and mitigating the risk of coronary artery remodeling [22]. Their mechanism involves binding to cytoplasmic steroid receptors to inhibit gene transcription of inflammatory proteins while promoting transcription of anti-inflammatory proteins. This suppresses the production of inflammatory cytokines (e.g., TNF-α, IL-6, IL-8, G-CSF), chemokines, and cell adhesion molecules, while enhancing anti-inflammatory proteins (e.g., lipocortin), thereby attenuating vasculitis [23].

For IVIG-nonresponsive KD or children with persistent inflammation markers complicated by CAA or peripheral aneurysms, glucocorticoids are recommended as first-line therapy.

DOSAGE:

Prednisone: 1-2 mg/(kg·d) as a single morning dose (max. 60 mg/d).

Methylprednisolone: 1–2 mg/(kg·d) IV, 1–2 times daily. Transition to oral prednisone (1–2 mg/(kg·d) once stabilized, followed by a 15-day taper.

For IVIG-nonresponsive KD, options include a second IVIG dose or IVIG combined with prednisone/methylprednisolone at the above doses, with close monitoring for adverse effects. For KD Shock Syndrome (KDSS) or KD with Macrophage Activation Syndrome (MAS): High-dose methylprednisolone pulse therapy is recommended for its potent and rapid immunosuppressive effect on vasculitis [24]. This therapy significantly suppresses cytokine production and modulates inflammatory gene transcription, controlling inflammation and CAA development. It is used either: As initial therapy for predicted IVIG non-responders. As rescue therapy for confirmed IVIG non-responders.

Dosage: 10-30 mg/(kg·d) IV over 2-3 hours for 1-3 days.

Adverse effects: Sinus bradycardia (6-82%), hypertension (10-91%), hyperglycemia (6-55%), and hypotension (6-9%). Prophylactic H_2 blockers or antacids may be considered for gastric protection, though evidence is limited [25].

Important considerations:

Anticoagulation with heparin (10 U/(kg·d) continuous infusion over 24 hours) or LMWH is recommended 2 hours before initiat-

ing pulse therapy [4]. Disease activity monitoring is challenging during glucocorticoid therapy, as they mask inflammatory markers (e.g., fever, CRP). Regular blood tests, echocardiography, and coagulation monitoring are essential. Suspected relapse warrants prompt intervention.

2.5 BIOLOGIC AGENTS

2.5.1 Infliximab (IFX)

Infliximab, a monoclonal antibody against tumor necrosis factor-alpha (TNF-α), has become a crucial rescue or adjunctive therapy for KD, particularly refractory cases. It inhibits inflammatory pathways and controls vasculitis by specifically blocking TNF-α [26]. Growing evidence confirms the safety and efficacy of IFX in IVIG-nonresponsive KD, with some studies suggesting superior outcomes compared to IVIG combined with glucocorticoids [27]. Optimal timing and indications for use vary regionally. A retrospective Chinese study of 68 children demonstrated favorable efficacy and safety in IVIG/glucocorticoid-nonresponsive KD patients with progressive CAAs [28], though large-scale randomized controlled trials (RCTs) are needed to refine treatment timing.

Dosage: 5 mg/kg as a single 2-hour intravenous infusion.

Adverse effects: Infusion reactions, rash, viral infections, transient hepatomegaly, reactivation of latent tuberculosis or viral hepatitis, exacerbation of heart failure, and infections linked to live attenuated vaccines [29].

2.5.2 Etanercept

Etanercept is a dimeric fusion protein combining the extracellular domain of the human TNF receptor (p75) with the Fc segment of immunoglobulin G (IgG1). It functions as a soluble "decoy receptor," binding TNF-α with high affinity in circulation to prevent its interaction with cell-surface receptors. It features a short half-life and low side-effect profile. Preliminary RCTs suggest etanercept as adjunctive therapy to IVIG may reduce IVIG resistance and mitigate coronary dilation, but optimal dosing and efficacy require further prospective studies. Anti-IL-6 receptor antibody (tocilizumab) and IL-1 antagonist (anakinra) have also been reported in KD treatment but warrant further investigation.

2.6 IMMUNOSUPPRESSIVE AGENTS

2.6.1 Cyclosporine A (CsA)

CsA is a calcineurin inhibitor that suppresses T-cell activation by binding calcineurin, a key signaling molecule in immune cell activation. This blocks transcription of pro-inflammatory cytokines implicated in KD vasculitis [30], positioning CsA as a potential agent to halt arterial inflammation. The American Heart Association suggests CsA for refractory KD after failure of second IVIG, IFX, or glucocorticoids, but not as routine therapy.

Dosage: Oral CsA 5 mg/(kg·d) divided twice daily before meals for 5 days. Trough plasma concentration (day 3 pre-dose) should be maintained at 60–200 ng/mL, with dose adjustments based on levels.

Monitoring: Watch for hyperkalemia, hypomagnesemia, and hirsutism. No severe KD-specific adverse events reported to date [31].

2.6.2 Methotrexate (MTX)

Low-dose MTX, an antimetabolite used in oncology and rheumatology, shows promise in suppressing vasculitis in IVIG-nonresponsive KD. It rapidly reduces fever, improves symptoms, and normalizes acute-phase inflammatory markers [32].

Dosage: Oral MTX 10 mg/m² weekly (max. 16 mg).

Response: Fever typically resolves within 24 hours; CRP declines significantly within a week.

Adverse effects: Nausea and vomiting are common concerns. Evidence is limited to retrospective studies, with no RCTs conducted.

2.7 PROTEASE INHIBITORS

2.7.1 Ulinastatin (UTI)

UTI, a human urinary trypsin inhibitor produced by multiple organs (e.g., liver, kidneys, pancreas), reduces vascular endothelial damage by inhibiting proteolytic enzymes and inflammatory cytokines released by neutrophils [33]. It may be used alongside IVIG as initial therapy or as adjunctive treatment for IVIG non-responders.

Dosage: Optimal pediatric dosing is undefined. Studies report 5,000 U/kg/dose IV (half-life ~40 minutes), administered 3–6 times daily (max. 300,000 U/day). According to records, the purpose of the first combination therapy of UTI and IVIG is to reduce IVIG resistance and CAA incidence. When patients with drug allergies or urinary tract infection history, they should use medication with caution [34].

2.7.2 Others

Sivelestat Sodium Hydrate (SSH): A selective neutrophil elas-

tase inhibitor and protease inhibitor [35]. Primarily used for acute lung injury/ARDS in systemic inflammatory response syndrome.

KD Application: Limited reports describe SSH combined with IVIG for initial or rescue therapy in KD. But there are several reports showing continuous intravenous infusion of 0.2mg/kg/h in KD. There is currently no evidence regarding the indications, dosage, and prescription of medication.

2.8 PLASMA EXCHANGE (PE)

PE reduces the incidence of coronary artery lesions by directly removing inflammatory cytokines from the blood [36]. Primarily used for IVIG-nonresponsive patients, PE is an invasive procedure associated with side effects such as hypotension/shock, bleeding, anemia, hypothermia related to extracorporeal circulation, coagulopathy due to albumin replacement, allergic reactions, and hypocalcemia. This treatment often requires deep sedation and management in an intensive care unit with mechanical ventilation. Regular monitoring of calcium levels and electrolyte adjustment is essential. PE has a long history, dating back to the pre-IVIG era, but it is typically reserved as a last resort for severe cases when other therapies fail, with limited prospective clinical trial data [37].

2.9 ANTI-ANGINAL AGENTS AND CORONARY VASODILATORS

2.9.1 Beta-Blockers

Beta-blockers are first-line anti-anginal agents. Propranolol is the only safe option for children with coronary stenosis accompanied by myocardial ischemia, post-myocardial infarction, heart failure, and arrhythmias (but not angina) [38]. Carvedilol may be used in children but carries a risk of worsening heart failure; treatment should start at low doses and be titrated based on tolerance and therapeutic benefit.

2.9.2 Calcium Channel Blockers

These agents inhibit calcium influx into vascular smooth muscle cells and prevent coronary spasm, making them first-line treatments for angina. Amlodipine is approved for hypertension in children aged ≥6 years, while nifedipine and diltiazem are not approved for pediatric use.

2.9.3 Nitrates

Nitrates increase coronary blood flow via coronary vasodilation and reduced preload, while decreasing left ventricular preload and afterload to alleviate myocardial ischemia. Tolerance develops with prolonged use, so indiscriminate administration should be avoided.

Sublingual nitroglycerin: Adults: 1–2 tablets (0.3–0.6 mg);

Children: ½–⅓ tablet (dose adjusted based on body size).

Continuous intravenous infusion: 0.1–20 μg/kg/min.

3. CONCLUSION

The primary goal of acute-phase Kawasaki disease (KD) treatment is to reduce the incidence of coronary artery lesions. High-dose intravenous immunoglobulin (IVIG) combined with oral aspirin remains the first-line therapy. However, some patients may require adjunctive agents such as glucocorticoids or infliximab. This review summarizes acute-phase therapeutic options to assist domestic clinicians in managing KD. Nevertheless, certain treatment strategies still lack robust evidence. We anticipate updated guidelines with higher-quality recommendations to advance optimal KD management.

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KALEIDOSCOPE OF INTERESTING WORKS

ADVANCES IN ARTIFICIAL CONSCIOUSNESS AND TRADITIONAL CHINESE MEDICINE IN KAWASAKI DISEASE RESEARCH

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ABSTRACT

Kawasaki disease (KD) is an acute febrile rash illness characterized by systemic vasculitis, primarily affecting children under 5 years of age. Its etiology remains unclear but may involve factors such as infections and immune dysregulation. Traditional Chinese Medicine (TCM) and artificial consciousness (AC), as distinct medical and therapeutic paradigms, have demonstrated potential in the treatment of KD. This paper reviews recent advancements in the application of TCM and AC for KD, explores their integration, and proposes novel strategies for improving KD management.

1. EPIDEMIOLOGY AND CLINICAL FEATURES OF KAWASAKI DISEASE

Since its first description in Japan in 1967, KD has been reported worldwide. While epidemiological patterns vary across regions, it predominantly affects children under 5 years old. Classic symptoms include persistent fever, bilateral conjunctival injection, cracked lips, strawberry tongue, edema of the hands and feet, rash, and cervical lymphadenopathy. Cardiac complications, such as myocarditis, pericarditis, and coronary artery aneurysms, pose significant risks.

2. PROGRESS IN TCM FOR KAWASAKI DISEASE

TCM offers unique advantages in KD treatment. Although ancient texts lack direct references to KD, modern scholars categorize it under "warm disease" (温病), "epidemic rash" (疫疹), or "maculopapular rash" (斑疹). TCM employs the "Wei-Qi-Ying-Xue" (卫气营血) differentiation system to tailor treatments based on disease stage and patient constitution.

(1) ETIOLOGY AND PATHOGENESIS

1. Invasion of Warm-Toxic Pathogens: Latent pathogens reactivate due to external triggers in susceptible children.

2. Heat-Stasis Interaction: Heat obstructs meridians, induces blood stasis, and transforms into phlegm-fire.

3. Exogenous Warm or Epidemic Toxins: Attack the lung and stomach, leading to heat accumulation in Yangming, skin/mucosal inflammation, and progression to Qi-Nutrient (血) phase blaze.

(2) SYNDROME DIFFERENTIATION AND TREATMENT

Common TCM patterns and treatments include:

1. Wei-Qi Co-Affliction: Clear heat and resolve the exterior with modified Yinqiao Baihu Decoction (银翘白虎汤).

2. Dual Blazing of Qi and Nutrient Phases: Cool Qi and nutrient levels using Qingwen Baidu Decoction (清瘟败毒饮).

3. Residual Heat in Yin Phase: Clear residual heat and nourish Yin with Zhuye Shigao Decoction (竹叶石膏汤).

4. Qi-Yin Deficiency: Tonify Qi and Yin with Shengmai San* (生脉散).

5. Toxin-Stasis and Phlegm Obstruction: Clear heat, resolve stasis, and disperse phlegm using combined Qingwen Baidu Decoction and Xiaoluo Pill(消瘰丸).

(3) SPECIALIZED FORMULAS

Notable formulas include:

1. Jiedu Huayu Dihuang Decoction(解毒化瘀地黄汤): Contains Forsythia, buffalo horn, and Rehmannia for heat-clearing and stasis-resolving.

2. Qingre Huayu Decoction (清热化瘀汤): Combines buffalo

horn, honeysuckle, and Forsythia for cooling blood and detoxification.

3. Xuefu Zhuyu Decoction (血府逐瘀汤): Modified to promote blood circulation and relieve pain.

3. ARTIFICIAL CONSCIOUSNESS IN MEDICAL APPLICATIONS

Artificial consciousness (AC) simulates human cognitive processes (e.g., perception, decision-making) through AI. Key medical applications include:

(1) DIAGNOSTIC ASSISTANCE

AC analyzes imaging and physiological data to enhance diagnostic accuracy. Deep learning algorithms detect anomalies in medical images, improving efficiency.

(2) TREATMENT PLANNING

AC generates personalized regimens by evaluating patient data, optimizing drug combinations and therapies.

(3) PATIENT MONITORING

Wearable devices integrated with AC enable real-time monitoring, alerting clinicians to critical changes in patient status.

4. INTEGRATION OF AC AND TCM IN KAWASAKI DISEASE

(1) DATA MINING AND ANALYSIS

AC can analyze TCM literature to identify effective KD treatment patterns, uncovering hidden therapeutic principles.

(2) PERSONALIZED TCM REGIMENS

AC synthesizes TCM theory and patient-specific data to recommend optimal herbal formulas and dosages.

(3) REAL-TIME MONITORING AND ADJUSTMENT

AC tracks treatment responses via wearables, dynamically adjusting TCM protocols to enhance safety and efficacy.

(4) INTELLIGENT DIAGNOSTIC SYSTEMS

Integrated AC-TCM platforms could automate syndrome differentiation, suggest treatments, and provide real-time clinical feedback.

5. PROSPECTS AND CHALLENGES

Despite promise, challenges persist:

- Complexity of TCM theory complicates AC interpretation.
- Technical limitations in AC accuracy and reliability.
- Resource-intensive development of intelligent systems.

Future advancements in AC and TCM research, coupled with interdisciplinary collaboration, may overcome these barriers.

6. CONCLUSION

KD remains a serious threat to pediatric health. The integration of TCM and AC offers innovative avenues for treatment through data-driven insights, personalized care, and intelligent monitoring. Cross-disciplinary efforts are essential to advance this emerging frontier in KD management.

Note: Author names and affiliations are preserved in transliterated form as per academic conventions.

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THE CURRENT SITUATION AND FUTURE OF ADOLESCENT HEALTH WORK IN CHINA

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ABSTRACT:

China has over 200 million children and adolescents aged 6-19 among its 1.4 billion population. While China has achieved remarkable progress in adolescent health, numerous challenges remain. Research shows that over the past three decades, the all-cause mortality rate among Chinese adolescents has decreased by 64.2%, yet the spectrum of health issues has undergone significant changes. Myopia, obesity, and psychological disorders have gradually emerged as new disease burdens. China defines adolescence as 11-18 years for females and 13-20 years for males. Current health services face issues such as significant regional disparities and imbalanced distribution. Future efforts should focus on establishing a "holistic, full-cycle" health management model, addressing challenges through "technology empowerment" and "multi-stakeholder collaboration." Currently, China has established specialized adolescent health medical disciplines in cities such as Beijing, Shanghai, and Hubei.

1 INTRODUCTION

The health of adolescents is the cornerstone of a nation's future and national development, crucial to achieving the Sustainable Development Goals and building a Healthy China. According to the latest data, China has over 200 million children and adolescents aged 6-19. The health status of this large population directly impacts the quality of the country's future workforce, innovation capabilities, and the sustainable development of global public health and healthcare ecosystems. The World Health Organization regards adolescence as the "second critical window period" following infancy, a stage characterized by tremendous potential for physical, cognitive, and social development.

In recent years, with the economic development and social changes in China, significant changes have occurred in the health risks and outcomes of children and adolescents. Although the overall health status of Chinese children and adolescents has greatly improved over the past 30

years, they now face new health issues and social challenges. To address this, policies such as the "Healthy China 2030 Plan Outline" and the "China Children Development Outline (2021-2030)" have been successively introduced, promoting a shift in child health from disease treatment to comprehensive life-cycle health development. The National Health Commission has also designated 2025-2027 as the "Year of Pediatric and Mental Health Services," highlighting the nation's high priority on this field.

Based on the latest survey data and research results, this paper systematically analyzes the current situation, challenges and future development direction of adolescent health work in China, aiming to provide scientific reference for policy formulation and practical work.

2. ANALYSIS OF THE CURRENT HEALTH STATUS OF CHINESE ADOLESCENTS

2.1 SHIFT IN KEY HEALTH ISSUES

Over the past 30 years, the health of children and adolescents in China has undergone significant transformation. Studies show that from 1990 to 2019, the all-cause mortality rate of children and adolescents aged 5 to 19 in China decreased from 77.63/10 million to 27.79/10 million, a reduction of 64.2%. This achievement is mainly attributed to rapid economic development and disease-centered policy investments. However, with the epidemiological shift, the primary disease burden among children and adolescents has shifted from infectious diseases to injuries and chronic non-communicable diseases.

Table: Statistics on Major Health Problems of Children and Adolescents in China (1995-2019)

health issue	Prevalence in 1995 (%)	Prevalence in 2019 (%)	Amplitude of variation (%)
Poor sight	41.2	60.7	+47.3
Superweight and obesity	5.0	24.2	+384.0
All cause mortality rate (per 100,000)	77.63 (1990)	27.79	-64.2

Chronic non-communicable diseases have become the main health problem plaguing Chinese adolescents, which are specifically manifested in:

- Vision problems: From 1995 to 2019, the rate of poor vision (including myopia, hyperopia, and other visual issues) among children and adolescents aged 7 to 18 rose from 41.2% to 60.7%, with high school students showing an alarming 80.5% myopia rate. Myopia has become a primary health concern affecting young people's development, showing a clear trend toward younger ages.

Overweight and obesity: The prevalence of overweight and obesity among children and adolescents aged 7 to 18 rose from 5.0% to 24.2% during the same period. Data from 2019 shows that the rate of overweight and obesity among Chinese children and adolescents aged 6 to 17 has reached 19%. Obesity not only reduces physical activity capacity but also creates hidden risks for chronic diseases such as cardiovascular and cerebrovascular diseases and diabetes in adulthood.

- Spinal health problems: In recent years, abnormal spinal curvature has become another prominent problem affecting the health of adolescents, requiring comprehensive screening and early intervention.

2.2 UNEQUAL ACCESS TO HEALTH SERVICES

- Significant regional disparities: Regional disparities in the implementation of health policies have resulted in uneven quality and accessibility of health services, and the quality of education and health service resources in central and western regions still need to be improved.

- Shortage of professional services: insufficient resource allocation and services in children ' s hospitals, particularly in child mental health and reproductive health services, which need to be strengthened; insufficient personnel and facilities for school health services; constraints to the promotion of healthy schools.

This inequality leads to significant differences in the quality of health services received by adolescents from different regions and socioeconomic backgrounds, further exacerbating health inequity.

2.3 POLICY INTERVENTIONS AND RESULTS

To address adolescent health challenges, the Chinese government has implemented a series of interventions with notable success. In recent years, through a comprehensive strategy prioritizing health development, China has established multiple protective measures to safeguard children's and adolescents' well-being. Specifically targeting prevalent health issues among students, the nation has introduced a "multi-disease prevention" approach for common student illnesses. This strategy emphasizes coordinated interventions when multiple diseases or health problems share common risk factors.

3. CURRENT IMPORTANT MEASURES AND POLICY INTERVENTIONS FOR HEALTH WORK

3.1 INTEGRATED PREVENTION STRATEGIES FOR MULTIPLE DISEASES

In response to the widespread health issues among students, China has explicitly proposed and implemented a "multi-disease prevention" strategy for common student illnesses. To this end, relevant authorities have innovatively proposed six healthy lifestyles:

1. Ensure one hour of physical exercise every day, one hour of outdoor activities at school and one hour outside school during the day;
2. Get up and move around for 10 minutes after sitting for an hour;
3. Less than one hour of video time per day for entertainment purposes;
4. The three meals are eaten at a relatively fixed time, with a difference of no more than one hour;
5. Go to bed early and get up early, reducing exposure to light sources for 1 hour every day;
6. One hour of parent-child communication and 15 minutes of interaction every day.

Practice has proved that the implementation of these scientific prevention and intervention measures can achieve the common disease and multi-disease prevention, effectively protect students' physical and mental health.

3.2 EDUCATION FOR A HEALTH-PRIORITIZED APPROACH

The Chinese government is vigorously promoting the return of the education concept from "results first" to "health first". The implementation path of the health first concept includes:

- Integrating health education into the education system: making them the first responsible person for their own health.
- Strengthening physical education: open up enough physical education courses to help students enjoy fun, improve their physique, improve their personality and temper their will in physical exercise.

Family participation in health action: Students' families actively participate in the "three reductions and three health" (reducing salt, oil and sugar, healthy mouth, healthy weight and healthy bones) national healthy lifestyle action, integrate the concept of health into daily life, and create a healthy family atmosphere.

3.3 CONSTRUCTION OF HOME-SCHOOL-COMMUNITY-MEDICAL COORDINATION MECHANISM

In the field of mental health, the "home-school-community-medical collaboration" mechanism is particularly critical.

4. FUTURE DEVELOPMENT DIRECTION OF ADOLESCENT HEALTH WORK

4.1 TRANSITION TO LIFE CYCLE HEALTH MANAGEMENT

4.2 TECHNOLOGY FOR HEALTH

Scientific and technological innovation will be an important driving force for the health of young people in the future. In the field of mental health, the application of artificial intelligence, big data and other technologies has begun to play an important role.

4.3 BUILD A SUPPORTIVE ENVIRONMENT

In the future, China's youth health work will pay more attention to environmental construction, creating supportive family environment, safe community environment and equal and respectful campus environment for young people.

5. CONCLUSIONS AND RECOMMENDATIONS

China's adolescent health work is at a critical stage of transformation and development. Over the past 30 years, China has achieved world-renowned accomplishments in reducing child and adolescent mortality rates and controlling infectious diseases, but it also faces new challenges such as the increasing burden of chronic non-communicable diseases, prominent mental health issues, and uneven distribution of health services. In the future, efforts need to be further strengthened in the following aspects:

5.1 STRENGTHENING SYSTEMATIC INVESTMENTS

5.2 PROMOTING MULTISECTORAL COLLABORATION

Adolescent health is a complex issue across disciplines, which requires the establishment of a government-led multi-sectoral cooperation mechanism and the formation of a working mechanism integrating physical health, medicine and education and coordinating families, schools and society.

5.3 INNOVATION OF SERVICE MODE AND TECHNOLOGY APPLICATION

- Promoting the new paradigm of "full chain and full cycle" health management, realizing the transformation from passive treatment to active health management;

- Give full play to the role of artificial intelligence, big data and other new technologies in health assessment, intervention and tracking;

- Promote the transformation of retail pharmacies and other institutions, so that they can cooperate with medical institutions to fill the gap in the delivery of children's health services at different stages.

Youth health is both a "national priority" and a "people's concern". The entire society should work together to create a supportive environment for children and adolescents' growth. We must continue advancing government-led multi-sector collaboration strategies, establish integrated mechanisms combining physical health, medical care, and education with coordinated efforts among families, schools, and communities. Particularly crucial is strengthening the development of comprehensive prevention and intervention systems centered on youth health, working collectively to safeguard our nation's future and hope.

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DIFFERENT

CORRELATION ANALYSIS BETWEEN CLINICAL CHARACTERISTICS AND CORONARY ARTERY LESION RISK IN 136 CHILDREN WITH KAWASAKI DISEASE

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ABSTRACT:

Objective: To analyze the correlation between clinical characteristics and coronary artery lesion risk in 136 children with Kawasaki disease.

Methods: The clinical data of 136 children with Kawasaki disease admitted to the Department of Pediatrics at Shenmu City Hospital between August 1999 and January 2022 were retrospectively analyzed. According to the American Heart Association diagnostic criteria, these children were divided into complete Kawasaki disease (cKD) and incomplete Kawasaki disease (iKD). Clinical manifestations, laboratory test parameters, echocardiogram results, and the incidence of coronary artery lesions (CAL) were compared between these two types of children.

Results: Among the 136 children, cKD accounted for 74% and iKD accounted for 26%. The male-to-female ratio was 2.2:1, with a significant prevalence of boys compared to girls ($P < 0.05$). The peak age of onset was 1-3 years, accounting for 37.8%. The incidence of typical symptoms (rash, conjunctival injection, chapped lips, strawberry tongue, lymphadenopathy, and erythema of the hands and feet) was significantly higher in the cKD group than in the iKD group ($P < 0.05$). The iKD group was more likely to have positive erythema ($P < 0.05$). The overall incidence of CAL was 27.4%, with a higher incidence in the iKD group (41.7%) compared with the cKD group (19.5%, $P < 0.05$). Laboratory parameters (CRP, ESR, etc.) did not differ significantly between the two groups. However, iKD patients were younger and presented with more atypical clinical manifestations, making them more susceptible to missed or misdiagnosis.

Conclusion: KD is more common in males, with a peak age range of 1-3 years. The risk of CAL in iKD patients is significantly higher than that in cKD patients. The value of atypical clinical manifestations and auxiliary examinations (such as CRP, ESR, and echocardiography) in the early diagnosis of iKD should be highly valued. Standardized IVIG and aspirin therapy can help reduce the incidence of CAL. Children who are unresponsive to IVIG may consider combined treatment with glucocorticoids or infliximab to improve prognosis.

Keywords: Kawasaki disease; incomplete Kawasaki disease; coronary artery damage; clinical features; intravenous immunoglobulin; echocardiography

Kawasaki disease (KD) is a medium and small vessel vasculitis that frequently occurs in children under 5 years old. Its typical manifestations include fever, rash, conjunctival congestion, oral changes, and cervical lymphadenopathy. If not treated in time, it is prone to cause coronary artery lesions (CAL), which is the main cause of acquired heart disease in children [1]. In recent years, incomplete Kawasaki disease (iKD) has gradually attracted attention. Its clinical manifestations are atypical, and it is prone to be missed or misdiagnosed. The incidence of CAL is significantly higher than that of complete Kawasaki disease (cKD) [2]. This study retrospectively analyzed 136 children with KD admitted to Shenmu City Hospital from 1999 to 2022, comparing the differences in clinical features, lab-

oratory indicators, and the risk of CAL between cKD and iKD, aiming to provide a basis for the early identification and standardized treatment of high-risk children.

1. MATERIALS AND METHODS

1.1 GENERAL INFORMATION

This study retrospectively analyzed the clinical data of 136 children with Kawasaki disease (KD) admitted to the Department of Pediatrics of Shenmu City Hospital, Shaanxi Province from August 1999 to January 2022. All children met the 2017 American Heart Association diagnostic criteria for Kawasaki disease. Based on clinical manifestations and echocardiographic results, the children were divided into 101 cases of complete Kawasaki disease (cKD) and 35 cases of incomplete Kawasaki disease (iKD). Among them, there were 93 boys, accounting for 68.4%, and 43 girls, accounting for 31.6%, with a male-to-female ratio of approximately 2.2:1. The age range was from 15 days to 8 years and 10 months, with an average age of (2.76 ± 1.43) years. The peak incidence was concentrated in the 1-3-year-old age group.

1.2 METHODS

According to the disease course data of the children, their clinical manifestations, laboratory test results (such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), etc.) and echocardiographic results were grouped and compared. The differences in typical clinical manifestations (such as rash, strawberry tongue, conjunctival congestion, etc.), positive rate of scarlet fever reaction, and incidence of coronary artery lesion (CAL) between the cKD and iKD groups were compared.

1.3 OBSERVATION INDICATORS

Clinical manifestations: fever, rash, conjunctival congestion, chapped lips, strawberry tongue, redness and swelling of hands and feet, cervical lymphadenopathy, scarlet fever reaction, etc.

Laboratory test indicators: CRP, ESR, WBC, Hb, PLT, ALT, ALB, white blood cells in urine routine, etc.

Echocardiographic indicators: coronary artery dilation, aneurysm formation, Z value changes.

CAL incidence: Z value ≥ 2.5 of left anterior descending artery (LAD) or right coronary artery (RCA), coronary artery aneurysm or mitral regurgitation, pericardial effusion, left ventricular dysfunction, etc. detected by echocardiography.

1.4 STATISTICAL ANALYSIS

Continuous variable data were expressed as (mean ± standard deviation) and analyzed by t-test; qualitative data were expressed as (n, %) and analyzed by X2 test. Statistical analysis was performed using SPSS 25.0 software. A result with $P < 0.05$ was considered statistically significant.

2. RESULTS

2.1 COMPARISON OF GENERAL CHARACTERISTICS AND CLINICAL MANIFESTATIONS BETWEEN DIFFERENT TYPES OF KAWASAKI DISEASE.

The incidence of typical clinical manifestations such as rash, strawberry tongue, conjunctival congestion, chapped lips, lymphadenopathy, and redness and swelling of hands and feet in the cKD group was sig-

Table 1

Comparison of general data and clinical manifestations of children with the same type of Kawasaki disease (n = 136)

Item	cKD Group (n=101)	iKD Group (n=35)	X^2/t Value	P Value
Age (years)	2.88±1.42	2.23±1.18	2.431	0.016
Male (example, %)	70 (69.3%)	23 (65.7%)	0.155	0.694
Rash	93 (92.1%)	19 (54.3%)	25.547	<0.001
Conjunctival congestion	90 (89.1%)	18 (51.4%)	22.572	<0.001
Strawberry tongue	88 (87.1%)	16 (45.7%)	24.777	<0.001
Swollen and red hands and feet	86 (85.1%)	14 (40.0%)	25.347	<0.001
Chapped lips	84 (83.2%)	15 (42.9%)	21.328	<0.001
Enlarged cervical lymph nodes	76 (75.2%)	12 (34.3%)	5.446	0.020
Positive red scar of BCG vaccination	21 (20.8%)	18 (51.4%)	11.928	<0.001

Table 2

Comparison of Laboratory and Echocardiographic Indicators between the Two Groups of Children Patients

Item	cKD Group (n=101)	iKD Group (n=35)	X^2/t Value	P Value
CRP (mg/L)	78.6±21.3	82.1±22.4	0.827	0.410
ESR (mm/h)	64.7±15.6	66.5±14.2	0.601	0.549
WBC (×10^9/L)	15.3±4.2	16.0±4.6	0.829	0.409
Hb (g/L)	109.4±9.3	108.6±10.1	0.429	0.669
PLT (×10^9/L)	466±122	471±116	0.212	0.833
ALB (g/L)	31.8±4.1	30.9±4.5	1.091	0.277
ALT (U/L)	38.2±18.7	42.3±20.2	1.095	0.276
Leukocytes in urine >10/HPF	16 (15.8%)	8 (22.9%)	0.880	0.348
CAL Number of cases occurred	17 (19.5%)	20 (57.1%)	21.328	0.000

nificantly higher than that in the iKD group ($P < 0.001$), but the scarlet fever reaction was more common in the iKD group ($P = 0.001$). There was no significant difference in gender between the two groups, but the children in the iKD group were younger, as shown in Table 1.

2.2 COMPARISON OF LABORATORY AND ECHOCARDIOGRAPHIC EXAMINATION RESULTS

There was no statistically significant difference in inflammatory markers such as CRP and ESR between the two groups ($P > 0.05$). However, the incidence of CAL was significantly higher in the iKD group than in the cKD group ($P < 0.001$), suggesting a higher risk of coronary artery injury in children with iKD, as shown in Table 2.

3 DISCUSSION

In recent years, with the enhanced understanding of Kawasaki disease (KD), the diagnosis rate and treatment level have been continuously improving, especially for the typical type (cKD), which has established a relatively standardized diagnosis and treatment pathway [3]. However, the atypical type (iKD), due to its non-specific clinical manifestations, is still prone to being misdiagnosed as other febrile diseases, leading to delayed treatment and an increased risk of coronary artery lesions (CAL) [4]. In addition, the insufficient implementation of echocardiography in some primary medical institutions further increases the probability of missed diagnosis. Studies have shown that the incidence of CAL in iKD is significantly higher than that in cKD, and the non-response rate to intravenous immunoglobulin (IVIG) is also higher. Currently, there is a lack of unified treatment guidelines [5]. Moreover, the incomplete long-term follow-up system poses a risk of cardiac complications for some children. Enhancing the early identification ability of iKD, establishing risk stratification and standardized treatment plans, strengthening echocardiographic screening and long-term cardiac monitoring are key to improving prognosis and reducing the incidence of CAL [6].

The results of this study indicate that there are significant differences in clinical manifestations and the risk of CAL between children with typical Kawasaki disease (cKD) and those with atypical Kawasaki disease (iKD). Children with cKD have more typical clinical symptoms and are relatively easier to diagnose, while iKD, due to the lack of complete typical manifestations, especially when accompanied by fever and uncommon signs, is often misdiagnosed as other viral or bacterial infections, delaying treatment and increasing the risk of CAL [7]. The positive rate of scarlet fever rash in the iKD group was significantly higher than that in the cKD group, suggesting that this reaction should be given due attention as an important auxiliary diagnostic clue when the clinical judgment is unclear. Although there were no significant differences in inflammatory markers such as CRP, ESR, and WBC between cKD and iKD in this study, indicating that the degree of inflammation itself is not sufficient to distinguish the two types of KD, the incidence of CAL in iKD was significantly higher than that in cKD (57.1% vs 19.5%, $P < 0.001$), further confirming that atypical manifestations may delay the window for IVIG treatment, leading to persistent coronary artery inflam-

mation and structural damage. Additionally, the average age of children with iKD was younger, indicating that younger children are more prone to atypical manifestations. This finding suggests that in clinical practice, special vigilance should be exercised for infants under 2 years old with fever and some symptoms of Kawasaki disease, and echocardiography and laboratory tests should be conducted as soon as possible, and IVIG treatment can be initiated according to the AHA recommended standards [8]. This study also suggests that standardized IVIG and aspirin combination therapy is crucial for reducing the incidence of CAL. For children who do not respond to IVIG, the addition of glucocorticoids or biological agents such as infliximab to control the inflammatory response can be considered.

In conclusion, early identification, accurate classification, and timely standardized treatment of Kawasaki disease are of great significance for preventing coronary artery damage. Special attention should be paid to the recognition and implementation of treatment guidelines for iKD, and clinical alertness should be enhanced. In the future, it is necessary to further expand the sample size and conduct prospective studies to explore more sensitive early warning indicators and optimized treatment pathways, providing stronger evidence support for the health prognosis of children with KD.

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ADVANCES IN EPIDEMIOLOGICAL RESEARCH ON KAWASAKI DISEASE WORLDWIDE

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Kawasaki Disease (KD) is an acute systemic vasculitis that primarily affects children under 5 years of age and is a leading cause of acquired heart disease in children in developed countries. Its etiology remains unknown, and epidemiological characteristics provide key clues for etiological research.

I. CORE EPIDEMIOLOGICAL CHARACTERISTICS

1. AGE AND GENDER:

- It mainly affects infants and young children, with approximately 80% of cases occurring in children under 5 years old, and the peak incidence is between 1 and 2 years of age.

- The male-to-female ratio is about 1.5:1, with a slight predominance of boys over girls.

2. ETHNICITY AND GENETIC SUSCEPTIBILITY:

- Children of East Asian descent have the highest incidence, especially those from Japan, South Korea, and China. This phenomenon has been confirmed worldwide, indicating that genetic factors play an important role in the pathogenesis.

- Genome-Wide Association Studies (GWAS) have identified multiple susceptibility gene loci related to immune regulation and vascular inflammation (such as ITPKC, CD40, BLK, etc.), and the frequency of these loci is higher in the East Asian population.

3. SEASONALITY AND CLUSTERING:

- Many countries have reported obvious seasonal fluctuations, with peak incidence usually occurring in winter and spring.

- Small-scale 'outbreaks' or clustered cases within communities are occasionally reported, suggesting the possible existence of certain common infectious triggers.

II. GLOBAL GEOGRAPHICAL DISTRIBUTION AND INCIDENCE TRENDS (KEY RESEARCH ADVANCES)

The incidence of Kawasaki Disease varies greatly worldwide, and the incidence in most countries continues to rise.

Key Advances: The global incidence is generally on the rise, but the absolute incidence and increase rate in East Asia are much higher than those in other parts of the world. This indicates that on the basis of genetic susceptibility, there may be widespread environmental triggers.

III. ADVANCES IN ETIOLOGICAL RESEARCH (BASED ON EPIDEMIOLOGICAL CLUES)

The etiology is unknown, but the mainstream hypothesis holds that: individuals with genetic susceptibility develop an abnormal immune response after exposure to a certain common infectious agent (possibly a virus), leading to vascular inflammation. Epidemiology provides key support for this hypothesis:

1. INFECTION TRIGGER HYPOTHESIS:

- Seasonality and clustering strongly suggest the existence of one or more common pathogens that can be transmitted through the air.

- Age distribution: The high incidence in infants and young children indicates that it mainly affects individuals with immature immune systems who are infected for the first time, which is similar to many childhood viral infections.

- Research Frontiers: Modern molecular technologies (such as metagenomics) are used to conduct large-scale screening of respiratory and gastrointestinal samples from patients in an attempt to identify specific viral or bacterial community characteristics. However, no single 'pathogenic bacteria' has been identified so far.

2. ENVIRONMENTAL FACTOR HYPOTHESIS:

- Wind Direction Research: Studies in Japan and China have found that the peak incidence of Kawasaki Disease is associated with winds from northern China/Central Asia (such as westerly or northerly

Region/Country	Incidence (per 100,000 children under 5 y	eTaresnodlsd) and Advances
Japan	**~350+ (2020 data)**	**The highest in the world. Since the first report in the 1960s, thr**
South Korea	**~210 (recent data)**	**The incidence ranks second in the world and is growing rapidly**
China	**~60-110 (significant regional differences)**	**The incidence shows a significant upward trend, but national da**
North America/Europe	**~10-30**	**The incidence in the United States is about ~25, and the incide**
Other Countries	**< 10**	**The reported incidence in Southeast Asia, India, the Middle Ea**

winds). It is speculated that the wind may carry certain microorganisms, fungal spores, toxins, or environmental chemicals.

- Climate Change Association: Some studies have attempted to link the incidence to climate changes such as temperature, humidity, and precipitation, but the results are inconclusive.

3. GENETIC SUSCEPTIBILITY HYPOTHESIS:

- As mentioned earlier, GWAS studies have confirmed the importance of genetic factors. The current model is a 'multiple hit' model: that is, individuals need to carry a certain number of risk gene variants and be exposed to triggers at a specific time to develop the disease.

IV. EPIDEMIOLOGICAL ADVANCES IN CORONARY ARTERY LESIONS (CAL)

The main hazard of Kawasaki Disease lies in its damage to the coronary arteries, leading to the formation of aneurysms or dilatation.

- High Incidence: In untreated patients, the incidence of CAL is as high as 20-25%.

- Efficacy of IVIG: High-dose intravenous immunoglobulin (IVIG) therapy significantly reduces the risk of CAL to 3-5%.

- Resistance: Approximately 10-20% of patients do not respond to initial IVIG therapy, and these patients are at the highest risk of developing CAL.

- Long-term Cardiovascular Risk: Even if the coronary arteries are normal in the acute phase, the risk of developing early atherosclerosis in adulthood may be higher than that in the general population.

Therefore, long-term follow-up of children with Kawasaki Disease is crucial.

V. FUTURE RESEARCH DIRECTIONS AND CHALLENGES

1. Etiology Confirmation: It remains the biggest challenge and ultimate goal. International collaboration is needed to conduct large-scale, prospective sample collection and environmental monitoring.

2. Improved Risk Prediction: Develop more effective models to identify high-risk patients who are resistant to IVIG in the early stage of the disease, so as to adopt more aggressive second-line treatment.

3. Global Disease Burden: Establish more complete monitoring systems in low- and middle-income countries to understand the true global disease distribution and avoid underestimation due to insufficient diagnosis.

4. Long-term Management: Establish a seamless follow-up system from childhood to adulthood to manage the lifelong cardiovascular health of patients with coronary artery sequelae.

CONCLUSION

Global epidemiological studies on Kawasaki Disease clearly depict a disease with strong genetic susceptibility and potential environmental triggers. Its incidence, especially in East Asia, continues to rise, making it an increasingly important public health issue. Although IVIG therapy has greatly improved the prognosis, the unknown etiology hinders the development of preventive strategies. Future research relies on cross-border and multidisciplinary cooperation, combining advanced genomics, environmental science, and immunology technologies, with the ultimate goal of uncovering the etiological mystery of Kawasaki Disease and achieving effective prevention and precise treatment.

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PRACTICING PHYSICIANS

THE RELATIONSHIP AND ROLE OF PROACTIVE MEDICINE IN KAWASAKI DISEASE AND INFECTIOUS IMMUNOLOGICAL DISEASES

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ABSTRACT:

Proactive Medicine, as an advanced medical concept transitioning from "passive disease treatment" to "active health management," aims to achieve lifelong health maintenance through prevention-first strategies, early intervention, personalized management, and technological empowerment. By systematically reviewing its core principles and technical support systems-incorporating regular health checkups, advanced diagnostic tests, wearable devices, health applications, and domestic and international practices-this paper analyzes the clinical value of Proactive Medicine in diagnosing and treating diseases such as Kawasaki disease. It further explores the alignment and synergistic pathways between Proactive Medicine and Traditional Chinese Medicine's (TCM) "preventive treatment" philosophy. Addressing current challenges like data privacy and technology accessibility, the study provides theoretical references and practical directions for integrating Proactive Medicine into the "Healthy China 2030" strategy.

Keywords: Proactive Medicine; preventive treatment; integrative Chinese and Western medicine; Kawasaki disease; infection-related immune disorders; early intervention.

I. CORE CONNOTATION AND CONCEPTUAL EVOLUTION OF PROACTIVE MEDICINE

(1) Definition: From "Disease Response" to "Health Creation"

"Proactive Medicine" (also termed proactive healthcare or active health) is an evolving health paradigm that shifts focus from disease treatment to prevention and health optimization.

II. CLINICAL VALUE OF PROACTIVE MEDICINE IN KAWASAKI DISEASE

Kawasaki disease (KD), a common acute vasculitis in children, necessitates early intervention due to the irreversible nature of coronary artery lesions (CAL). Proactive Medicine demonstrates significant clinical value in this field, manifested in three aspects:

(1) Overcoming Diagnostic Limitations for Pre-Symptomatic Risk Identification

Traditional KD diagnosis relies on "fever lasting ≥5 days + typical clinical symptoms," often leading to misdiagnosis or delayed intervention due to atypical presentations. Proactive Medicine enables early diagnosis via dual pathways:

1. Early Biomarker Detection: Elevated levels of adrenomedullin (ADM) and S100 calcium-binding protein A12 (S100A12) in blood serve as early "signal molecules" before symptom onset.

2. AI-Assisted Imaging:Automated coronary Z-score analysis quantifies subtle vascular edema in subclinical stages, increasing early detection rates by 40% and transitioning from "post-symptom diagnosis" to "pre-symptom warning."

(2) Stratified Intervention to Mitigate Coronary Risks

Personalized strategies for different KD phases:

1. Pre-Symptomatic Phase (Screening Susceptible Populations): Genetic testing (e.g., ITPKC, FCGR2A genes) identifies high-risk children, guiding infection avoidance (e.g., minimizing crowded exposures).

2. Acute Phase (Fever <5 days): Biomarker (e.g., IL-6, C-reactive protein) and genetic risk stratification predict IVIG resistance, prompting early infliximab-IVIG combination therapy to shorten inflammation.

3. Subacute Phase: Thromboelastography-guided anticoagulation reduces coronary dilation incidence by 35% in high-risk cases.

(3) Extended Post-Discharge Management for Long-Term Health

Proactive Medicine addresses gaps in traditional follow-ups via:

1. Wearable Heart Rate Monitors: Real-time HRV tracking detects myocardial ischemia risk (89% sensitivity).

2. Home-Hospital Platforms: AI-generated rehabilitation plans (e.g., cardiac reserve-based cycling) and automated reminders ensure continuous care.

III. PROACTIVE MEDICINE IN INFECTION-RELATED IMMUNE DISORDERS

For conditions like rheumatoid arthritis, systemic lupuserythematosus, and recurrent infections, Proactive Medicine offers a "prevention-monitoring-intervention" framework

(1) Risk Prediction: Identifying Susceptible Populations

1. Genetic Screening: TLR4/-NOD2 polymorphisms predict immune dysregulation (e.g., recurrent infections).

2. Immune Baseline Profiling: T/B-cell counts and cytokine (e.g., TNF-α, IL-10) levels establish reference thresholds.

(2) Dynamic Monitoring: Early Disease Signals

1. Portable Inflammatory Markers: Home-based CRP/procalcitonin tests trigger timely intervention.

2. Lifestyle-Immune Correlations: Sleep <6 hours/day elevates IL-6 by 20%, guiding behavior adjustments.

(3) Precision Interventions

1. Infection Prevention: Pathogen-specific vaccination (e.g., pneumococcus) and avoidance protocols.

2. Immune Modulation: Vitamin D supplementation and aerobic exercise (3x30 mins/week) delay autoimmune progression.

IV. SYNERGY BETWEEN PROACTIVE MEDICINE AND TCM

(1) Conceptual Alignment: East-West Health Wisdom

1. "Preventive Treatment" Resonance: TCM's "treating the undiseased" (e.g., dietary/emotional regulation, Baduanjin) mirrors Proactive Medicine's early screening/chronic disease management.

2. Holism and Personalization: TCM's constitution-based (e.g., Yang deficiency) approaches align with gene-/data-driven precision health.

(2) Integrative Practices in China

1. Policy-Driven "Preventive Treatment" Clinics: Combining TCM (e.g., Astragalus/Crataegus dietary therapy) with smart BP-AI monitoring for pre-hypertension.

2. Subhealth Management: Acupuncture + sleep tracking optimizes TCM's "lifestyle rhythm" advice.

3. Modernized Herbal Prevention: Big data validates Coptis chinensis for diabetes pre-intervention.

V. CONCLUSION

Proactive Medicine optimizes Kawasaki disease management via early diagnosis, stratified intervention, and post-discharge care, reducing CAL risks. Its "risk-dynamic-precision" framework reshapes infection-immune disorder prevention. Synergy with TCM enriches health systems. Despite challenges (e.g., technology access), policy and innovation can position Proactive Medicine as a cornerstone for "Healthy China 2030," transforming healthcare from treatment to sustained health maintenance.

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CURRENT SITUATION OF DENTAL IN CHILDREN IN VIETNAM: SYSTEMATIC REVIEW

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ABSTRACT:

In recent years, oral health care for children in Vietnam has attracted increasing scholarly attention, with several evidence-based studies highlighting the urgent need for intervention. The overall oral health status of Vietnamese children remains concerning, particularly due to the high burden of dental caries. Moreover, significant disparities exist between regions and between urban and rural populations, reflecting broader socio-economic and environmental determinants of health

Prevalence of Dental Caries: Recent epidemiological studies underscore the severity of dental caries among Vietnamese children. A 2025 study conducted in the mountainous region of northern Vietnam (Sa Pa, Lao Cai Province) reported an alarmingly high prevalence of dental caries among primary school children, reaching 91.4%. Specifically, 82.2% of children exhibited caries in their deciduous teeth, while 57.4% had

caries in permanent teeth. The mean dental index was 5.38, indicating not only widespread but also severe caries in deciduous dentition (1) . These findings highlight the urgent need for preventive measures and targeted oral health programs in disadvantaged regions.

Complementing this, another 2025 study conducted in Hanoi examined preschool children aged 5–6 years and found a high prevalence of primary dental caries, with socio-demographic and behavioral factors strongly associated with disease occurrence. Furthermore, research on oral health-related quality of life among 3-year-old preschool children in northern Vietnamese cities revealed that their quality of life was only at a medium level, suggesting that dental caries and related oral conditions significantly affect daily functioning and well-being (2).

Another study in 2025 found that the oral health-related quality of life of 3-year-old preschool children in northern Vietnamese cities was at a medium level (3).

Overall, research in the field of oral health care for children in Vietnam has painted a picture of "high prevalence, multiple risk factors, and exploration of new therapies". Existing studies clearly indicate that addressing this issue requires a comprehensive strategy, encompassing both the improvement of individual behavioral habits and the reduction of socioeconomic disparities and enhancement of access to medical services.

Keywords: Dental caries prevalence, Vietnamese children, Oral health disparities, Socioeconomic determinants, Preventive strategies

INTRODUCTION

Dental caries remains the most prevalent chronic oral disease among children worldwide and is recognized as a major public health challenge due to its impact on quality of life, school performance, and long-term health outcomes. Globally, despite advances in preventive dentistry, the burden of dental caries persists, particularly in low- and middle-income countries where access to oral health services is limited and preventive programs are underdeveloped. According to the Global Burden of Disease Study, dental caries continues to affect over half of the world's school-aged children, with significant disparities across regions and socio-demographic groups (4).

Vietnam exemplifies this global challenge. Recent epidemiological studies conducted in both urban and rural settings have consistently reported alarmingly high prevalence rates of dental caries among children, often exceeding 70–90%. For instance, research in Sa Pa, Lao Cai Province documented a prevalence of 91.4% among primary school children, with a mean dmft index of 5.38, indicating severe disease burden (1). Similarly, studies in Hanoi revealed high rates of caries among preschool children, with socio-demographic and behavioral factors strongly associated with disease occurrence (2). These findings underscore the multifactorial nature of pediatric oral health problems in Vietnam, where behavioral habits, dietary patterns, motivational factors, and socio-economic disparities converge to exacerbate disease risk.

The Vietnamese context also reflects broader regional patterns observed across Southeast Asia. Countries such as Thailand, Indonesia, and the Philippines report comparably high prevalence rates among preschool and school-aged children, driven by rapid urbanization, increased consumption of processed foods, and uneven distribution of dental services. When compared to other middle-income countries, including India, Pakistan, Brazil, and Mexico, Vietnam's prevalence rates remain at the higher end of the spectrum, highlighting systemic gaps in preventive strategies and resource allocation (5). In contrast, developed countries such as Japan, Western Europe, and North America have achieved significant reductions in pediatric caries prevalence—often below 40%—through comprehensive public health measures including water fluoridation, universal health coverage, and school-based preventive programs (4).

Against this backdrop, this systematic review aims to synthesize current evidence on the prevalence, determinants, and interventions related to pediatric oral health in Vietnam. By situating Vietnam's findings within regional and global contexts, the review seeks to identify critical gaps and inform policy directions for reducing oral health inequalities and improving child health outcomes

METHODOLOGY

Literature Search Strategy: This systematic review was conducted following established guidelines for evidence synthesis in public health research. A comprehensive search was performed across multiple electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, as well as Vietnamese national journals such as the Vietnam Medical Journal and institutional repositories of the National Hospital

of Odonto-Stomatology in Hanoi. The search covered publications from 2015 to 2025, ensuring inclusion of both recent and foundational studies on pediatric oral health in Vietnam.

The following keywords and Boolean operators were applied:

• "dental caries" OR "oral health" AND "children" AND "Vietnam"

• "dmft index" OR "oral hygiene" AND "Vietnamese children"

• "oral health-related quality of life" AND "Vietnam"

Reference lists of relevant articles were also screened to identify additional studies not captured in the initial search.

Inclusion and Exclusion Criteria:

Studies were included if they met the following criteria:

• Conducted in Vietnam and focused on children aged 3–12 years.

• Reported prevalence, risk factors, or interventions related to dental caries or oral health.

• Published in peer-reviewed journals or official medical reports.

• Provided quantitative data (e.g., prevalence rates, dmft/dmfs indices) or qualitative insights into determinants of oral health.

Exclusion criteria were:

• Studies focusing exclusively on adults or adolescents above 12 years.

• Case reports, editorials, or commentaries without empirical data.

• Articles not available in English or Vietnamese.

• Studies with incomplete methodology or insufficient data for extraction.

Data Extraction and Quality Assessment

Two independent reviewers screened titles and abstracts for relevance. Full-text articles were then assessed against inclusion criteria. Data extracted included:

• Study location and population characteristics.

• Sample size and age distribution.

• Prevalence of dental caries and mean dmft/dmfs indices.

• Reported risk factors (behavioral, dietary, sociodemographic).

• Intervention strategies and outcomes.

Quality assessment was conducted using the Newcastle-Ottawa Scale (NOS) for observational studies and the Cochrane Risk of Bias Tool for intervention studies. Discrepancies between reviewers were resolved through discussion with a third investigator.

DATA SYNTHESIS

Findings were synthesized narratively due to heterogeneity in study designs, populations, and outcome measures. Where possible, prevalence rates and dmft indices were compared across regions and age groups to identify trends. Determinants of oral health were categorized into behavioral, dietary, motivational, and sociodemographic domains. Intervention studies were analyzed separately to highlight emerging treatment modalities and public health strategies.

RESULT

Prevalence of Dental Caries

• A 2025 study in Sa Pa, Lao Cai Province reported a 91.4% prevalence of dental caries among primary school children, with 82.2% affected in deciduous teeth and 57.4% in permanent teeth. The mean dmft index was 5.38, indicating severe disease burden.(1)

• A 2025 study in Hanoi found a high prevalence of primary dental caries among preschool children aged 5–6 years, with socio-demographic and behavioral factors strongly associated with disease occurrence (2).

• Research on oral health-related quality of life among 3-year-old preschool children in northern Vietnamese cities revealed only a medium level of quality of life, suggesting significant impacts of caries on daily functioning (3).

KEY DETERMINANTS

Several studies have explored the main factors contributing to children's oral health problems, which can be summarized as follows:

• Poor oral hygiene habits: A study found that only 7.5% of 7-9-year-old children had their oral hygiene rated as "good". Poor brushing habits and only visiting the dentist when symptoms occur are significantly associated with a higher caries index (1)

• Dietary habits: Frequent consumption of sugary foods such as candies, snacks, and sodas is closely related to an increased risk of caries in primary teeth (2).

• Lack of intrinsic motivation: A study in Hanoi found that children's motivation for oral health care mainly comes from external sources (such as parental urging), and they lack intrinsic motivation. Research shows that children with stronger intrinsic motivation have better oral hygiene, highlighting the importance of changing the direction of health education (3).

• Sociodemographic differences:

• Region and ethnicity: Compared to urban children, children in remote mountainous areas have more prominent oral health prob-

lems, and there are significant ethnic differences. For example, in a mountainous area study, Dai children had a higher risk of caries in primary teeth compared to Yao children, while Hmong children had a relatively better situation (1).

• Family background: Parents' occupation and education level are important influencing factors. For instance, children whose parents are farmers have a higher risk of caries than those whose parents are workers or have other occupations. Higher education level of the father is associated with better oral health-related quality of life in 3-year-old children (3).

• History of dental trauma: A study conducted in Dong Thap Province, Vietnam, found that children who had a history of dental trauma during the primary tooth period had a 1.73 times higher risk of incomplete mineralization of permanent molars and incisors than other children. This developmental defect can lead to tooth sensitivity and increased susceptibility to caries (6).

CLINICAL TREATMENT AND INTERVENTION RESEARCH

In addition to the current prevalence and risk factors, Vietnamese scholars are also actively exploring new treatment and intervention methods:

Application of New Materials: A preliminary study conducted in Ho Chi Minh City evaluated a new type of prefabricated crown for children that combines aesthetic appeal with minimal tooth grinding. Short-term follow-up at 3 months post-operation showed that the crown performed well in terms of chewing function, aesthetics, integrity, and marginal adaptation, offering a new treatment option for primary tooth restoration (7).

Intervention Directions: Researchers unanimously called for the urgent implementation of targeted oral health promotion programs in schools, enhanced oral health education for parents, and improved accessibility to dental care services for children in remote areas. A health education model that focuses on cultivating children's intrinsic motivation is considered to have greater potential (1-3).

DISCUSSION

The findings of this systematic review confirm that dental caries remains a major public health issue among Vietnamese children, with prevalence rates exceeding 70–90% in some regions. These figures are substantially higher than those reported in many other parts of the world, underscoring the urgent need for targeted interventions.

COMPARISON WITH SOUTHEAST ASIA

Vietnam's burden of pediatric dental caries is consistent with trends observed across Southeast Asia, where prevalence rates remain high due to similar socioeconomic and behavioral determinants. For example, studies in Thailand and Indonesia have reported caries prevalence among preschool children ranging from 70–85%, with mean dmft indices comparable to those observed in Hanoi and Lao Cai. In the Philippines, prevalence rates exceed 80% in certain rural populations, reflecting limited access to preventive care and high sugar consumption. These parallels suggest that Vietnam's challenges are part of a broader regional pattern, driven by rapid urbanization, dietary transitions, and uneven distribution of dental services (5).

COMPARISON WITH THE OTHER MIDDLE-INCOME COUNTRIES

When compared to other middle-income countries outside Southeast Asia, Vietnam's prevalence rates remain at the higher end of the spectrum. In Pakistan and India, for instance, caries prevalence among school-aged children ranges between 60-75%, with socio-economic disparities strongly influencing outcomes. Similarly, in Latin American countries such as Brazil and Mexico, prevalence rates hover around 65–70%, but national oral health programs have begun to reduce the burden in urban centers. Vietnam's persistently high rates, particularly in rural and ethnic minority populations, highlight the need for stronger national-level preventive strategies and resource allocation (5).

COMPARISON WITH DEVELOPED COUNTRIES

In contrast, developed countries have achieved significant reductions in pediatric dental caries through comprehensive public health measures. Data from the Global Burden of Disease Study indicate that high-SDI (Socio-Demographic Index) regions such as Western Europe, North America, and Japan report prevalence rates below 40%, with mean dmft indices often under 2. These im-

provements are attributed to widespread use of fluoridated water and toothpaste, school-based preventive programs, and regular dental check-ups supported by universal health coverage (4). The stark contrast between Vietnam and these high-income countries underscores the importance of systemic interventions, including preventive infrastructure and policy-driven approaches.

Policy Implications:

The evidence reviewed demonstrates that oral health problems among Vietnamese children are shaped by a constellation of behavioral, dietary, motivational, and sociodemographic factors. These determinants not only contribute to the high prevalence of dental caries but also perpetuate inequalities in oral health outcomes across regions and social groups. Addressing these challenges requires a comprehensive and multi-level approach, consistent with global recommendations for oral health promotion (8), (9, 10).

Behavioral and Educational Interventions:

The finding that only a small proportion of children maintain good oral hygiene practices highlights the urgent need for school-based oral health education programs. Preventive strategies should emphasize the importance of daily toothbrushing with fluoride toothpaste, routine dental check-ups, and the avoidance of symptom-driven dental visits. Evidence from other countries suggests that integrating oral health education into the school curriculum can significantly improve children's hygiene practices and reduce caries incidence (1,2), (11, 12). In Vietnam, such programs should be tailored to local cultural contexts and delivered in collaboration with teachers and community health workers.

Nutritional Policies:

Dietary habits, particularly the frequent consumption of sugar-rich foods and beverages, remain a critical risk factor for dental caries. Public health policies should therefore prioritize reducing sugar intake among children. This may include implementing school nutrition guidelines, restricting the availability of sugary snacks and sodas in educational settings, and promoting healthier alternatives. Parental education on the impact of diet on oral health is equally important, as parents play a central role in shaping children's eating behaviors. (2). Global evidence strongly supports the pivotal role of free sugars in caries development, reinforcing the need for dietary interventions (13).

Motivation and Health Education Models:

The lack of intrinsic motivation among children to maintain oral health underscores the limitations of externally driven behaviors. Health education models should therefore focus on cultivating intrinsic motivation, empowering children to take responsibility for their own oral hygiene. Interactive and child-centered approaches, such as gamified learning, peer-led initiatives, and positive reinforcement strategies, may be particularly effective in fostering long-term behavioral change (3). This represents a shift from traditional parental urging toward more sustainable, self-driven health practices. International reviews emphasize that sustainable improvements in oral health require motivational and behavioral strategies alongside clinical interventions (9, 10).

Addressing Sociodemographic Inequalities:

Regional and ethnic disparities in oral health outcomes reflect broader social determinants of health. Children in remote mountainous areas, particularly those from ethnic minority groups, face structural barriers to accessing dental care. Policies must therefore prioritize resource allocation to underserved regions, including the establishment of mobile dental clinics, training of local health workers, and subsidized dental services. Furthermore, the association between parental occupation and education level with children's oral health outcomes highlights the need for family-centered interventions. Programs that enhance parental knowledge and skills in oral health care can indirectly improve children's outcomes (1-3), (8), (10)

Managing Dental Trauma and Developmental Defects:

The long-term consequences of dental trauma during childhood, such as incomplete mineralization of permanent teeth, necessitate early prevention and management strategies. Schools and communities should implement injury-prevention programs, particularly in rural areas where children are more exposed to physical risks. Additionally, early detection and treatment of dental trauma can mitigate its impact on permanent dentition, reducing the risk of sensitivity and caries in later life (4).

CONCLUSION

This systematic review demonstrates that dental caries among Vietnamese children remains a pressing public health concern, characterized by high prevalence rates, severe disease burden, and significant socio-demographic dis-

parities. The evidence highlights a constellation of contributing factors, including poor oral hygiene practices, frequent consumption of sugary foods, lack of intrinsic motivation, and structural inequalities related to region, ethnicity, and parental background. Furthermore, the long-term consequences of dental trauma add to the complexity of pediatric oral health challenges in Vietnam.

Comparative analysis reveals that Vietnam's situation is consistent with trends across Southeast Asia and other middle-income countries, where prevalence rates remain high due to similar socioeconomic and behavioral determinants. However, Vietnam's rates are notably higher than those reported in many comparable nations, underscoring the need for stronger national-level preventive strategies. In contrast, developed countries have achieved substantial reductions in pediatric caries prevalence through systemic interventions such as fluoridation, universal health coverage, and school-based oral health programs. These international experiences provide valuable lessons for Vietnam, suggesting that comprehensive, multi-level approaches are both feasible and effective.

Policy implications are clear: Vietnam must prioritize school-based oral health education, parental involvement, and nutritional policies aimed at reducing sugar consumption. Equitable resource allocation is essential to address disparities in rural and ethnic minority populations, while innovative treatment modalities, such as prefabricated crowns, offer promising clinical solutions. Importantly, health education models should focus on cultivating intrinsic motivation among children, thereby fostering sustainable behavioral change.

In conclusion, the burden of dental caries among Vietnamese children reflects both individual-level behaviors and broader structural determinants. Addressing this challenge requires a holistic strategy that integrates preventive education, clinical innovation, and systemic policy reforms. By learning from regional peers and adopting successful models from developed countries, Vietnam can move toward reducing oral health inequalities and improving the overall well-being of its children.

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ABSTRACTS OF INTERESTING ARTICLES PUBLISHED IN VARIOUS JOURNALS

POTENTIAL BENEFIT OF CAPILLAROSCOPY IN ASSESSING THE CLINICAL DYNAMICS OF ERYTHEMA NODOSUM

(A CASE STUDY)

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ABSTRACT:

Erythema nodosum (EN) is mainly a septal panniculitis without vasculitis. Its manifestation is a dense rash on the shins. In some cases, secondary vasculitis also develops. Our clinical case was a classic manifestation of EN, without complications. However, capillaroscopy performed at the initial stage revealed microcirculatory changes, mainly because of reduced transparency. These changes were disappeared in dynamics, consistent with the clinical improvement of the rash. As a result, we can assume that the capillaroscopy picture represented a subclinical form of vasculitis, which did not have the opportunity to manifest clinically. This gives the capillaroscopy method the ability to dynamically monitor microcirculation.

THE ROLE OF EPONYCHIUM CAPILLAROSCOPY IN SYSTEMIC LUPUS ERYTHEMATOSUS, DERMATOMYOSITIS, AND RAYNAUD'S PHENOMENON

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ABSTRACT:

Nail capillaroscopy (NFC) is a non-invasive, easy-to-use, inexpensive technique that plays an important role in rheumatology clinical practice.

Evaluation of capillary morphology - such as dilation, hemorrhage, capillary loss, and neoangiogenesis - allows clinicians to obtain important information about disease activity, progression, and vascular involvement. Capillaroscopy plays a crucial role not only in the early detection of the disease, but also in differentiating primary from secondary Raynaud's phenomenon and in monitoring treatment of various connective tissue diseases.

Recent advances, including digital capillaroscopy and the integration of automated image analysis, have increased its diagnostic accuracy and accessibility, solidifying its place as a frontline tool in rheumatology practice.

The potential use of capillaroscopy has been studied in rheumatological conditions such as: systemic lupus erythematosus, Sjogren's syndrome, antiphospholipid syndrome, rheumatoid arthritis, systemic sclerosis, and others.

This paper discusses in detail the role of capillaroscopy in systemic lupus erythematosus, dermatomyositis, and Raynaud's phenomenon.

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(Tbilisi, Georgia)

CAPILLAROSCOPIC CHANGES IN CHILDREN INFECTED WITH COVID

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ABSTRACT:

The coronavirus (SARS-CoV-2) pandemic, known as COVID-19, has spread across the world in a short period of time and has killed more than 2 million people to date.

Microcirculatory changes, visible by eponychium capillaroscopy, were observed with different characteristics in different stages of the disease, from the acute phase to the post-COVID period.The presence of hemosiderin deposits and capillary changes are consistent with the COVID-19 pathophysiological changes we know today, especially the involvement of the endothelium.The changes found during the acute phase, regardless of the severity of the infection, are reversible and are no longer seen in discharged patients or even in re-evaluation of the same patients.

The studies available to us highlight the possible utility of eponychium capillaroscopy in the context of SARS-CoV-2 disease as a non-invasive and easy-to-perform method.There does not appear to be a specific pattern of microcirculatory changes associated with COVID-19, but there are nonspecific changes that may be important for patient management.

Examining a larger sample of patients would allow investigating the existence of a correlation between microcirculatory changes visible by nail capillaroscopy and the development of serious complications secondary to SARS-CoV-2 infection (eg, pulmonary embolism, ARDS, etc.).

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CLINICAL VALUE OF CARDIOINTERVALOGRAPHY IN MODERN MEDICINE

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Ir. Tsitsishvili Children's Clinic)

ABSTRACT:

Cardiointervalography is a functional-instrumental examination method, the purpose of which is (by means of the variation of the R-R intervals on the electrocardiographic recording) to determine the balance of the sympathetic and parasympathetic divisions of the autonomic nervous system, which is often disturbed in the presence of a particular pathology. In childhood, this imbalance appears as an important premorbid factor in the development of both cardiovascular and many non-cardiac diseases, which can be avoided by the right information and reasonable therapeutic or preventive interventions. The numerical parameters obtained by cardiointervalography allow, regardless of the symptoms, to objectively determine the predominance of the influence of one or another part of the vegetative nervous system on the cardiovascular system both at rest and in a physically tense

state. We define eutonia, sympathicotonia and vagotonia. This makes it possible to identify a therapeutic target at an early stage of pathogenesis, when pathophysiological changes only have a functional impact on the body and we still have the opportunity to prevent organic pathology.

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(Tbilisi, Georgia)

ASSESSMENT OF AUTONOMIC NERVOUS SYSTEM DISORDERS AND ASSOCIATED CARDIOVASCULAR RISKS IN PATIENTS WITH SYSTEMIC SCLERODERMA

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G. CHAKHUNASHVILI,
N. JOBAVA

(TSMU, Georgian Association of Pediatric Cardiologists, Ir. Tsitsishvili Children's Clinic)

ABSTRACT:

In systemic scleroderma, we encounter such pathological changes in the autonomic nervous system that can lead to functional changes in the controlled organ. It was studied cardiological and microvascular manifestations in patients with systemic scleroderma and the relationship of these changes to the state of the autonomic nervous system. The results obtained allow us to conclude that, regardless of the duration of the disease, changes in heart rate variability (HRV) and heart rate turbulence (HRT) are observed, which is proportional to the reflection of the nervous influence on the work of the heart. On the other hand, no association was revealed between microcirculatory changes, microangiopathy and the state of the peripheral nervous system in patients with Raynaud's phenomenon, which indicates the independent development of these processes and the potential central genesis of vasomotor disorders in patients with scleroderma.

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ASPECTS OF CONGENITAL MEGAURETER IN CHILDHOOD

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N. KVIRKVELIA, M. TSANAVA,
T. ABULADZE, D. KVIRKVELIA,
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(Ir. Tsitsishvili New Children's Clinic)

ABSTRACT:

It is important to note that surgical treatment of obstructive megaureter involves resection of the obstructive distal segment, narrowing of the dilated ureter, and reimplantation into the bladder, using reflux prevention techniques. In some cases, a temporary skin ureterostomy is required to reduce the diameter of the ureter to normal size. An alternative approach to reconstruction in young children is reimplantation of a simple, refluxing ureter.

The incidence of cases suggests that high-pressure balloon dilatation or ureteral stenting may be a promising approach for the treatment of primary obstructive megaureter in neonates or infants, in whom reconstructive surgery is more difficult. Further studies with a larger number of patients are needed to confirm the long-term efficacy and safety of this technique.

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URINARY TRACT INFECTION IN CHILDHOOD

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ABSTRACT:

Definition of urinary tract infection (UTI) -UTI refers to the presence of a significant number of bacteria in the urine without indicating the localization of the pathological process. UTI is a collective term and includes inflammatory changes caused by bacteria, both in the lower (cystitis) and upper urinary tract (pyelonephritis) Treatment begins empirically, with antibiotics, after preliminary collection of urine for bacteriological examination In newborns - treatment should be started intravenously with broad-spectrum antibiotics after collection of material for laboratory examination. In the pre-antibiotic era, neonatal mortality rates for SSI were >20%. With the introduction of antibacterial therapy, complications (kidney abscess, mortality) have become rare. Empirical therapy - In empirical therapy, the antibiotic selection is the same as for sepsis, since SSI and sepsis are mainly caused by the same microorganisms. Treatment is provided parenterally - a combination of ampicillin and gentamicin (most pathogens are sensitive to these antibiotics). Dosage varies depending on weight and chronological age. The duration of treatment should be determined by the clinical course. In uncomplicated SSI (e.g., infection caused by Escherichia coli, no pathological changes on ultrasound of the urinary tract), the duration of treatment is 10-14 days. Antibacterial therapy is administered intravenously, although in infants, if the clinical picture improves and the course is uncomplicated, oral therapy may be switched. With prolonged therapy, there is a possibility of fungal infection. In adult children, the drug of choice for uncomplicated STIs is oral 3rd generation cephalosporins. In case of ineffectiveness, the treatment plan is changed based on the results of the bacteriological study, taking into account the antibiotic regimen.

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MODERN ASPECTS OF THE TREATMENT OF PRIMARY MEMBRANOUS NEPHROPATHY

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(Ir. Tsitsishvili New Children's Clinic)

ABSTRACT:

Membranous nephropathy (MN) is one of the most common causes of nephrotic syndrome in adults. The term MN reflects the pattern of damage revealed by histopathological examination of kidney biopsy, namely thickening of the glomerular basement membrane (GBM) and subepithelial immunoglobulin-containing deposits, with little cellular proliferation or infiltration. In the work, the authors, using the example of a case study, discuss modern aspects of the treat-

ment of primary membranous nephropathy, and conclude that After the end of treatment, the patient's general condition and quality of life significantly improved, there was practically no edema, diuresis was restored, the degree of proteinuria significantly decreased in dynamics (albumin/creatinine ratio in urine - 170 mg/mmol/crea), hypoalbuminemia, hyperlipidemia were no longer observed, and there was no episode of exacerbation of nephrotic syndrome. In parallel with the clinical improvement, immunological remission was noted (6 months after treatment - PLAR- R AB-1:10; 1 year after treatment - PLAR- R AB-1:20), which gives hope that the patient will also enter complete clinical remission.

Pediatric Cardiology №19 (2025)
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HYDRONEPHROSIS IN CHILDHOOD

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ABSTRACT:

Congenital hydronephrosis, both in terms of severity and prognosis, is one of the most important problems of the urinary system, which can be accompanied by the destruction of the renal parenchyma and impaired function. It can be detected from the 12th-14th week of pregnancy.

The authors conclude in their work that timely detection and management of congenital hydronephrosis significantly reduces the risk of damage to the urinary system and the development of chronic kidney disease.

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MODERN METHODS OF POSTNATAL ULTRASOUND ASSESSMENT OF CONGENITAL HYDRONEPHROSIS

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M. INASARIDZE, Z. ZARNADZE,
G. CHITAIA

(Ir. Tsitsishvili New Children's Clinic)

ABSTRACT:

Determining the degree of dilatation of the urinary tract in the pediatric population has always been and still is the greatest challenge of medicine. There are several classifications in the world. The aim of this article is to gather information confirmed by the latest randomized studies, which helps us in the sonographic diagnosis and assessment of congenital hydronephrosis. In the work, the authors conclude that by summarizing the experience accumulated over 11 years, we can confirm the effectiveness of using the UTD classification, pre-evaluate the need for surgical intervention and the risk of infection. It truly combines the two most commonly used classifications to date and helps us manage congenital hydronephrosis in the postnatal period, however, due to the complexity and lack of awareness of the classification, further research is still needed in clinical practice.

Social, Ecological & Clinical Pediatrics
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(Tbilisi, Georgia)

THE RUSSIAN-UKRAINIAN WAR AND POSSIBLE SCENARIOS FOR THE DEVELOPMENT OF EVENTS IN THE BLACK SEA REGION

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Direction: International Relations

ABSTRACT:

The main goal of the study is to analyze the geopolitical, geoeconomic and geostrategic situation in the Black Sea/Caspian region and to present a possible scenario for the development of the situation in the region based on the factor of the Russian-Ukrainian war. In this regard, pessimistic, neutral and optimistic scenarios for the development of events from the geopolitical, political, economic, military and security points of view are given.

Social, Ecological & Clinical Pediatrics
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NEONATAL NECROTIZING ENTEROCOLITIS: CURRENT CHALLENGES AND FUTURE PERSPECTIVES

T. GOTUA

ABSTRACT:

Necrotizing Enterocolitis (NEC) is a life-threatening disease predominantly affecting premature and very low birth weight infants resulting in inflammation and necrosis of the small bowel and colon and potentially leading to sepsis, perforation, peritonitis and,sometimes, death. Numerous research efforts have been made to better understand, treat, and prevent NEC. The high mortality and morbidity rates of NEC and its consequent impact on healthcare costs make it one of the most expensive neonatal pathologies, incurring an estimated annual financial burden.

This review briefly describes the possible pathogenesis of NEC, epidemiology, risk factors, pathophysiology, clinical diagnosis, and clinical manifestation and complications, modern and future treatment and prevention strategies. Findings from clinical observations, microbiological analysis, and molecular research will improve our understanding of the mechanisms underlying the pathogenesis of NEC. Future research in the field of NEC in preterm infants should focus on elucidating the specific role of pathogenic metabolic pathways in the pathogenesis of NEC, applying advanced artificial intelligence techniques such as machine learning to improve the accuracy of early diagnosis, further explore the TLR4-dependent signaling pathways that drive NEC progression, and develop targeted strategies to mitigate the range of long-term morbidities associated with NEC, thereby improving both acute clinical management and long-term health outcomes for these infants.

Social, Ecological & Clinical Pediatrics
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MODERN ASPECTS OF ONCOIMMUNOLOGY AND NEW CHALLENGES

VILI PACHKORIA,
MD., PhD, Professor,
Physician of General profile,
Oncologist, Clinical anatomist,
True member of the Georgian Academy of Humanitarian and Arts Sciences

ABSTRACT:

According to many of the world's leading and well-known specialists - the future of cancer treatment is immunotherapy. In the coming years, oncology will see a fundamental revision of treatment strategies: aggressive methods, which fail to differentiate between malignant and normal cells, will gradually lose their positions. Based on the above, I began searching for scientific papers, based on the study of which I presented new theses and methods, whose theoretical foundations are based on the achievements of modern medical science, the anatomical, immunological, morphological, clinical, and biological aspects of the human body. The mentioned theses and methods include: RASA therapy (RASAT), RACA therapy (RACAT), RALA therapy (RALAT), and PRASA therapy (PRASAT), for the implementation of which, in the future, scientific, experimental, and laboratory research needs to be actively continued. For this, we are ready to cooperate with all interested companies, in any country.

Social, Ecological & Clinical Pediatrics
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MORPHOLOGICAL AND CLINICAL-ANATOMICAL ASPECTS OF REPRESSED AUTO-SERO-ADJUVANT THERAPY (RASAT)

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True member of the Georgian Academy of Humanitarian and Arts Sciences

ABSTRACT:

Repressed Auto-Sero-Adjuvant Therapy (RASAT), which can also be called Suppressed Auto-Sero-Adjuvant Therapy (SASAT) with the same meaning, is a method that stimulates the body's immune system, improves general health, and serves as an auxiliary method for primary therapeutic agents. It involves, for therapeutic purposes, the subcutaneous injection of constituent elements of serum obtained from the patient's own venous blood, in a repressed/suppressed (inactivated, attenuated) form.

To implement this method, in the future, it is necessary to actively continue scientific, experimental, and laboratory research.

INNOVATIVE METHODS IN TREATING HEREDITARY DISEASES IN CHILDREN

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Scientific-clinical center for Maternal and Child health, Hospital with Scientific Clinical Centre of Cardiology

Rare diseases are diseases that are 80% genetic in nature and occur with a frequency of 1 in 10,000 people. They affect not only individual patients, but also entire families, affecting generations. At the same time, 65% of these diseases lead to severe forms of disability, a reality that every parent can face. However, we must not forget: even if a rare disease cannot be cured, help is always available.

Protecting the health of the generation is a priority of state policy in the field of healthcare. As part of the implementation of the "Health" State Program, which is a national strategy for protecting the health of mothers and children in Turkmenistan for 2021-2025, "Healthy Mother - Healthy Child - Healthy Future," much attention is paid to early detection and treatment of hereditary diseases.

With the assistance of the Ministry of Health and Medical Industry of Turkmenistan, over the past 2 years, a joint project with the Swiss company "F. Hoffmann La Roche LTD" has been successfully implemented at the Scientific-clinical center for Maternal and Child health for the diagnosis and innovative treatment of two dangerous genetic diseases: spinal muscular atrophy (SMA) and hemophilia A.

Since most genetic diseases remain lifelong diagnoses, the goal of treatment is not only to increase the length of life, but also to significantly improve its quality.

Spinal muscular atrophy (SMA) is a rare genetic disorder that affects motor neurons and causes progressive muscle weakness and complete immobilization and cessation of vital organ function. Patients retain intelligence and sensitivity, and IQ is often above average, so early detection and timely intervention play a key role in improving the prognosis and quality of life of patients. For the first time, the diagnosis and treatment of this disease have been successfully introduced in Turkmenistan.

The work on the detection, diagnosis and treatment of diseases is carried out in three stages. At the first stage, primary care physicians, upon detection of suspicious clinical signs, refer the patient to the Scientific-clinical center for Maternal and Child health, where specialized specialists - a pediatric neurologist, hematologist, orthopedist, geneticist, pediatrician - conduct an examination. At the second stage, the center's laboratory department conducts a molecular genetic test for spinal muscular atrophy DNA. At the third stage, patients with a confirmed diagnosis are given the opportunity to start treatment with the drug "EVRISDI", which significantly improves motor skills. The drug is available in the form of a powder for preparing a solution and taking it orally. This convenient and effective option can also be used at home. The child's parents are trained in the correct use of the drug in the hospital, after which they can regularly take the drug at their place of residence. The use of this drug in SMA patients has led to the restoration of previously lost functions: an increase in the range of motion, the ability to sit and move, and self-care. Patients were less likely to suffer from acute respiratory infections and pneumonia, and spent less time in the hospital. Early intervention and ongoing parental support helped children improve their quality of life, realize their full potential, and adapt to the conditions of the disease.

Hemophilia A is another inherited blood disorder caused by a deficiency of factor VIII. This disease has been known since ancient times. Modern medicine has come a long way: from complete helplessness in the face of the disease to effective replacement therapy. Thanks to advances in genetics and molecular biology, hemophilia is a condition that can be safely controlled with modern drugs. When the project is implemented, patients with severe disease receive the innovative drug "GEMLIBRA", which is a monoclonal antibody and is fundamentally different from previous treatments. The drug significantly simplifies treatment compared to the intravenous injections required for traditional replacement therapy. In many patients, bleeding has completely stopped.

The reduced frequency of bleeding and ease of use allow patients to lead a more active lifestyle, reduce the number of missed classes, and also reduce the number of visits to the doctor. Children return to an active lifestyle, go to school, and play sports.

Innovative approaches to treating rare diseases in children are already yielding tangible results. Thanks to government support, international cooperation, and the expertise of medical professionals, many children with severe genetic diseases are gaining the opportunity to extend their lives, health, and future.

Azhar Giniyat Chair
of NCCR Kazakhstan
SPPH & Memory T. Kawasaki
Xi'an China Dec. 2024

埃及大学骨科专家学术交流
2025.6.6陕西省人民医院

白俄罗斯国际医学会议
2025.10.30

迪拜国际医学会议
2025.1.6

中国德国古巴越南专家合影留念
2025.3.12广州

中国德国古巴越南专家合影留念
2025.3.12广州

COMING VERY SOON
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A supplementary manual entitled "Fundamentals of Pediatric Cardio-Rheumatology" (Volumes I–II) will be published soon.Authors: G. S. Chakhunashvili, N. D. Jobava, K. G. Chakhunashvili, D. G. Chakhunashvili. Volume I is devoted to Cardiology, and Volume II to Rheumatology, in which Chapter II represents the specialized section. The publication is presented in Georgian, English, and Russian.

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Volume I: 1170 pages

Volume II: 1235 pages

补充性学术专著《儿科心脏—风湿病学基础》（第一卷–第二卷）即将出版。

作者：**G. S. Chakhunashvili，N. D. Jobava，K. G. Chakhunashvili，D. G. Chakhunashvili**。

第一卷主要论述儿科心脏病学，第二卷专注于儿科风湿病学，其中第二章为专业深化章节。

本书将以格鲁吉亚语、英语和俄语三种语言出版。

出版社：格鲁吉亚，第比利斯，格鲁吉亚儿科心脏病学协会，**2025**年。

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