Hindawi
Dermatologic Therapy
Volume 2024, Article ID 7835561, 12 pages
https://doi.org/10.1155/2024/7835561

Review Article

MicroRNAs as Potential Biomarkers for the Diagnosis, Treatment, and Prognosis of Sexually Transmitted Diseases: Recent Advances and Future Directions

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Received 13 October 2023; Revised 5 January 2024; Accepted 27 February 2024; Published 18 March 2024

Academic Editor: Mahlatse Kgokolo

Sexually transmitted diseases (STDs), including condyloma acuminatum (CA), syphilis, gonorrhea, genital *Chlamydia trachomatis* (CT), and acquired immune deficiency syndrome (AIDS)/human immunodeficiency virus (HIV) infection, are a group of diseases primarily transmitted through sexual contact, similar behaviors, and indirect contact. These diseases exert a profound impact on both the physical and mental health of patients and impose a substantial socioeconomic burden. Nonetheless, there is a lack of satisfactory treatment options and preventive strategies currently. Research has revealed aberrant expression patterns of microRNAs (miRNAs) in the tissues and blood of individuals with STDs, which are involved in the regulation of essential cellular processes, including proliferation, differentiation, and apoptosis. Consequently, miRNAs hold promise as crucial biomarkers for early diagnosis, disease assessment, prognosis, and potential therapeutic targets for STDs. This systematic review presents pertinent research on miRNAs in the context of STDs to establish a theoretical foundation for clinical diagnosis and treatment strategies.

1. Introduction

STDs refer to a widespread epidemic that primarily transmits through sexual contact, similar behaviors, indirect contact, etc. This category includes conditions such as condyloma acuminatum (CA), syphilis, gonorrhea, genital *Chlamydia trachomatis* (CT), and acquired immune deficiency syndrome (AIDS)/human immunodeficiency virus (HIV) infections. These diseases have far-reaching public health implications on individuals' sexual and reproductive health and notably impact their physical and mental well-being, thereby imposing a substantial economic burden on society [1]. Presently, both treatment modalities and preventive strategies exhibit certain limitations. In recent years, the development of high-throughput sequencing and bioinformatic techniques has stimulated advancements in molecular biology, bioinformatics, and translational research. Numerous studies have suggested the involvement of miRNAs in the occurrence and progression of STDs through various pathways. This review presents an extensive overview of pertinent research on miRNAs in the context of STDs, with the ultimate objective of providing a theoretical framework to enhance clinical diagnosis and treatment.

2. Methods

We reviewed the literature on miRNAs associated with sexually transmitted diseases, including condyloma acuminatum, syphilis, gonorrhea, genital chlamydia infection, and HIV.

3. Structure and Function of miRNAs

MiRNAs are a highly conserved class of noncoding, single-stranded small RNA molecules in eukaryotes. They are typically composed of 21–25 nucleotides in length. MiRNAs regulate gene expression at the post-transcriptional level [2], thereby facilitating the binding of the RNA-induced silencing complex to the 3′-untranslated region (UTR) of target genes. This interaction leads to the degradation of the miRNAs or the inhibition of translation [3], contributing to the maintenance of cellular homeostasis. Since their initial discovery in 1993, researchers have identified a wide range of miRNAs, ranging from 5,000 to 10,000 in mammalian species. These miRNAs collectively represent a notable proportion (1%–5%) of all genes in the human genome [4]. MiRNAs exert regulatory control over a substantial proportion (20%–60%) of genes responsible for protein synthesis. Their influence extends to crucial cellular processes, including cell development, morphogenesis, proliferation, apoptosis, differentiation, immune regulation, and the mechanistic underpinnings of wound healing [5]. Nevertheless, miRNAs are also closely associated with various inflammatory diseases, neoplastic diseases, and STDs. Under diseased conditions, miRNAs can induce gene expression, thereby resulting in abnormal phenotypes. Conversely, miRNAs also possess the ability to impart protective capabilities by restoring cellular homeostasis [6]. Therefore, the balance of miRNAs is pivotal in maintaining cellular physiology's stable functionality.

4. Correlation between miRNAs and STDs

4.1. Role of miRNAs in Genital Warts. Genital wart also referred to as condyloma acuminatum (CA), is a common STD primarily caused by infection with human papillomavirus (HPV) types 6 and 11 [7]. The HPV lifecycle commences with the infection of basal cells through minor abrasions [8]. Subsequently, the virus maintains its genome at minimal copy numbers within the basal cells of the host. Upon differentiation of epithelial cells, the virus undergoes robust replication, leading to a significant increase in copy numbers and the subsequent activation of capsid genes (L1 and L2). This process results in the production of progeny viral particles released from the surface of the epithelium. Genital warts are typically categorized into the following four types: classic CA, keratotic warts, papular warts, and flat warts [9]. These warts are characterized by high transmissibility, rapid growth, and propensity to recur [10]. The precise pathogenic mechanisms that drive the localized changes in genital epithelial tissues following HPV infection are yet to be fully elucidated. However, with the gradual exploration of miRNAs, researchers have discovered that miRNAs exhibit abnormal expression during the formation of CA lesions, impacting processes such as cell proliferation, apoptosis, and differentiation.

Previous research has underscored the potential of miRNA-34a-5p as an innovative serological marker for the diagnosis of CA. An examination of the correlation between miRNA-34a-5p expression and the mRNA expression of PD-L1 in tissues from 81 patients with CA revealed that miRNA-34a-5p was downregulated and PD-L1 mRNA was upregulated, with a negative correlation between their expression levels. This finding suggests a joint influence of miRNA-34a-5p and PD-L1 on the occurrence and progression of CA. Further investigation found that the combined use of miRNA-34a-5p and PD-L1 for CA diagnosis yielded an area under the curve (AUC) of 0.954, demonstrating a sensitivity of 86.4% and a specificity of 91.4%. These results indicate that the combination of miRNA-34a-5p and PD-L1 has a favorable diagnostic value for CA [11]. The upregulation of miRNA-26a leads to enhanced degradation of phosphatase and tensin homolog (PTEN) mRNA, which weakens the action of PTEN. Loss of miRNA-143 or miRNA-145 can perturb the NRAS/PI3K/AKT signaling pathway. In addition, the downregulation of miRNA-99b and upregulation of its target gene, insulin-like growth factor 1 receptor (IGF-1R), can excessively induce the PI3K/AKT signaling pathway. All of these alterations can lead to the dysregulation of CA cell proliferation [12–14]. Autophagy has been recognized to be closely associated with the occurrence and progression of CA. Wu et al. [15] conducted a verification analysis of miRNA-30a-5p and miRNA-514a-3p, both of which are highly correlated with autophagy in CA, along with autophagy-related (Atg) proteins Atg5, Atg12, and Atg3. They found that the expression levels of miRNA-30a-5p and miRNA-514a-3p were significantly reduced in patients with CA compared to healthy controls. In contrast, the expression levels of Atg proteins Atg5, Atg12, and Atg3 were significantly increased. These findings suggest that the downregulation of miRNA-30a-5p and miRNA-514a-3p represses the expression of target genes Atg5, Atg12, and Atg3, thus participating in the regulation of the autophagy system in the context of CA.

In addition, dysregulated expression of miRNA-34a-5p, miRNA-22-3p, miRNA-31, miRNA-9, miRNA-143, miRNA-155, and miRNA-203 can impact CA various aspects, including the course of disease, wart size, HPV infection subtype, and recurrence frequency, through multiple different pathways. However, the specific mechanisms underlying their action are still under investigation [16–23] (Table 1).

4.2. Role of miRNAs in Syphilis. Syphilis is a chronic infectious disease caused by the spirochete bacterium *Treponema pallidum* (TP). TP can be transmitted through sexual contact, including oral contact, or the introduction of unfiltered blood or blood products, leading to chronic infection with different clinical stages. Syphilis can be categorized into acquired syphilis and congenital syphilis [24]. Currently, commonly used laboratory tests include specific treponemal antibody tests and nonspecific treponemal antibody tests [25]. Research has demonstrated that the expression and function of miRNAs confer important roles in early diagnosis, disease assessment, and prognosis of syphilis.

The expression of miRNA-338-5p was found to be elevated in serum treponemal immobilization-positive patients compared to healthy controls. Its target genes were

Table 1: MiRNAs modulate condyloma acuminatum infection by regulating host proteins.

miRNA	Target(s)	Action	Experimental strategy	References
miR-34a-5p	PD-L1	Course of disease, wart size, HPV infection subtype, and diagnostic value	In vitro	[11]
miR-143/miR-145	NRAS, PI3 K p110a, and p-AKT	Dysplasia of cell proliferation	In vitro	[12]
miR-99b	IGF-1R	Dysplasia of cell proliferation	In vitro	[13]
miR-26a	PTEN	Dysplasia of cell proliferation	In vitro	[14]
miR-30a-5p/miR-514a-3p	Atg5, Atg12, Atg3	Involved in the regulation of the CA autophagy system	In vitro	[15]
miR-22-3p	VEGF	HPV infection type	In vitro	[17]
miR-9	HK2	Course of disease, wart size, and HPV infection subtype	In vitro	[23]
miR-149-3p	HE4	Course of disease, wart size, and HPV infection subtype	In vitro	[22]
miR-143/miR-155	NRAS, PI3 K p110a, and p-AKT	Course of disease, wart size, and HPV infection subtype	In vitro	[19]
miR-203	p63	HPV infection subtype	In vitro	[21]
miR-203	Survivin	HPV infection subtype	In vitro	[20]

closely related to the T cell receptor signaling pathway and growth metabolism, suggesting its potential as a biomarker for identifying serum treponemal immobilization-positive patients and diagnosing latent syphilis [26]. In addition, Huang et al. [27] revealed that three miRNAs (hsa-miR-195-5p, hsa-miR-223-3p, and hsa-miR-589-3p) showed significant differences in the serofast and serologically cured states. Among these miRNAs, hsa-miRNA-195-5p showed higher expression in untreated syphilis and serum treponemal immobilization-positive patients compared to those healthy controls. The combination of these three miRNAs holds potential as a diagnostic tool and predictor of serological response following syphilis treatment. In another study by Jia et al. [26], it was demonstrated that the level of miRNA-101-3p was significantly increased in peripheral blood mononuclear cells of patients with serum treponemal immobilization-positive syphilis. This miRNA downregulated the TLR2 signaling pathway by targeting TLR2 3′UTR in patients with syphilis, leading to a decrease in macrophage cytokine production [28, 29]. The upregulation of miRNA-142-3p expression inhibited phagocytosis by dendritic cells and macrophages in patients with secondary syphilis. The phagocytic function of macrophages played a crucial role in the immune clearance of TP, thereby promoting the progression of syphilis infection [30] (Table 2).

4.3. Role of miRNAs in Gonorrhea. Gonorrhea, an infection caused by *Neisseria gonorrhoeae*, primarily leads to suppurative infections of the genitourinary system. It can also involve infections in the eyes, throat, rectum, etc [31]. Gonorrhea has a short incubation period and high infectivity, leading to various complications and sequelae, including disseminated gonococcal infection, such as infectious arthritis, heart disease, and meningitis [32]. The World Health Organization (WHO) estimated that in 2012, there were 78.3 million new cases in adults (15–49 years of age) worldwide. In 2017, ~556,000 cases of gonorrhea were reported in the USA [33]. Gonorrhea has emerged as a major global public health problem. In addition, with the widespread use of antibiotics, it has been demonstrated to develop antibiotic resistance. Reports of treatment failures have emerged from various parts of the world [34]. Thus, early diagnosis and prompt and effective treatment methods are crucial for improving prognosis and preventing recurrence.

Liu et al. [35] investigated the impact of *Neisseria gonorrhoeae* or purified lipooligosaccharide (LOS) on human monocytic leukemia cell THP-1 cells. Their findings revealed that gonococcal LOS treatment induced the upregulation of miRNA-146a in human monocytic THP-1 cells. They also elucidated that the expression level of miRNA-146a was closely associated with the tolerance of cells. Their further studies have highlighted that LOS treatment results in the downregulation of IL-1R-associated kinase 1 (IRAK1) (89ILOS), TNFR-associated factor 6 (TRAF6) (89I and 1291LOS), TNF-α, and IL-1β. Both IRAK1 and TRAF6 are downstream signaling adapters of NF-κB, indicating that gonococcal LOS may reduce miRNA-146a levels, which may be involved in the survival and dissemination of *Neisseria gonorrhoeae* [35]. In another study, it was observed that the expression of miRNA-718 was decreased in macrophages upon infection with *Neisseria gonorrhoeae*. MiRNA-718 was found to directly modulate the PI3K/AKT signaling pathway by downregulating PTEN, consequently enhancing AKT phosphorylation and suppressing the production of proinflammatory cytokines [36]. Phosphorylated AKT induced the expression of let-7e, which downregulated TLR4 and weakened TLR4-mediated proinflammatory signaling. This finding suggests that miRNA-718 may increase the susceptibility to *Neisseria gonorrhoeae* infection [36] (Table 3).

4.4. Role of miRNAs in Genital CT Infection. Genital CT infection is a common STD affecting the urinary and reproductive systems. Recent statistics from the WHO reveal approximately 127 million new cases of CT infection annually, with nearly 60% of these infections primarily affecting young individuals between the ages of 14 and 24 years [37, 38]. The majority of CT infections exhibit a hidden or prolonged course with mild or no obvious symptoms. They have the potential for widespread transmission and commonly result in various complications [39]. Prior research has provided evidence suggesting that CT infections can inflict substantial harm on the female reproductive system [40]. The range of potential consequences includes, but is not limited to, fallopian tube injury, pelvic inflammatory disease, cervicitis, endometritis, and ectopic pregnancy. These complications may lead to the development of tubal abnormalities, which can ultimately result in female infertility [41]. In males, genital CT infection can contribute to urethritis, epididymitis, prostatitis, and infertility.

Accumulating studies have indicated the changes in the expression levels of multiple miRNAs in host cells infected with CT, signifying their pivotal involvement in host cell changes and responses. Understanding the mechanisms of human-specific host defense and complications in CT infection holds significant importance in preventing adverse pathologies. Li et al. [42] used fluorescence quantitative polymerase chain reaction (PCR) to analyze the association of the expression levels of miRNA-146a and miRNA-155 with vaginal microbiota imbalance in cervical exfoliated cells of HPV-infected patients. Their study further corroborated that elevated miRNA-146a and miRNA-155 expression could affect the T cell immune system and consequently alter the vaginal microbiota environment, thereby increasing the infection rate of CT in the reproductive tract.

MiRNAs play a crucial role in the assessment of the effectiveness and prognosis of treatment for CT infection in the reproductive tract. Batteiger et al. [43] examined samples from 83 symptomatic and asymptomatic CT-infected females and analyzed the differences in miRNA expression. Compared to healthy individuals, in the symptomatic infection group, miRNA-142 and miRNA-147 showed a 2.2–6.9-fold increase in expression, while the asymptomatic infection group

Table 2: MiRNAs modulate syphilis infection by regulating host proteins.

miRNA	Target(s)	Action	Experimental strategy	References
miR-195-5p/miR223-3p/ miR-589-3p	Several genes	Diagnostic tool and predictor of serological response	In vitro	[27]
miR-101-3p	TLR2 3, UTR	Macrophage cytokine decreased	In vitro	[29]
miR-338-5p	RANBP 17, XPO 1 and XPO 6	Identification of patients with serological fixation and diagnosis of latent syphilis	In vitro	[26]
miR-142-3p	DC	Promoting the progression of syphilis infection	In vitro	[30]

Table 3: MiRNAs modulate gonorrhea infection by regulating host proteins.

miRNA	Target(s)	Action	Experimental strategy	References
miR-146a	TNF-α	Involved in the survival and dissemination of *Neisseria gonorrhoeae*	In vitro	[35]
miR-718	PTEN	Macrophage cytokine decreased	In vitro	[36]

exhibited a 3.9–9.0-fold increase in miRNA-449c, miRNA-6779, miRNA-519d, miRNA-449a, and miRNA-2467 expression. These findings suggest that miRNA expression profiles at the infection site may serve as potential indicators for monitoring disease prognosis. Benyeogor et al. [44] compared the differential expression of reproductive tract miRNAs in mouse models infected with murine CT and focused on the differences between single and repeat CT infections. Their observations revealed significant abnormalities in the expression of 10 miRNAs, including mmu-miRNA-378b, mmu-miRNA-142-3p, mmu-miRNA-128-3p, mmu-miRNA-335-3p, mmu-miRNA-195a-3p, and mmu-miRNA-142-5p. These findings suggest that miRNAs may serve as potential biological markers for reinfection. The loss of miRNA-378b prevents CT clearance in mice while also playing a protective role in the pathological development of the reproductive tract. The research team employed CRISPR/Cas technology to generate miRNA-378b knockout (miRNA-378b$^{-/-}$) mice and infected them with CT and then compared the infectivity and reproductive pathology of the CT-infected mice to that of wild-type mice [44]. The results demonstrated that miRNA-378b$^{-/-}$ mice were unable to clear the infection compared to wild-type mice. However, miRNA-378b$^{-/-}$ mice also exhibited a mitigating effect on reproductive tract pathology changes throughout the infection period. This observation suggests that miRNA-378b deficiency inhibited the inflammatory response in mice, thereby controlling CT replication and influencing complications such as infertility. The deficiency of miRNAs, leading to prolonged CT infection with attenuated pathology, provides new insights for future studies on the prevention of complications associated with CT.

The absence of miRNA-30c-5p expression leads to the upregulation of the mitochondrial fission regulator and p53 target gene, Drp1, significantly impeding CT growth and altering the mitochondrial network [45]. Keck et al. [46] observed that miRNA-135a regulated CCR5 expression and $CD4^+$ T cell proliferation induced by murine CT, as well as the migration of these cells towards the reproductive tract cells infected with murine CT. This regulation was achieved through immune activation mediated by the CXCL10/CXCR3 axis, thereby influencing effector T cell activation and homing to the infection site. These findings underscore the crucial role of miRNAs in immune cell trafficking and modulation following infection (Table 4).

4.5. Role of miRNAs in HIV/AIDS Infection. Acquired immune deficiency syndrome (AIDS) is a kind of infectious disease by the human immunodeficiency virus (HIV) infection, which does great harm to human health [47]. More than 75 million people worldwide are infected with HIV [48], and an estimated 38 million people are currently living with HIV [49]. Approximately, 1.5 million people become infected with HIV each year, and approximately 0.65 million people die from HIV-related complications [50]. HIV enters activated CD4+T lymphocytes mainly through interaction with CD4 and chemokine receptors (CCR5 or CXCR4), leading to the progressive reduction of CD4+T lymphocytes, accompanied by activation of CD8+T lymphocytes, resulting in abnormal and functional depletion of immune cell subsets (T lymphocytes and B lymphocytes) [51]. The resistance to internal and external pathogens decreased significantly, causing a variety of symptoms and complications. HIV infection can lead to abnormalities in host-specific miRNA expression profiles and participate in the regulation of HIV invasion, replication, latency, and activation through specific signaling pathways, leading to the progression of HIV/AIDS-related diseases.

Shahbaz et al. [52] found that elevated plasma levels of ATP in HIV-infected patients enhanced the expression of miRNA30b, 30c, and 30e in T lymphocytes in vitro and significantly inhibited the upregulation of CD73 in CD8+ T lymphocytes, which, in turn, may reduce the risk of developing multiple sclerosis. Bao et al. [54] analyzed the gene sequencing of colonic intestinal mucosal tissue specimens from two male AIDS patients and found that miR-1297 could inhibit the repair of intestinal barrier damage by negatively regulating phospholipase Cβ1 (PLCβ1) and its tightly linked downstream protein ZO-1 in lipopolysaccharide (LPS) injured CCCHIE-2 cells, suggesting that PLCβ1 and miR-1297 may be an important target for intestinal barrier damage repair. HIV-1 Vpr protein induces miR-210-5p expression, downregulates TGIF2, regulates p50 phosphorylation to activate the NF-κB pathway, and promotes G2 phase blockade, which may contribute to viral replication and induce pathological changes [53]. In a cohort study of HIV-infected patients with or without ocular damage, miR-192-5p and miR-543 expression levels were found to be downregulated in HIV-infected patients with ocular damage. miR-192-5p and miR-543 are strongly associated with chronic low-level inflammation, which can help to identify the disease state of HIV patients and diagnose HIV patients with immune recovery uveitis (IRU) [55]. Da Fonseca Ferreira et al. [56] selected mature apoE−/− mouse models that were fed a high-fat/high-cholesterol diet and injected with HIV^{posEVs}, HIV PL^{depEVs}, or HIV^{negEVs}. The researchers found that the development of atherosclerosis was exacerbated in mice injected with the HIV^{posEVs} group, whereas mice in the HIV PL^{depEVs} or HIV^{negEVs} mice did not affect the atherosclerotic load. Further studies showed that the overexpressed miR-let-7 b-5 p in the HIV^{posEVs} group acted through Hmga2 to partially mediate the role of HIV^{posEVs} in lineage negative bone marrow cells (lin-BMCs), which provides a new therapeutic target for people living with HIV (PLHIV) atherosclerosis exacerbation (Table 5).

Table 4: MiRNAs modulate genital chlamydia infection by regulating host proteins.

miRNA	Target(s)	Action	Experimental strategy	References
miR-146a/miR-155	Not mentioned	Change vaginal microecological environment	In vitro	[42]
miR-142/miR-147/miR-449c/miR-6779/miR-519d/miR-449a/ miR-2467 et al.	Several genes	Indicators for monitoring disease prognosis	In vitro	[43]
miR-378b	EMT	Controls CT replication and affects infertility	In vitro	[44]
miR-30c-5p	p53	CT growth was affected and the mitochondrial network was significantly affected	In vitro	[45]
miR-135a	CXCL10	Affects immune cell transport and regulation	In vitro	[46]

Table 5: MiRNAs modulate HIV/AIDS infection by regulating host proteins.

miRNA	Target(s)	Action	Experimental strategy	References
miRNA-30b/miRNA-30c/miRNA-30e	CD73	Multiple sclerosis	In vitro	[52]
miRNA-210-5p	TGIF2	Viral replication and induction of pathological changes	In vitro	[53]
miRNA-1297	Plc-β1	Repair of intestinal barrier injury	In vitro	[54]
miRNA-192-5p/miRNA-543	—	Identify the disease state and diagnose	In vitro	[55]
miRNA-let-7b-5p	Hmga2	Atherosclerotic	In vitro	[56]

5. Discussion

MiRNAs are involved in cell differentiation, apoptosis, signal transduction, cell cycle, and gene expression, which are closely related to the development of STDs and are also important biomarkers for the diagnosis, treatment, and prognosis of STDs, but their mechanisms have not yet been fully elucidated. CA is caused by the continuous replication of HPV infection in tissue cells, resulting in papillomatous proliferation of the epidermis. MiRNAs can affect the Notch1 signaling pathway by targeting and binding related genes, downregulating PI3K-p85 expression, and phosphorylation of AKT inhibiting the translation of proteins related to PI3K/AKT and MAPK signaling pathways, thereby affecting the proliferation and invasion of keratinocytes [13, 57]. Sabnam and Pal [58] found that 2-chloroethyl ethyl sulfide (CEES) exposed keratinocytes would initiate cellular stress through the PI3K/AKT signaling pathway, which disrupts antioxidant defenses, increases the accumulation of intracellular free oxygen and nitrogen radicals, and leads to apoptosis of keratinocytes. In patients with gonorrhea, miRNAs regulate the PI3K/AKT signaling pathway, promote AKT phosphorylation, and indirectly inhibit the expression of Toll-like receptor 4 (TLR4) and its downstream signaling molecules (such as IRAK-1 and NF-κB), which affects bacterial loading of *Neisseria gonorrhoeae* [36]. The PI3K/AKT pathway is a key signal transduction pathway in eukaryotic cells, which is involved in apoptosis, metabolism, growth, and other important life activities. The PI3K/AKT signaling pathway exists in both patients with CA and gonorrhea and influences the progression of the disease, and an in-depth investigation of the PI3K/AKT signaling pathway is conducive to the development of targeted therapeutic drugs for CA and gonorrhea.

Syphilis serum fixation is defined as the disappearance of clinical symptoms in patients with syphilis after regular treatment, but the nontreponemal serological tests persistently positive ($\leq 1:4$ or $\leq 1:8$), and it does not increase fourfold [59, 60]. Syphilis serum fixation is a worldwide problem, and about 20% of early syphilis patients may still be in a state of syphilis serum fixation after standardized antisyphilis treatment [61], which is related to over- and relatively undertreatment of syphilis. Through the Toll-like receptor (TLR) pathway, miRNAs cause T-cell subsets, NK-cell disorders and imbalances in CD4+/CD8+ T-cells and Thl/Th2 cytokines, resulting in reduced delayed-type hypersensitivity to syphilis spirochete antigens, which results in immune imbalance and eventually syphilis serum fixation [26]. In addition, miRNAs bind to the 3′- UTR of TLR, rescuing rtp17-induced inflammatory factor production and inhibition of the TLR4-MYD88 signaling pathway [62] and alleviating the inflammatory response in syphilis patients. Therefore, exploring the TLR pathway helps solve the problem of syphilis serum fixation and improving inflammation in syphilis patients. MiRNAs can regulate the expression of CCR5 and the proliferation of Ct-infected CD4+T cells through CXCL10/CXCR3 axis-mediated immune activation to facilitate their migration to reproductive tract cells, but the exact mechanism is not fully understood [46].

HIV has become a global public problem due to its high rate of morbidity and mortality and the difficulty of treatment. MiRNAs can participate in the regulation of HIV latency, replication, cell cycle, and other processes through a variety of specific signaling pathways, leading to the progression of HIV/AIDS-related diseases. It was found that miRNAs promote viral latency by targeting and inhibiting the expression of the TRIM32 gene (which is involved in assisting the activation of latent HIV), thereby reducing the NF-κB inhibitor kinase activity in the NF-κB signaling pathway [63]. At the same time, it also binds to HIV-dependent factor (HDF), inhibits the transcriptional replication of viral gene histone deacetylase sirtuin 1 (SIRT1), and then inhibits the signaling molecule NF-κB, affect the downstream NF-κB signaling pathway, and suppress the activation of HIV-1 [64]. Positive transcription elongation factor B (P-TEFb) consists of cell cycle protein-dependent kinase 9 (CDK9) and cell cycle protein T1 (CycT1), which are closely related to HIV-1 viral transcription. The overexpression of activated miRNAs downregulates cyct1 and decreases P-tefb expression, thereby reducing HIV-1 replication in monocytes [65]. Of course, miRNAs can also be directly targeted to the HIV-1 genome, such as targeting and inhibiting HIV Vpr protein expression to inhibit viral infection, targeting the Nef gene to inhibit viral replication, and targeting the TATA box in the 5′ LTR region of HIV-1 to up-regulate promoter activity and activate viral transcription [65, 66]. In a word, miRNAs are a double-edged sword for HIV/AIDS, driving disease progression as well as being potential targets for therapy.

6. Conclusion and Prospects

In recent years, miRNAs have garnered increasing attention in global research. Numerous studies have highlighted their potential as markers for early diagnosis, disease severity assessment, and prognosis evaluation. Nonetheless, current research on miRNAs in the context of STDs predominantly revolves around the identification of expressed miRNAs differentially. These studies often suffer from limited sample sizes and a lack of investigations into the functional roles and mechanisms of these miRNAs. Hence, it is an urgent task to expand sample sizes and delve deeper into the regulatory effects of relevant miRNAs on downstream targets in STDs. In addition, researchers should endeavor to bridge the gap between basic research and clinical studies, thus offering novel perspectives for the diagnosis, prevention, and treatment of STDs.

Data Availability

No new data generated or the article describes entirely theoretical research. Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Disclosure

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Shiyang Li and Xiaohua Tao conceptualized the study. Shiyang Li wrote the original draft. Yi Xu, Changxia Li, and Yue Huang performed data curation. Ming Wang, Meihua, and Xiaohua Tao supervised the study. All the authors contributed to performing the literature search and taking responsibility for the integrity of the work as a whole. All the authors have read and agreed to the published version of the manuscript.

Acknowledgments

This work was supported by the Nanchang Science and Technology Support Project (HongKezi (2021) 129 Item 24).

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