

Dysregulated expression of circulating microRNA-134 in adolescents with major depressive disorder

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Abstract: Major depressive disorder (MDD) is a significant global health issue. Adolescence, in particular, represents a critical period marked by peak onset, heightened vulnerability, and poorer response to treatment, highlighting the urgent need for improved diagnostic and therapeutic strategies in this population. Accumulating evidence has proposed miR-134 as a potential molecular biomarker for the diagnosis of major depressive disorder (MDD). However, as with most research on miRNAs in depression, these investigations have been limited to adult populations, leaving the adolescent group underexplored. To extend this work, the present study examined circulating miR-134 expression in adolescents with MDD. A total of forty-two participants, including twenty adolescents with MDD and twenty-two healthy adolescents (HC), were recruited for plasma sampling, RNA extraction, and real-time RT-PCR to quantify the expression of circulating miR-134. Despite the relatively small sample size, circulating plasma miR-134 was significantly downregulated in adolescents with MDD compared with HC. Receiver operating characteristic (ROC) curve analysis showed that miR-134 had a moderate diagnostic potential for MDD (area under the curve 0.75). Plasma miR-134 distinguished MDD from HC with 70% sensitivity and 72,7% specificity. Our findings confirm decreased plasma miR-134 levels in adolescents with MDD, consistent with previous observations in adults. This cross-age consistency reinforces the potential of miR-134 as a reliable peripheral biomarker for major depressive disorder, relevant to both adolescent- and adult-onset depression.

Keywords: Depression; miR-134; Adolescent; Major depressive disorder.

1.0 INTRODUCTION

Major depressive disorder is a prevalent health condition that significantly impairs psychosocial functioning and diminishes quality of life. In 2025, the World Health Organisation (WHO) estimated that 332 million individuals worldwide have depression, approximately 4% of the global population. Depression is also a significant factor in approximately 700,000 suicide deaths annually. Notably, adolescence represents a peak period for the onset of major depressive disorder (MDD), with incidence rising sharply during mid- to late adolescence. Although the World Health Organisation traditionally defines adolescence as 10–19 years, recent perspectives suggest extending this range to 10–24 years to reflect better ongoing biological development and delayed social role transitions ([Sawyer et al., 2018](#)). Approximately one in seven 10–19-year-olds (about 14.3%) experience a mental disorder, among which depression represents one of the most prevalent conditions. Depression, anxiety, and behavioural disorders are among the most disabling conditions during adolescence, with profound effects on education, social relationships, and overall health. Furthermore, suicide remains a critical concern, ranking as the third leading cause of death among individuals aged 15–29 years ([World Health Organization, 2025](#)). Importantly, adolescent depression is often associated with poor treatment outcomes, which amplify its long-term burden. Early-onset depression is further linked to more severe manifestations in adulthood, including a higher frequency of depressive episodes, increased likelihood of hospitalisation, and elevated risk of self-harm and suicide. Beyond psychiatric consequences, it is also associated with poorer social and occupational functioning, as well as adverse physical health outcomes, such as increased risk of obesity, diabetes, and cardiovascular disease ([Korczak et al., 2023](#)). Despite this considerable burden, recognition and treatment of depression in adolescents remain limited, with many cases underdiagnosed or untreated.

Currently, the diagnosis of depression is mainly based on patient-reported symptoms and assessed through a psychodynamic interview conducted by a physician, with depressed mood or loss of interest or pleasure serving as the key criterion ([Ortega et al., 2021](#)). This process remains challenging because symptom assessment is inherently subjective, relying on both

patients' self-reports and clinicians' interpretations, which can differ. This issue is particularly evident in adolescents, whose limited life experience may hinder their ability to accurately interpret and respond to survey scale questions, thereby reducing the reliability of disease severity assessments compared to adults. Therefore, conducting molecular-level studies is crucial to identifying biological markers that can enhance diagnostic accuracy and specificity alongside clinical interviews and self-report questionnaires, particularly in adolescents.

Despite our knowledge of the neurobiology of MDD having advanced, the mechanisms associated with the pathogenesis of MDD remain unclear. Multiple hypotheses have been proposed, including genetic vulnerability, dysregulation of neurotransmitter systems, hyperactivity of the hypothalamic–pituitary–adrenal (HPA) axis, impaired neuroplasticity and neurogenesis, neuroinflammation, and disturbances in the microbiome–gut–brain axis ([Nguyen et al., 2025](#); [Tian et al., 2022](#)). Within this complex framework, microRNAs (miRNAs) have gained attention as critical post-transcriptional regulators. These small non-coding RNAs (20–25 nucleotides) specifically bind to complementary sequences in the 3'UTR of target mRNAs, resulting in either mRNA degradation or translational inhibition ([He & Hannon, 2004](#); [Shen & Li, 2016](#)). Highly expressed in the brain, miRNAs play a crucial role in various brain functions, especially in neurogenesis, neuronal plasticity, and neuronal development ([Kosik, 2006](#); [Zeng, 2009](#)). Emerging evidence suggests that miRNA dysregulation contributes to multiple pathophysiological mechanisms of depression, positioning miRNAs as promising biomarkers and potential therapeutic targets ([Ding et al., 2023](#)). For example, miR-200a, miR-30a, miR-30e, miR-135a, miR-1202, miR-329, miR-362, and miR-124 are involved in serotonin signalling, glutamate regulation, and vesicle transport. In addition, miR-124-3p, miR-128-3p, and miR-139-5p regulate key signalling pathways associated with neuroplasticity and neurogenesis. Notably, miR-124-3p also plays a critical role in stress-related neuroendocrine responses and hypothalamic–pituitary–adrenal (HPA) axis alterations, while miR-9-5p may contribute to neuroinflammatory processes in depression ([Nguyen et al., 2025](#)).

Among brain-enriched microRNAs, miR-134 is predominantly localised in the synapto-dendritic compartment of hippocampal neurons, where it regulates neuronal development and synaptic function ([Gaughwin et al., 2011](#); [Schratt et al., 2006](#)). To date, miR-134 has been mainly studied in animal models, where it shows a strong association with depression-related mechanisms. Altered expression of miR-134 disrupts neuroplasticity through the SIRT1, CREB/BDNF, and Limk1/cofilin pathways, ultimately contributing to stress-induced depressive-like behaviors ([Fan et al., 2018](#); [Gao et al., 2010](#); [Wang et al., 2022a](#)).

In contrast, human research remains scarce, with only two published studies examining miR-134 in MDD patients, both limited to adult populations. Consequently, its role in adolescent depression—an especially vulnerable developmental stage for the onset of mood disorders—remains unclear. To address this gap, we conducted a cross-sectional observational study to evaluate plasma miR-134 levels in adolescents with MDD. We hypothesized that plasma miR-134 levels would be lower in adolescents with MDD than in healthy controls, consistent with downregulation patterns reported in adults. Our findings suggest miR-134 involvement in adolescent MDD and support its potential diagnostic value in this age group.

2.0 MATERIALS AND METHODS

2.1 Participants

This preliminary study enrolled 20 adolescents diagnosed with major depressive disorder (MDD) at Children's Hospital 1 and Ho Chi Minh City Psychiatric Hospital, Vietnam. We collected samples between October 2023 and October 2024. We determined the sample size based on recruitment feasibility during the study period. MDD was diagnosed according to DSM-IV criteria, and depression severity was assessed using the Patient Health Questionnaire-9 modified for adolescents (PHQ-9-M), a widely used and validated screening tool for depressive symptoms in adolescent populations ([Nandakumar et al., 2019](#)). The scale consists of nine items corresponding to DSM depressive symptoms and provides a quantitative measure of symptom severity. Only participants with PHQ-9-M scores greater than 10, indicating at least moderate depression severity, were included in the MDD cohort.

Additional inclusion criteria were: (1) age 10–24 years, consistent with the extended definition of adolescence proposed by Sawyer et al. (2018); (2) medication-naïve or medication-free for at least eight weeks prior to enrollment; (3) willingness to participate and provide informed consent. Participants with a history of

psychiatric conditions (including bipolar I or II disorder, autism spectrum disorder, schizophrenia spectrum disorder, or other psychiatric disorders), prior use of psychotropic medications, or a high suicide risk determined by a clinician were excluded. We also excluded pregnant or lactating individuals. The control group included 22 healthy volunteers recruited from relatives and acquaintances of the research team members. All healthy controls were assessed using the PHQ-9-M, with inclusion limited to those scoring ≤ 4 and meeting no DSM-5 diagnostic criteria for mental disorders. The Institutional Review Board of Children's Hospital 1, Vietnam, reviewed and approved the study protocol, and all participants provided written informed consent.

2.2 Human plasma samples

Whole blood (4 mL) was collected from each participant via the brachial vein using EDTA anticoagulant tubes and processed within 2 hours. Plasma was obtained by two sequential centrifugation steps using a refrigerated centrifuge (Eppendorf 5702R, Eppendorf, Germany): first at $1900 \times g$ for 10 minutes at 4°C , followed by a second centrifugation at $3000 \times g$ for 15 minutes at 4°C to remove residual cellular components. The resulting plasma was aliquoted into nuclease-free tubes and stored at -80°C until RNA extraction.

2.3 RNA extraction

RNA was extracted from plasma samples using the miRNeasy Serum/Plasma Advanced Kit (Qiagen, Germany). Briefly, plasma samples were thawed on ice, and 200 μL was transferred to new tubes for RNA extraction according to the manufacturer's instructions. The extracted RNA was stored at -80°C until further analysis. Purified total RNA samples were quantified with a NanoDrop BioSpectrometer Basic (Eppendorf, Germany) via absorbance measurements at 260 and 280 nm. The miRNA concentration was measured using a Qubit[®] 4 Fluorometer (Thermo Fisher Scientific, United States) with the Qubit[™] microRNA Assay Kits.

2.4 Real-time RT-qPCR

cDNA synthesis was carried out using the TaqMan[™] Advanced miRNA cDNA Synthesis kit. The samples were diluted 1:10 before running the real-time qPCR experiments. For real-time qPCR reactions, 5 μL of diluted cDNA template was mixed with 10 μL of TaqMan[™] Fast Universal PCR Master Mix (2X), no AmpErase[™] UNG, 1 μL of TaqMan Advanced miRNA Assay, and 4 μL of RNase-free water. We performed all reactions in duplicate/triplicate, including negative controls. We ran the experiments in 96-well plates using

the 7500 Real-Time PCR System (Applied Biosystems, United States). We used the following conditions: 20 seconds of enzyme activation at 95 °C, followed by 40 cycles of 3 seconds of denaturation at 95 °C and 30 seconds of annealing/extension at 60 °C. Raw Ct values were collected using the SDS 2.3 software (Applied Biosystems, Inc.).

TaqMan™ Advanced miRNA assays (Applied Biosystems, USA) were used for the quantification of miR-134-5p and the reference miRNA (miR-423-5p). The assay details are provided in **Table 1**. MiR-423-5p was selected as the internal reference for the TaqMan real-time PCR method because it has been identified as a suitable reference gene for plasma-based studies in MDD ([Liu et al., 2014](#)). The relative levels of miR-134 were calculated using the $2^{-\Delta\Delta Ct}$ method ([Schmittgen & Livak, 2008](#)). In each analysis, healthy control samples served as calibrators and were assigned a relative expression value of 1.0. All other quantities were expressed as *n*-fold differences relative to the calibrator.

Table 1. TaqMan™ Advanced miRNA Assays used for qPCR analysis.

	Assay Name	Assay ID	T _a	Manufacturer
Target miRNA	hsa-miR-134-5p	477901_mir	60°C	Applied Biosystems, USA
Endogenous control	hsa-miR-423-5p	478090_mir	60°C	Applied Biosystems, USA

Note: Each assay is a specific pre-formulated TaqMan™ Advanced miRNA Assay containing a TaqMan MGB probe and target-specific forward and reverse primers. T_a : Annealing temperature.

2.5 Statistical analysis

Statistical analyses were performed in RStudio (version 2026.01.1+403, Posit Software, PBC) using the R statistical environment and relevant packages. We assessed categorical variables, such as gender, using Chi-square tests. We first tested continuous variables for normal distribution using the Shapiro-Wilk test. Because the data were not normally distributed, we evaluated differences in age and miR-134 expression levels between patients with major depressive disorder (MDD) and healthy controls using the Wilcoxon rank-sum test. We calculated effect size using the rank-biserial correlation (*r*) to quantify the magnitude of the between-group difference. Continuous variables are presented as mean ± standard deviation (SD). A *p*-value less than 0.05 was considered statistically significant.

To assess miR-134's ability to distinguish adolescents with MDD from healthy controls, we performed receiver operating characteristic curve analysis. The ROC curve plots sensitivity (true-positive rate) against 1–specificity (false-positive rate) across different threshold values. We evaluated the diagnostic performance of miR-134 using the Area under the curve (AUC), where higher AUC values indicate better discrimination between the two groups. The optimal cut-off value was determined using the Youden index (*J* = sensitivity + specificity – 1). Sensitivity, specificity, and overall classification accuracy were calculated to evaluate the diagnostic performance of miR-134.

Figure 1 shows a schematic overview of the study workflow.

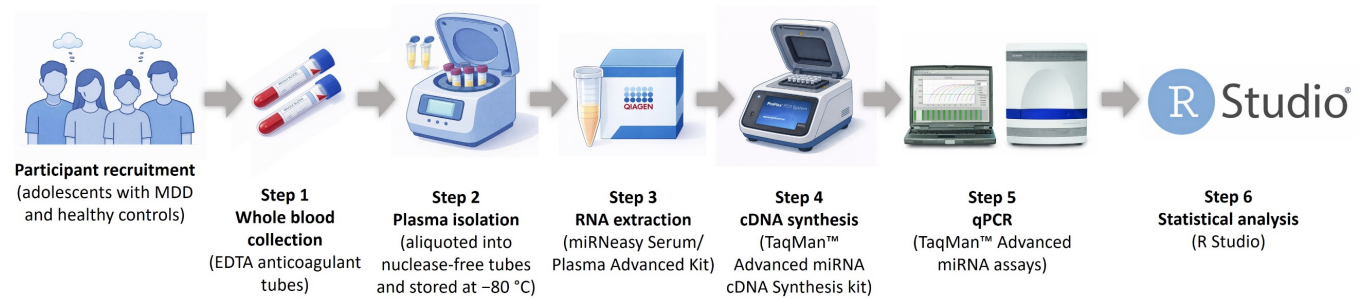


Figure 1. Overview of the study design and experimental workflow.

3.0 RESULTS

3.1 Demographic and clinical characteristics of patients and controls

Table 2 presents the basic demographic and clinical characteristics of all participants included in the study. A

total of 42 adolescents were recruited, comprising 20 individuals diagnosed with major depressive disorder (MDD group) and 22 healthy controls (HC group). The MDD group consisted of 13 males and 7 females, with a mean age of 17.950 ± 3.634 years. The HC group

included 15 males and 7 females, with a mean age of 18.545 ± 2.198 years. The two groups did not differ significantly in sex distribution or age. All patients with MDD had significantly higher PHQ-9 scores than healthy control subjects. In the MDD group, PHQ-9 scores ranged from 10 to 26, with a mean of 17.842 ± 4.925 , corresponding to moderate (10–14), moderately severe (15–19), and severe (20–27) depression. In contrast, the HC group had PHQ-9 scores ranging from 0 to 4, with a mean of 2.045 ± 1.588 , which falls within the minimal depression category.

3.2 Lower levels of miRNA-134 in plasma in the MDD group

We analysed differential plasma miR-134 expression in adolescents diagnosed with MDD compared with HC. As shown in **Figure 2**, miR-134 expression level was statistically significantly reduced in the MDD group (0.3855 ± 0.3130) compared with the HC group (1.000 ± 0.8520) (Wilcoxon rank-sum test: $W = 332$, $p = 0.005$). On average, plasma miR-134 level in the MDD group was approximately 0.4-fold that in the HC group (**Table 2**), suggesting a notable downregulation associated with the disorder. The effect size, measured using rank-biserial correlation, was $r = 0.435$, indicating a moderate effect.

Table 2. Demographic and clinical characteristics data of participants.

Variable	HC	MDD	p-value
Sample size	22	20	-
Sex (F/M)	15/7	13/7	1 ^a
Age (years)	18.545 ± 2.198	17.950 ± 3.634	0.6077 ^b
PHQ-9	2.045 ± 1.588	17.842 ± 4.925	$<0.001^b$ ($4.417e^{-08}$)
MiR-134 ($2^{-\Delta\Delta Ct}$)	1.000 ± 0.8520	0.3855 ± 0.3130	0.005 ^b

HC: healthy control subjects; MDD: major depressive disorder subjects; M: male; F: female. Data on age and PHQ-9 score were presented as mean $\pm$ SD. ^a Pearson's Chi-squared test; ^b Wilcoxon rank-sum test

3.3 Confirming the statistical relevance of dysregulated miR-134 by ROC curves

ROC curve analysis was performed to evaluate miR-134's ability to distinguish adolescents with MDD from healthy controls. The analysis yielded an area under the curve (AUC) of 0.75, with a 95% confidence interval (CI) ranging from 0.609 to 0.900, as shown in **Figure 3**.

Although this AUC does not reach the commonly accepted threshold of 0.80 for high diagnostic accuracy, it still indicates moderate discriminatory power. The relatively broad confidence interval may be attributed to the limited sample size or population variability ([Çorbacioğlu & Aksel, 2023](#)). The optimal cut-off value determined using the Youden index was 0.492, yielding a sensitivity of 70% and a specificity of 72.73%, with an overall classification accuracy of approximately 71.4%.

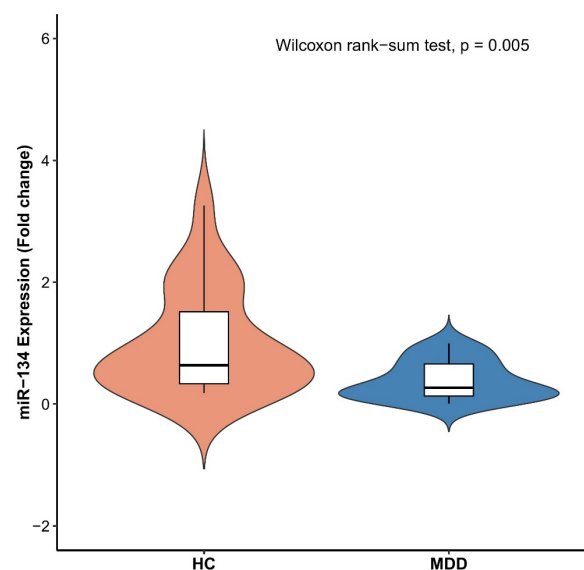


Figure 2. Plasma miR-134 levels in HC and MDD subjects

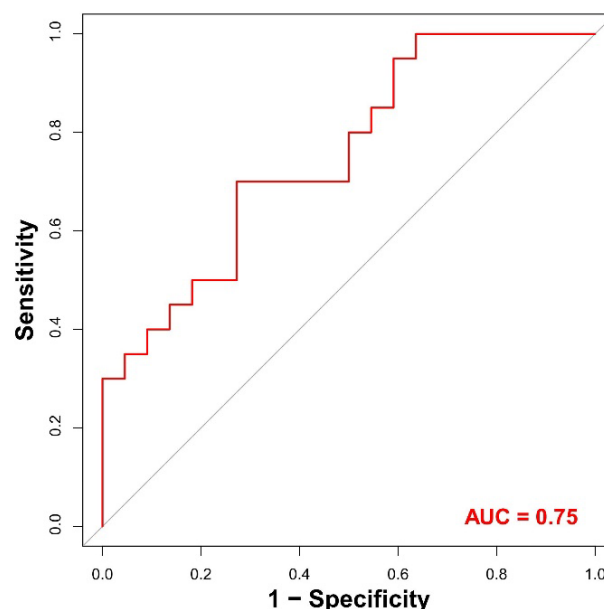


Figure 3. ROC analysis of miR-134 for discriminating MDD patients from healthy controls. miR-134 yields an area under the ROC curve of 0.75 (sensitivity of 70% with a specificity of 72.73%)

4.0 DISCUSSION

MicroRNAs (miRNAs) have emerged as crucial regulators of post-transcriptional gene expression and are expected to remain central to future neurobiological research. Among them, miR-134 is a brain-enriched microRNA that is strongly linked to stress responses and depressive phenotypes. To date, researchers have extensively studied miR-134 in animal models, primarily in brain tissues. Meerson et al. (2010) showed that miR-134 expression in adult male rats increased in the amygdala after acute immobilisation stress but decreased under chronic stress. These stress-induced alterations in miR-134 may influence cholinergic neurotransmission by regulating the splicing factor SC35 and its downstream targets in the brain (Meerson et al., 2010). Similarly, Zhang (2020) also observed that chronic unpredictable mild stress (CUMS) significantly reduced miR-134 levels in rat plasma, hippocampus, and prefrontal cortex (Zhang et al., 2020). In addition, mice exhibited enhanced anxiety-like and depression-like behaviors during the cocaine extinction phase of conditioned place preference, accompanied by markedly increased miR-134 levels and decreased expression of 19 genes associated with synaptic plasticity, glial activity, and neurochemical microenvironments in the ventral hippocampus (Li et al., 2020).

A key study on molecular signaling showed that miR-134 serves as a key negative regulator of synaptic plasticity by inhibiting CREB and BDNF expression. MiR-134 expression is tightly regulated by SIRT1, an NAD⁺-dependent class III histone deacetylase that participates in oxidative stress response, neuroprotection, autophagy, and mitochondrial regulation. SIRT1 normally suppresses miR-134 transcription through a repressor complex containing the transcription factor YY1, and loss of SIRT1 function leads to excessive miR-134 expression, resulting in reduced CREB and BDNF levels and impaired synaptic plasticity (Gao et al., 2010). Consistent with these findings, tetrahydroxystilbene glucoside and resveratrol restored hippocampal memory and synaptic plasticity in stress-induced mice through activation of the SIRT1/miR-134/CREB/BDNF pathway (Chen et al., 2016; Shen et al., 2018). Similarly, exposure to an enriched environment ameliorated depressive-like behaviors and cognitive deficits, likely through activation of the SIRT1/miR-134 pathway, which enhanced dendritic spine density and branching, increased postsynaptic density, and elevated the expression of synaptic proteins SYN, PSD95, and BDNF in the hippocampus (Shen et al., 2019). Through another mechanism, CUMS increased miR-134 expression and

downregulated Limk1/cofilin in the medial prefrontal cortex, indicating that miR-134 modulates structural neuroplasticity via the Limk1/cofilin signaling pathway. Treatment with ginsenoside Rg1 ameliorated both behavioral and neuronal structural changes induced by CUMS and normalized the dysregulated miR-134–Limk1/cofilin pathway (Fan et al., 2018). More recently, Wang et al. (2022b) showed that miR-134-5p knockdown alleviates depression-like behaviours, restores dendritic spine morphology, and enhances mitophagy by activating AMPK signalling. Therefore, miR-134-5p acts as a negative regulator of AMPK-mediated mitophagy, and its suppression can promote neuronal resilience and recovery of synaptic function (Wang et al., 2022b). Wang et al. (2022a) observed that brain-specific miR-134 directly binds to the BDNF 3'UTR and was significantly downregulated by ginsenoside Rb1 in the hippocampus of CUMS-exposed mice. These findings suggest that the antidepressant-like effects of ginsenoside Rb1 involve potentiation of synaptic plasticity via the miR-134-mediated BDNF signaling pathway in a mouse model of chronic stress-induced depression (Wang et al., 2022a).

Although the role of miR-134 in the pathogenesis of depression has been extensively studied in animal models, research in humans remains limited, with only two studies in adults identified. Zhang et al. (2020) demonstrated that plasma miR-134 levels were significantly downregulated in patients with depression compared to healthy controls, and these alterations could distinguish depression from other psychiatric conditions. Circulating miR-134 exhibited high diagnostic performance, with a sensitivity of 79% and a specificity of 84%. Based on these findings, the authors proposed that plasma miR-134 may serve as a potential biomarker for MDD. In addition, the authors discussed that in MDD, miR-134 downregulation may enhance CREB translation amid reduced BDNF levels and CREB activity, highlighting the need for further studies to clarify this potential feedback loop (Zhang et al., 2020). More recently, Lou et al. (2023) reported that peripheral blood miR-134 expression was significantly downregulated in MDD patients compared to healthy controls, suggesting its pivotal role in functional brain networks relevant to depression. In this study, using a novel multi-omics approach that integrated blood genomics, neuroimaging, transcriptomics, and behavioral data, the authors showed that individual exosomal miR-134 levels affect clinical symptoms of MDD by modulating ACC-related functional dysconnectivity. The downregulation of miR-134 and subsequent inhibition of target gene transcription may

play a role in mediating pathological depressive behavior. Taken together, the study highlights miR-134 as a potential key biomarker of depression (Lou et al., 2023). In the present study, we found that miR-134 expression was significantly dysregulated in adolescents with MDD, which is consistent with findings previously reported in adult populations (Lou et al., 2023; Zhang et al., 2020). The similar pattern of miR-134 dysregulation across age groups suggests that this microRNA may play a biologically relevant role in MDD pathophysiology. However, compared with the results reported by Zhang et al. (2020), our study showed slightly lower diagnostic accuracy, with a sensitivity of 70% and a specificity of 72.73%. This difference in diagnostic performance may reflect developmental factors influencing miRNA regulation during adolescence. Adolescence is a critical developmental stage characterized by substantial synaptic remodeling and maturation of neural circuits, particularly in brain regions involved in emotion regulation, such as the prefrontal cortex and limbic system. Emerging evidence suggests that microRNAs play an important role in regulating gene expression during adolescent brain development and help refine neuronal connectivity and synaptic plasticity (Morgunova & Flores, 2021; Vázquez-Ágredos et al., 2022). In this context, altered miR-134 expression during adolescence may reflect disruptions in activity-dependent synaptic plasticity or adaptive responses to changes in neurotrophic signaling. Furthermore,

hormonal fluctuations and neuroendocrine changes that occur during this developmental period may influence miRNA expression patterns and regulatory networks, potentially affecting miRNA-mediated pathways involved in synaptic function and neurodevelopment (Vázquez-Ágredos et al., 2024). Several limitations should be considered when interpreting these findings. First, the relatively small sample size represents an important limitation. Despite recruitment efforts from two major hospitals in Ho Chi Minh City, the study included only 20 adolescents with MDD and 22 healthy controls, which may limit the representativeness and generalizability of the findings. In addition, several potential confounding factors that may influence circulating miRNA expression—such as sex, body mass index (BMI), sleep patterns, and comorbid anxiety disorders—were not controlled for in the current analysis. These factors may contribute to biological variability in circulating miRNA levels and should therefore be considered in future studies. Future investigations with larger sample sizes, multicenter designs, and appropriate control of potential confounding factors are needed to evaluate further the clinical utility of circulating miR-134 as a biomarker for depression. Ideally, such studies should include both adolescent and adult cohorts within the same study protocol to enable direct comparisons across developmental stages.

Table 3. Studies on miR-134 in humans with major depressive disorder.

Reference	Method	Sample size	Age	Results
(Zhang et al., 2020)	PCR measurement of plasma miR-134 levels in patients with depression and validation in CUMS rat model.	100 MDD	35.9 ± 11.5	Plasma miR-134 is significantly down-regulated in MDD patients and can effectively distinguish depression from other mental illnesses. Circulating miR-134 exhibited high diagnostic performance, with a sensitivity of 79% and a specificity of 84%.
		100 HC	32.4 ± 11.8	
(Lou et al., 2023)	Analysis of blood genomics, neuroimaging, transcriptomics, and behavioural data.	Discovery set: 56 MDD	30.696 ± 9.073	Downregulation of miRNA-134 is closely associated with changes in synaptic plasticity and functional connectivity of brain regions in patients with depression.
		51 HC	30,824 ± 12.168	
		Validation set: 57 MDD	28.544 ± 8.982	
		52 HC	32.692 ± 12.450	
In this research	PCR measurement of plasma miR-134 levels in adolescents with depression	20 MDD	17.950 ± 3.634	Plasma miR-134 is significantly down-regulated in adolescents with depression, with a sensitivity of 70% and a specificity of 72.73% in diagnosis.
		22 HC	18.545 ± 2.198	

MDD, Major depressive disorder; HC, healthy control

Although the preliminary findings further support the diagnostic relevance of plasma miR-134, depression is a highly heterogeneous disorder, and no single biomarker is likely to capture its full molecular complexity. Nevertheless, the consistent dysregulation of miR-134 across both adolescent and adult cohorts suggests that it may represent a biologically meaningful and developmentally stable marker within the MDD spectrum. To enhance its clinical applicability, future studies should consider integrating miR-134 into a broader biomarker panel that includes other depression-associated miRNAs such as miR-221, miR-124, and miR-132, potentially improving diagnostic sensitivity and specificity. Furthermore, combining miRNA profiles with additional biological indicators, clinical characteristics, and neuroimaging measures could provide a more comprehensive and biologically grounded framework for diagnosis and prognosis in MDD.

5.0 CONCLUSIONS

Our findings reinforce the role of miR-134 in the pathophysiology of major depressive disorder (MDD) and suggest that its dysregulation may represent a

biologically stable feature across developmental stages. The present results further highlight the potential of plasma miR-134 as a promising molecular marker for adolescent depression. Nevertheless, larger studies including direct age-group comparisons are needed to validate these findings. Future research should also aim to integrate miRNA profiles with biological, clinical, and neuroimaging markers to establish a more comprehensive framework for MDD diagnosis and prognosis.

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