Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(2), 2298-2309 | ISSN:2251-6727

MicroRNA-144 in COPD: Mechanistic Insights and Clinical Relevance

Ms. Samjhana. B, Ph.D[1]., Dr. Reeta.R, M. D[2]., Dr.Vimal Raj.R.,M.D,D.N.B[3]

[1]Research Scholar, Department of Biochemistry, Mahatma Gandhi Medical College &Research Institute, SBV, Puducherry, India.

[2]Professor and HOD, Department of Biochemistry, Mahatma Gandhi Medical College &Research Institute, SBV, Puducherry, India.

[3]Professor and HOD, Department of Respiratory Medicine, Sri Venkateshwara Medical College Hospital and Research Centre, Ariyur, Puducherry, India.

(Received: 16 January 2026 Revised: 25 February 2026 Accepted: 17 March 2026)

KEYWORDS

COPD, microRNA-144, oxidative stress, inflammation, airway remodelling, biomarker, DNMT3A

ABSTRACT:

Introduction: Chronic obstructive pulmonary disease (COPD) is a progressive disorder characterised by persistent inflammation, oxidative stress, and airway remodelling. MicroRNAs (miRNAs) act as key post-transcriptional regulators of gene expression, and among them, microRNA-144 (miR-144) has emerged as a significant contributor to COPD pathogenesis. However, a comprehensive understanding of its mechanistic roles and clinical applicability in COPD remains limited.

Objectives: To critically evaluate and synthesise current evidence on the molecular mechanisms, clinical relevance, and therapeutic potential of miR-144 in COPD.

Methods: A narrative review of original research studies involving COPD patients and experimental models was conducted. Studies analysing miR-144 expression in serum, plasma, sputum, and lung tissue were included

Results: miR-144 negatively regulates NRF2-dependent antioxidant signaling, thereby impairing cellular defense against oxidative stress. It further contributes to airway remodeling through epithelial–mesenchymal transition and extracellular matrix alterations. Aberrant miR-144 expression is associated with increased disease severity, airflow limitation, and exacerbation risk, supporting its role as a potential non-invasive biomarker.

Conclusions: miR-144 plays a multifaceted role in COPD pathophysiology and represents a promising candidate for integration into diagnostic and therapeutic strategies. Further large-scale, well-designed studies are required to validate its clinical utility and advance miRNA-based precision approaches in COPD management.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder characterised by persistent airflow limitation and chronic inflammatory responses in the airways [1,2]. These changes result from chronic lung inflammation, damage to air sacs and changes in lung structure [3,4]. Long-term exposure to cigarette smoke remains the most significant risk factor associated with COPD development. Additional contributors include occupational exposures, environmental air pollutants, and genetic susceptibility [5,6]. With current treatments that focus on opening airways and preventing acute exacerbations, there is currently no cure for COPD. This underscores the need for deeper mechanistic insights into COPD pathogenesis and the development of robust strategies for early diagnosis and targeted intervention [3,4]. COPD involves inflammation, an imbalance of certain proteins and problems with tissue repair [7,8]. Certain cells like neutrophils, macrophages and T lymphocytes get into the

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(2), 2298-2309 | ISSN:2251-6727

airways and lung tissue. They release chemicals that make airways narrower and damage air sacs [4,9]. Oxidative stress, driven by a disruption in redox homeostasis between reactive oxygen species and endogenous antioxidant systems, plays a central role in COPD pathophysiology [10]. In addition to transcriptional regulation, cellular processes are influenced by post-transcriptional mechanisms that control gene expression. MicroRNAs (miRNAs) play a key role in this process [11]. MicroRNAs (miRNAs) are small non-coding RNA molecules that regulate gene expression at the post-transcriptional level by binding to target messenger RNAs, thereby promoting mRNA degradation or inhibiting translation. They play a role in many cellular processes like cell growth, differentiation and death [12,13]. Some miRNAs are linked to lung diseases like asthma, lung fibrosis, lung cancer and COPD [14,15]. In COPD certain miRNAs help control inflammation, stress responses and changes in the matrix. This suggests that miRNAs might be involved in the start and progression of COPD [16]. One miRNA, microRNA-144 or miR-144 seems to play a role in COPD. When human bronchial epithelial cells are exposed to cigarette smoke miR-144 levels go up. This leads to the suppression of TGF-β and immunoglobulin receptor, which hurts the immune function of the airway [13,14]. In mouse models of COPD, miR-144-3p targets Toll-like receptor 2. This alters the TLR2/MMP9 signaling pathway and promotes epithelial–mesenchymal transition, which is linked to airway remodelling [15]. miR-144 can also suppress NRF2, which is important for protecting against oxidative stress. This suggests that miR-144 may exacerbate oxidative injury in COPD [17]. These observations demonstrate miR-144 might contribute to inflammation, oxidative stress and structural changes seen in COPD. Altered miR-144 levels have been found in human COPD lung tissues. This suggests that miR-144 could be a non-invasive biomarker for disease severity and progression [17,18,]. RNA-based treatments that target miRNAs, like mimics and inhibitors are promising strategies for changing disease-related pathways in COPD [17].

Given the growing evidence linking miR-144 to COPD, a review of its molecular mechanisms, clinical relevance, and therapeutic potential is needed. This review brings together findings from studies to provide insights into miR-144 as a potential target for precision medicine, in COPD management.

2. **Objectives:** The objective of this review is to critically analyse and summarise the available literature on the role of microRNA-144 (miR-144) in chronic obstructive pulmonary disease (COPD). The review focuses on its involvement in oxidative stress, inflammatory pathways, and epigenetic regulation, along with its potential clinical significance as a biomarker and therapeutic target.

3. **Methods:** An in-depth examination of previously published studies on miR-144 in COPD was conducted using available scientific databases. Research data were retrieved from PubMed, Google Scholar, ScienceDirect, Scopus, Web of Science, Springer, and Taylor & Francis.
   For the literature survey, relevant keywords such as “miR-144”, “COPD”, “oxidative stress”, “inflammation”, “NRF2”, “TLR2”, “MMP9”, “CFTR”, and “DNMT3A” were used in various combinations in the information retrieval system.
   Original research articles involving COPD patients and experimental models were included. Studies analysing miR-144 expression in serum, plasma, sputum, and lung tissue were considered.

Molecular Mechanisms of miR-144 in COPD

1.1 miR-144 Regulation of Oxidative Stress Pathways:

Oxidative stress plays a central role in COPD pathogenesis and arises when the generation of reactive oxygen species exceeds the capacity of endogenous antioxidant defence systems, resulting in cellular and tissue injury within the respiratory tract. Cigarette smoke, a primary environmental risk factor for COPD, introduces large quantities of oxidants and free radicals that damage airway epithelial cells and activate redox-sensitive signaling pathways [8,10]. Sustained oxidative stress contributes to epithelial damage, increased mucus production, chronic airway inflammation, and progressive decline in lung function.

MicroRNAs represent an important control mechanism in oxidative stress modulation in lung disease. Through these interactions, miRNAs participate in regulating

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(2), 2298-2309 | ISSN:2251-6727

multiple cellular processes including inflammation, oxidative stress responses, and tissue repair mechanisms.[12] Therefore, the dysregulation of some miRNAs is proposed to be implicated in the molecular mechanisms of COPD. Of these molecules, miR-144 was identified as a key regulator of antioxidant signaling pathways since it was shown to directly target nuclear factor erythroid-2 related factor 2 (NRF2) , the primary transcription factor responsible for the expression of many antioxidant enzymes. Elevated miR-144 expression has been shown to attenuate NRF2 activity, leading to reduced transcription of antioxidant genes and increased vulnerability to oxidative stress [17].

In recent molecular research papers based over miRNAs, it was seen that the cigarette smoke induced alterations are predominant in COPD patients and the expression of miRNAs are responsible for the disruption of the oxidative stress response pathway. These altered expression of miRNAs were also seen lung tissue samples of the COPD patients. This result suggests the involvement of miRNAs in the pathogenesis of COPD through the disruption of the oxidative stress response pathway. This disruption is responsible for the inflammatory response observed in COPD patients [18,19].

Apart from the antioxidant response regulation, the role of miR-144 has been observed in the regulation of ion transport functions of airway epithelial cells. The ion transport function on the epithelial cells is regulated by the cystic fibrosis transmembrane conductance regulator chloride channel. Few experimental studies have shown that the miR-144 is responsible for the downregulation of the expression of the CFTR chloride channel [16].

This may point towards the increased risk of oxidative stress-induced damage observed in the COPD patients.

1.2 miR-144 and Inflammatory Signalling :

Persistent airway inflammation is a central pathological characteristic of COPD and significantly contributes to disease progression. There are other environmental exposures that may lead to a chronic airway inflammation such as prolonged exposure to inhaled irritants like Cigarette, results in stimulation of the macrophages, neutrophils and lymphocytes within the airway and lung parenchyma. Activated inflammatory cells release cytokines, chemokines, and proteolytic enzymes that promote tissue injury and contribute to progressive airflow limitation [4,9].

MicroRNAs are now recognized as critical modulators of inflammatory signaling networks in chronic lung diseases of inflammatory signaling pathways in the chronic lung diseases. Any alteration in the miRNA expression will influence the immune cell activation, cytokine production, and regulate the intracellular signaling cascade for inflammatory response. Previous studies have demonstrated that microRNA- mediated regulatory inflammatory cytokines modulate the lung inflammation and immune cell activity in CODP patients [11].

Recent experimental studies have provided vast evidence linking miR-144 to the inflammatory signalling cascades. Investigations have shown that the circRERE/miR-144-3p/TLR2/MMP9 regulatory axis promotes inflammatory responses and epithelial-mesenchymal transition (EMT) in COPD models, leading to increased matrix metalloproteinase activity and extracellular matrix degradation [15].

Adding on to this a study showed evidence that indicates that miR-144 may also influence that airway immune responses by regulating TGF-β dependant pathway, which is involved in the epithelial barrier function and mucosal immune defence mechanism. Thus, dysregulation of any of this pathway often leads to impaired immune responses and prolonged airway inflammation in COPD patients [13].

So, the upcoming transcriptomic analyses of COPD lung tissue will further support the role of miRNAs in regulating inflammatory gene networks associated with chronic airway inflammation and tissue injury [20].

Taken together, these observations highlight the contributory role of miR-144 in COPD-associated inflammatory processes.

1.3 miR-144 in Airway Remodelling and Extracellular Matrix Regulation:

Emerging evidence indicates that miR-144 contributes to airway structural remodelling through regulation of extracellular matrix dynamics and epithelial cell differentiation by regulating the genes involved in the extracellular matrix (ECM) turnover and epithelial cell differentiation. Alterations in the expression of miR-144

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(2), 2298-2309 | ISSN:2251-6727

have been shown to affect the molecular pathways controlling collagen deposition, matrix degradation and tissue repair. Downregulation of these processes disturbs the balance between the ECM synthesis and degradation, which leads to an excessive accumulation of structural protein within the airway wall. Thus, changes like these contribute to the airway wall thickening and progressive deterioration of the small airways seen in COPD cases. Additionally, altered miR-144 expression may affect the epithelial regeneration and inflammatory signaling, further promoting the bronchial fibrosis [3,21,22].

miRNAs contribute to post-transcriptional regulation and are implicated in various biological processes, including inflammation, tissue repair, and cell differentiation. These regulatory molecules affect pathways linked to the ECM turnover and airway structural integrity, and their altered expression has been progressively linked to the development of long-term respiratory disorders. Among these, it has been discovered that COPD patients and bronchial epithelial cells treated with cigarette smoke extract had significantly higher levels of miR-144-3p. Experimental results indicate that increased miR-144-3p can target the epigenetic regulator EZH2 through the SNHG4/miR-144-3p/EZH2 signalling pathway, hence causing inflammation, mortality, and damage to the epithelium [14].

By its association with signalling pathways that control the epithelial-mesenchymal transition, experimental research has shown that miR-144 essentially contributes to airway remodelling. Stimulation of the circRERE/miR-144-3p/TLR2/MMP9 signaling axis increases extracellular matrix breakdown and EMT in airway epithelial cells in COPD models [15]. The lung parenchyma's emphysematous degradation and structural tissue damage are both influenced by elevated MMP9 activity.
It has been demonstrated that miR-144-related regulatory RNA networks connect to epigenetic signaling pathways linked to airway remodelling. For example, cigarette smoke-induced immune responses and structural alterations in COPD models have been linked to lncRNA-mediated modulation of the EZH2/miR-144-3p axis [14].

Apoptosis and damage to epithelial cells are significant processes that contribute to the advancement of COPD, in addition to normal extracellular matrix remodelling. Chronic inflammation and excessive oxidative stress cause epithelial cell apoptosis, which damages airways and destroys alveolar structures [8,9]. It is becoming more well understood that microRNA-mediated control of signalling pathways linked to apoptosis plays a significant role in determining the survival of epithelial cells in chronic pulmonary conditions [23]. Consequently, epithelium damage and the gradual loss of functioning airway structures in COPD may be caused by dysregulated miR-144 expression.

The molecular pathways regulated by miR-144 in COPD are summarized in Table 1.

Molecular Pathway	Target Mechanism	Biological Effect	Clinical Relevance
Oxidative stress regulation	miR-144 suppresses NRF2 signaling	Increased reactive oxygen species	Contributes to epithelial injury
Inflammatory signaling	Activation of NF-κB pathways	Increased cytokine production	Chronic airway inflammation
Epigenetic regulation	Interaction with DNMT3A	Altered DNA methylation	Persistent gene dysregulation
Epithelial cell function	Regulation of CFTR expression	Impaired epithelial homeostasis	Reduced mucociliary clearance

1.4 Epigenetic Regulation via DNMT3A

Epigenetic mechanisms play a critical role in mediating the biological effects of environmental and chemical exposures in chronic obstructive pulmonary disease (COPD). Among these mechanisms, DNA methylation represents a key regulatory process in which methyl groups are added to cytosine residues within CpG islands, leading to suppression of gene transcription. Exposure to chemical components of cigarette smoke, including reactive aldehydes, polycyclic aromatic hydrocarbons, and oxidant gases, has been shown to alter DNA methylation patterns in airway epithelial cells. These exposure-induced methylation changes can disrupt the regulation of genes involved in oxidative

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(2), 2298-2309 | ISSN:2251-6727

stress responses and inflammatory signaling pathways associated with COPD development [23].

DNA methyltransferase 3A (DNMT3A) is a major enzyme responsible for **de novo DNA methylation**, establishing new methylation marks in response to cellular stress and environmental stimuli. Alterations in DNMT activity have been reported in lung tissues exposed to cigarette smoke, indicating that inhaled chemical toxicants can influence methylation-dependent gene regulation in respiratory epithelial cells [24]. Such epigenetic modifications may contribute to sustained inflammatory responses and impaired tissue repair mechanisms in the lungs of individuals chronically exposed to environmental pollutants.

MicroRNAs are increasingly recognized as important regulators of epigenetic enzymes. These small non-coding RNAs can modulate the expression of DNA methyltransferases and thereby influence methylation patterns of genes involved in inflammatory and oxidative stress pathways. Experimental evidence indicates that certain microRNAs are capable of regulating DNMT3A expression, suggesting that altered microRNA profiles observed in COPD may influence DNA methylation patterns within airway epithelial cells [25].

In addition, genome-wide methylation analyses have identified several differentially methylated loci associated with lung function decline and COPD susceptibility in individuals exposed to tobacco smoke and environmental pollutants [26]. These findings indicate that DNMT3A-mediated methylation changes may represent an important molecular mechanism through which chemical exposures contribute to chronic airway inflammation and structural lung damage. Therefore, investigating the relationship between miR-144 expression and DNMT3A activity may help clarify how environmental chemical exposures influence epigenetic regulation in COPD pathogenesis. The interaction of miR-144 with oxidative stress, inflammatory pathways, and epigenetic regulators highlights its multifaceted role in COPD pathogenesis (Figure 1).

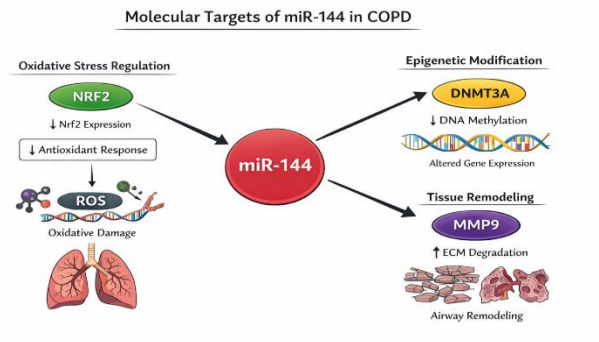

Figure 1. Proposed molecular mechanisms of miR-144 in COPD pathogenesis Environmental exposures, such as cigarette smoke and air pollutants, induce dysregulation of miR-144 expression in lung tissues. Elevated miR-144 levels contribute to oxidative stress by suppressing antioxidant defence pathways, including NRF2 signaling, resulting in increased reactive oxygen species production. In addition, miR-144 promotes inflammatory responses by activating NF-κB–mediated cytokine signaling. Emerging evidence also suggests interactions between miR-144 and epigenetic regulators, such as DNA methyltransferases, including DNMT3A, leading to altered gene expression patterns. These molecular events collectively contribute to airway epithelial injury, chronic inflammation, and structural remodelling characteristic of COPD

2. Clinical Significance of miR-144 in COPD

2.1 miR-144 as a Diagnostic Biomarker

Clinical signs of chronic obstructive pulmonary disease (COPD) frequently do not manifest until significant airway damage has occurred, making early identification difficult. Finding molecular biomarkers that can identify the early pathological alterations linked to the start of disease is therefore becoming more and more important. Because they can reflect underlying molecular changes in disease states and are stable in blood circulation and other biological fluids, microRNAs have become promising diagnostic biomarkers. Numerous studies have shown that circulating miRNAs are expressed differently in COPD patients than in healthy people, indicating that these miRNAs may be used to detect the disease [19]. Because of its role in a state of oxidative stress and pathways of inflammation linked to the pathophysiology of COPD, miR-144 received special attention among these molecules. Lung tissue cells exposed to cigarettes have been shown in experimental

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(2), 2298-2309 | ISSN:2251-6727

investigations to express more miR-144, indicating that environmental exposure may influence circulating miRNA profiles associated with respiratory diseases [27]. Clinical studies investigating miR-144 as a biomarker for COPD are summarized in Table 2.

Table 2: miR-144 as a biomarker for COPD

Study	Year	Sample Source	Method	Key Findings
Hassan et al.	2012	Lung epithelial cells	qRT-PCR	miR-144 regulates CFTR expression
Van Pottelberge et al.	2011	Induced sputum	miRNA profiling	Differential miRNA expression in COPD
Ezzie et al.	2012	Lung tissue	Microarray	miRNA networks altered in COPD
Osei et al.	2015	Lung tissue	Sequencing	MicroRNAs linked to inflammatory pathways

MiR-144 can be detected in serum and plasma samples. According to experimental research, it can be used as a minimally invasive biomarker to identify patients at risk of COPD or even to monitor the early stages of the disease. Circulating miRNAs have also shown promising diagnostic potential in distinguishing patients with COPD from healthy controls through molecular profiling approaches. Current evidence supports the possible inclusion of miR-144 in biomarker panels aimed at enhancing early detection of COPD in individuals exposed to environmental risk factors such as tobacco smoke and air pollution.

2.2 miR-144 and Disease Severity:

Along with the diagnostic value, the change in miR-144 expression is also linked with the disease severity and disease progression. The disease severity in COPD is often evaluated using the clinical parameters such as airflow limitations, symptoms associated and the frequency of exacerbations. Moreover, from the recent researches it's evident that with the use of molecular biomarkers in finding out the exact underlying disease mechanism for COPD disease may help us understand the disease progression and the heterogeneity of the disease better.

Studies examining the miRNA expression patterns linked to the changes in inflammatory signals in the lungs of the COPD patients. They also found specific miRNA profiles to correlate between specific miRNAs and lung function parameters, suggesting that miRNA expression levels any effect and reflect the disease severity [27,28].

In view of the fact that the miR-144 plays a regulating antioxidant role in the defense pathway and epithelial cell responses to the oxidative injury, in the light of the increased expression it may also contribute to enhanced oxidative stress and airway inflammation in advanced COPD stages.

Thus, Quantification of miR-144 expression may assist in stratifying patients based on disease severity and underlying molecular profiles. Several experimental and clinical studies have investigated the role of miR-144 in COPD pathogenesis and progression. Key studies evaluating miR-144 expression and related molecular pathways in COPD are summarized in Table 3.

Author	Year	Sample Type	Method	Key Findings
Hassan et al.	2012	Lung epithelial cells	qRT-PCR	miR-144 regulates CFTR expression in lung tissue, suggesting a role in airway epithelial

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(2), 2298-2309 | ISSN:2251-6727

				dysfunction.
Ezzie et al.	2012	Lung tissue from COPD patients	MicroRNA microarray and validation	Identified multiple dysregulated microRNAs in COPD, including miR-144, associated with inflammatory signaling pathways.
Van Pottelberge et al.	2011	Induced sputum	miRNA expression profiling	Demonstrated altered microRNA expression patterns in COPD airway samples, indicating potential biomarker utility.
Osei et al.	2015	Lung tissue	Next-generation sequencing	Identified microRNAs linked to inflammatory and structural pathways in COPD pathogenesis.
Li et al.	2022	Peripheral blood monocytes	qRT-PCR and functional assays	circRERE/miR-144-3p/TLR2/MMP9 axis promoted epithelial–mesenchymal transition contributing to COPD progression.
Song & Chen	2023	Lung epithelial cells exposed to cigarette smoke	qRT-PCR and molecular assays	SNHG4 aggravated cigarette smoke–induced COPD through regulation of the miR-144-3p/EZH2 signaling pathway.
Liu et al.	2025	Airway epithelial cells	qRT-PCR and pathway analysis	miR-144 modulated airway immune dysfunction through the TGF-β/pIgR signaling pathway.

(Abbreviations: qRT-PCR, quantitative reverse transcription polymerase chain reaction; CFTR, cystic fibrosis transmembrane conductance regulator; EMT, epithelial–mesenchymal transition.)

2.3 miR-144 and Risk of Acute Exacerbations:

Episodes of acute exacerbation in COPD are often distinguished based on the severe worsening of the respiratory symptoms that often requires immediate hospitalization or additional medical support. These repeated occurrences increase the COPD disease morbidity, mortality and healthcare expenses. Consequently, identifying biomarkers that may help predict the likelihood of exacerbations has become a key objective in COPD research. MicroRNAs have been suggested as potential indicators for identifying the

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(2), 2298-2309 | ISSN:2251-6727

inflammatory activity and immune dysregulation during these exacerbation events. MiRNA profiles may change during illness exacerbations, as evidence of reports there are researches that resulted in altered expression of circulating miRNAs during inflammatory responses in COPD patients [27].

Because miR-144 is involved in the regulation of oxidative stress and inflammatory signaling pathways, abnormal expression of this microRNA may contribute to a heightened susceptibility to exacerbations triggered by infections or environmental pollutants. Therefore, monitoring circulating miR-144 levels could provide valuable information regarding inflammatory activity and the risk of acute disease worsening in patients with COPD.

2.4 Potential for Personalized Medicine:

Given the variability of COPD, customised treatment strategies may be necessary to strengthen the disease's management. The designing of individualized treatment plans may be aided by molecular biomarkers that may recognize unique illness characteristics. Because microRNAs control several biological processes related to inflammation, oxidative stress, a phenomenon and tissue repair, they are becoming more widely acknowledged as attractive candidates for precision medicine. MiR-144 may be a viable therapeutic target due to its participation in multiple molecular pathways related to the pathophysiology of COPD. Additionally, determining patient subgroups with unique molecular profiles who can profit from targeted therapy may be made easier by detecting circulating miR-144 levels.

Therefore, further research exploring the clinical utility of miR-144 as a biomarker and therapeutic target may contribute to the development of personalized approaches for COPD diagnosis, risk assessment and disease management. Circulating miR-144 has been proposed as a promising biomarker for COPD diagnosis, disease severity assessment, and prediction of exacerbations (Figure 2).

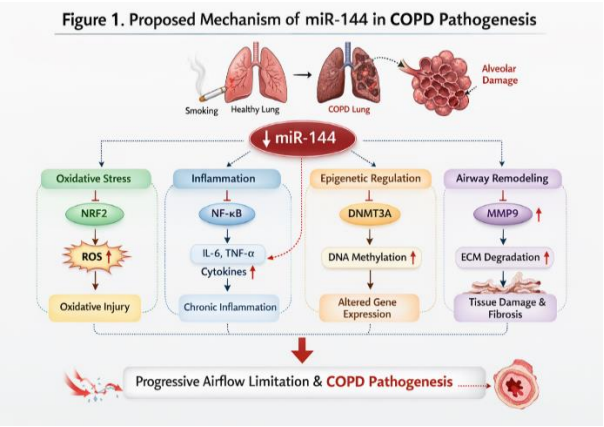

Figure 2. Clinical implications of circulating miR-144 in COPD diagnosis and management Circulating miR-144 detected in the blood, serum, or sputum has emerged as a potential biomarker for COPD. Increased miR-144 expression has been associated with disease presence, severity, and inflammatory activity in patients with COPD. The diagnostic performance has been evaluated using receiver operating characteristic (ROC) curve analysis in several clinical studies. Furthermore, dysregulated miR-144 levels may help predict acute exacerbations and support patient stratification for personalized management approaches in COPD.

2.5 Diagnostic Performance of miR-144: ROC/AUC Evidence:

Receiver operating characteristic (ROC) curve analysis, which evaluates a biomarker's sensitivity and specificity in differentiating disease cases from controls, is frequently used to assess the diagnostic value of circulating biomarkers. Using ROC curve analysis, a number of studies examining miRNA expression profiles in COPD have shown encouraging diagnosis accuracy. Circulating miRNAs had moderate to high discriminating power in separating COPD patients from healthy persons in these investigations, suggesting that they may serve as non-invasive biomarkers for disease diagnosis. The information that is now available indicates that miR-144 may contribute to biomarker panels that can increase diagnostic accuracy, despite the fact that research explicitly assessing this microRNA are still scarce [30].

Significant alterations in miR-144 expression in reaction to exposure to cigarette smoke and oxidative damage pathways that are pertinent to the pathophysiology of COPD have been shown by experimental studies. These

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(2), 2298-2309 | ISSN:2251-6727

molecular changes imply that the pathophysiological changes linked to airway inflammation and epithelium damage are reflected in circulating miR-144 levels [27,28].

When evaluating circulating miRNAs in biomarker studies, ROC analyses often reveal area under the curve (AUC) values between 0.70 and 0.85, indicating a reasonable clinical evaluation in identifying COPD cases [29,30]. The degree of specificity and sensitivity of biomarker panels for the early identification of COPD may be improved by combining miR-144 with other molecular markers linked to oxidative stress and cytokine signalling. In order to determine the exact analytical performance of miR-144 in a variety of patient demographics and environmental exposure situations, more clinical validation research is needed.

When considered collectively, the data suggest that miR-144 is implicated in several molecular pathways related to the pathophysiology of COPD, such as a state of oxidative stress regulatory mechanisms, inflammatory mediated signaling, and epigenetic modification. Circulating miR-144 levels may represent the underlying biological reactions to inhaled chemical toxicants, according to a modified expression of this microRNA in response to certain environmental exposures like cigarette smoke. As a result, miR-144 may be a promising prospective biomarker for COPD patients' early illness identification, severity evaluation, and exacerbation risk prediction. To confirm miR-144's potential use in biomarker-specific screening and classification of risk techniques for environmentally caused respiratory illnesses, more clinical trials assessing its ability to diagnose and longitudinal alterations are needed.

4. Results

Environmental exposures strongly influence chronic obstructive pulmonary disease (COPD); particularly inhaled chemical toxicants present in cigarette smoke and air pollutants. Accumulating evidence highlights the pivotal role of microRNAs in modulating cellular responses to environmental exposures. Among these regulatory molecules, miR-144 has emerged as an important modulator of oxidative stress signalling, inflammatory pathways, and epigenetic mechanisms involved in COPD pathogenesis. Dysregulated expression of miR-144 may contribute to airway epithelial injury, persistent inflammation, and altered gene regulation through interactions with antioxidant defence systems and DNA methylation pathways. In addition to its mechanistic relevance, circulating miR-144 shows potential as a non-invasive biomarker for disease detection, severity assessment, and prediction of exacerbation risk. Large-scale, well-designed clinical studies are warranted to validate the diagnostic and therapeutic potential of miR-144 in COPD.

5. Discussion

Chronic obstructive pulmonary disease (COPD) is a complex respiratory disorder characterised by persistent airflow limitation, chronic inflammatory responses, and progressive structural damage to the airways and lung parenchyma. Recent studies, particularly those involving microRNAs (miRNAs), which influence cellular responses for environmental exposures including air pollution and cigarette smoke, have highlighted the importance of molecular regulatory mechanisms in the pathophysiology of COPD. In addition to these regulatory molecules, miR-144 has gained increasing attention due to its regulatory influence on oxidative stress, inflammatory signalling, and epigenetic mechanisms. These processes are thought to play a significant role in the onset and advancement of COPD [21,27].

As discussed earlier, oxidative stress plays a central role in COPD pathogenesis. Oxidative stress remains a central mechanism in COPD and is closely linked to miR-144–mediated dysregulation of antioxidant pathways, particularly through modulation of NRF2 signalling [19]. These observations suggest that miR-144 may serve as a molecular link between environmental exposures and COPD-related cellular alterations. In addition to regulating oxidative stress, miR-144 appears to influence inflammatory signalling pathways that contribute to chronic airway inflammation. Persistent inflammatory responses involving macrophages, neutrophils, and lymphocytes are characteristic of COPD pathology. Altered miRNA expression profiles observed in lung tissues and airway samples from patients with COPD suggest that miRNAs participate in the regulation of cytokine production, immune cell activation, and tissue injury processes [21,28]. Given its involvement in multiple signalling pathways, dysregulation of miR-144 may amplify inflammatory responses and contribute to

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(2), 2298-2309 | ISSN:2251-6727

progressive airway remodelling and lung function decline in patients with COPD.

Another important aspect highlighted in this review is the potential interaction between miR-144 and epigenetic regulatory mechanisms in cancer. DNA methylation mediated by DNA methyltransferases, such as DNMT3A, is a key epigenetic process that can alter gene expression patterns in response to environmental stimuli. Evidence from molecular studies indicates that miRNAs can regulate the expression of epigenetic enzymes, thereby linking post-transcriptional gene regulation with DNA methylation pathways. This interaction suggests that altered miR-144 expression may influence DNMT3A activity and contribute to aberrant methylation patterns affecting genes involved in inflammatory responses and oxidative stress regulation in COPD patients.

Beyond its mechanistic role, the potential clinical significance of miR-144 has been increasingly recognised. Circulating miRNAs have demonstrated promising diagnostic and prognostic value in several

respiratory diseases owing to their stability in biological fluids and ability to reflect underlying molecular processes. Studies evaluating circulating miRNA profiles have reported moderate to high diagnostic performance using ROC curve analysis, indicating that miRNA-based biomarkers may assist in the early detection and risk stratification of COPD [29]. Given its involvement in key pathogenic pathways, miR-144 could be a valuable component of biomarker panels designed to improve diagnostic accuracy and monitor disease progression.

Furthermore, the relationship between miR-144 expression and environmental exposure is particularly relevant in COPD. Cigarette smoke contains numerous reactive chemical compounds that can induce oxidative stress, DNA damage, and epigenetic alterations in airway epithelial cells. Dysregulation of microRNA expression, including miR-144, may represent a molecular response to chemical exposure, linking environmental risk factors to the biological processes underlying COPD development. Understanding these exposure-related molecular mechanisms may provide valuable insights into how environmental toxicants contribute to chronic respiratory diseases.

Despite these promising findings, several limitations persist in the current literature. Many studies examining miRNA expression in COPD involve relatively small sample sizes or rely on cross-sectional study designs, which restrict the ability to establish causal relationships between miRNA dysregulation and disease progression. Additionally, variability in biological sample types, including serum, plasma, sputum, and lung tissue, may contribute to differences in reported miRNA expression patterns across studies. Therefore, standardising analytical methods and validating findings in large, well-characterised patient cohorts are essential to confirm the clinical utility of miR-144 as a COPD biomarker.

Future research should focus on longitudinal studies examining how miR-144 expression changes over time in relation to disease progression, environmental exposure levels, and treatment responses. Integration of miR-144 with other molecular biomarkers involved in oxidative stress and inflammatory signalling may also improve diagnostic performance and enable the development of multi-marker panels for COPD risk assessment. In addition, further mechanistic investigations into the interactions among miR-144, DNMT3A-mediated DNA methylation, and oxidative stress pathways may provide deeper insights into the molecular mechanisms driving COPD pathogenesis.

6 References

1. Bhatt, S. P.; Kim, Y. I.; Harrington, K. F.; Hokanson, J. E.; Lutz, S. M.; Cho, M. H.; *et al.* Smoking Duration Alone Provides Stronger Risk Estimates of Chronic Obstructive Pulmonary Disease Than Pack-Years. *Thorax* **2018**, *73* (5), 414–421. https://doi.org/10.1136/thoraxjnl-2017-210722.
2. Mannino, D. M.; Buist, A. S. Global Burden of COPD: Risk Factors, Prevalence, and Future Trends. *Lancet* **2007**, *370* (9589), 765–773. https://doi.org/10.1016/S0140-6736(07)61380-4.
3. Hogg, J. C.; Buzatu, L.; Coxson, H. O. The Nature of Small-Airway Obstruction in Chronic Obstructive Pulmonary Disease. *N. Engl. J. Med.* **2004**.
4. Saetta, M. Airway Inflammation in Chronic Obstructive Pulmonary Disease.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(2), 2298-2309 | ISSN:2251-6727

5. Eisner, M. D.; Anthonisen, N.; Coultas, D.; Kuenzli, N.; Perez-Padilla, R.; Postma, D.; *et al.* An Official American Thoracic Society Public Policy Statement: Novel Risk Factors and the Global Burden of Chronic Obstructive Pulmonary Disease. *Am. J. Respir. Crit. Care Med.* **2010**, *182* (5), 693–718. https://doi.org/10.1164/rccm.200811-1757ST.

6. Salvi, S. S.; Barnes, P. J. Chronic Obstructive Pulmonary Disease in Non-Smokers.

7. Kubo, H.; Asai, K.; Kojima, K.; Sugitani, A.; Kyomoto, Y.; Okamoto, A.; *et al.* Astaxanthin Suppresses Cigarette Smoke-Induced Emphysema through Nrf2 Activation in Mice. *Mar. Drugs* **2019**, *17* (12), 673. https://doi.org/10.3390/md17120673.

8. Kirkham, P. A.; Barnes, P. J. Oxidative Stress in COPD. *Chest* **2013**, *144* (1), 266–273. https://doi.org/10.1378/chest.12-2664.

9. Di Stefano, A.; Caramori, G.; Oates, T.; Capelli, A.; Lusuardi, M.; Gnemmi, I.; *et al.* Increased Expression of Nuclear Factor-κB in Bronchial Biopsies from Smokers and Patients with COPD. *Eur. Respir. J.* **2002**, *20* (3), 556–563. https://doi.org/10.1183/09031936.02.00272002 .

10. Rahman, I.; Adcock, I. M. Oxidative Stress and Redox Regulation of Lung Inflammation in COPD. *Eur. Respir. J.* **2006**, *28* (1), 219–242. https://doi.org/10.1183/09031936.06.00053805 .

11. Sanwlani, R.; Gangoda, L. Role of Extracellular Vesicles in Cell Death and Inflammation. *Cells* **2021**, *10* (10), 2663. https://doi.org/10.3390/cells10102663.

12. Bartel, D. P. MicroRNAs: Target Recognition and Regulatory Functions. *Cell* **2009**, *136* (2), 215–233. https://doi.org/10.1016/j.cell.2009.01.002.

13. Liu, H.; Zhao, Y.; Cao, J.; Liang, L.; Zhou, J. The Role of MicroRNA-144 in Regulating Airway Immune Dysfunction in COPD Through the Transforming Growth Factor-Beta/Polymeric Immunoglobulin Receptor Pathway: An In Vitro Study. *Chronic Obstr. Pulm. Dis. J. COPD Found.* **2025**, *12* (4), 285–293. https://doi.org/10.15326/jcopdf.2024.0592.

14. Song, B.; Chen, Y. Long Non-Coding RNA SNHG4 Aggravates Cigarette Smoke-Induced COPD by Regulating miR-144-3p/EZH2 Axis. *BMC Pulm. Med.* **2023**, *23* (1), 513. https://doi.org/10.1186/s12890-023-02818-5.

15. Li, Y.; Lu, X.; Li, W.; Shi, Z.; Du, W.; Xu, H.; *et al.* The circRERE/miR-144-3p/TLR2/MMP9 Signaling Axis in COPD Pulmonary Monocytes Promotes the Epithelial–Mesenchymal Transition of Pulmonary Epithelial Cells. *Biochem. Biophys. Res. Commun.* **2022**, *625*, 1–8. https://doi.org/10.1016/j.bbrc.2022.07.119.

16. Song, J.; Wang, Q.; Zong, L. LncRNA MIR155HG Contributes to Smoke-Related Chronic Obstructive Pulmonary Disease by Targeting miR-128-5p/BRD4 Axis. *Biosci. Rep.* **2020**, *40* (3), BSR20192567. https://doi.org/10.1042/BSR20192567.

17. Jadeja, R. N.; Jones, M. A.; Abdelrahman, A. A.; Powell, F. L.; Thounaojam, M. C.; Gutsaeva, D.; *et al.* Inhibiting MicroRNA-144 Potentiates Nrf2-Dependent Antioxidant Signaling in RPE and Protects against Oxidative Stress-Induced Outer Retinal Degeneration. *Redox Biol.* **2020**, *28*, 101336. https://doi.org/10.1016/j.redox.2019.101336.

18. Schembri, F.; Sridhar, S.; Perdomo, C.; Gustafson, A. M.; Zhang, X.; Ergun, A.; *et al.* MicroRNAs as Modulators of Smoking-Induced Gene Expression Changes in Human Airway Epithelium. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106* (7), 2319–2324. https://doi.org/10.1073/pnas.0806383106.

19. Ezzie, M. E.; Crawford, M.; Cho, J. H.; Orellana, R.; Zhang, S.; Gelinas, R.; *et al.* Gene Expression Networks in COPD: MicroRNA and mRNA Regulation. *Thorax* **2012**, *67* (2), 122–131. https://doi.org/10.1136/thoraxjnl-2011-200089.

20. Van Pottelberge, G. R.; Mestdagh, P.; Bracke, K. R.; Thas, O.; Van Durme, Y. M. T. A.; Joos, G. F.; *et al.* MicroRNA Expression in Induced Sputum of Smokers and Patients with Chronic Obstructive Pulmonary Disease. *Am. J. Respir. Crit. Care Med.* **2011**, *183* (7), 898–906. https://doi.org/10.1164/rccm.201002-0304OC.

21. Cañas, J. A.; Rodrigo-Muñoz, J. M.; Sastre, B.; Gil-Martinez, M.; Redondo, N.; Del Pozo, V. MicroRNAs as Potential Regulators of Immune Response Networks in Asthma and Chronic Obstructive Pulmonary Disease. *Front. Immunol.* **2021**, *11*, 608666. https://doi.org/10.3389/fimmu.2020.608666.

22. Pan, H. L.; Wen, Z. S.; Huang, Y. C.; Cheng, X.; Wang, G. Z.; Zhou, Y. C.; *et al.* Down-Regulation of MicroRNA-144 in Air Pollution-Related Lung Cancer. *Sci. Rep.* **2015**, *5*, 14331. https://doi.org/10.1038/srep14331.

23. Wan, E. S.; Qiu, W.; Baccarelli, A.; Carey, V. J.; Bacherman, H.; Rennard, S. I.; *et al.* Systemic Steroid Exposure Is Associated with Differential Methylation in Chronic Obstructive Pulmonary Disease. *Am. J. Respir. Crit. Care Med.* **2012**, *186* (12), 1248–1255. https://doi.org/10.1164/rccm.201207-1280OC.

24. Sundar, I. K.; Yin, Q.; Baier, B. S.; Yan, L.; Mazur, W.; Li, D.; *et al.* DNA Methylation Profiling in Peripheral Lung Tissues of Smokers and Patients with COPD. *Clin. Epigenet.* **2017**, *9* (1), 38. https://doi.org/10.1186/s13148-017-0335-5.

25. Fabbri, M.; Garzon, R.; Cimmino, A.; Liu, Z.; Zanesi, N.; Callegari, E.; *et al.* MicroRNA-29 Family Reverts Aberrant Methylation in Lung Cancer by Targeting DNA Methyltransferases 3A and 3B. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104* (40), 15805–15810. https://doi.org/10.1073/pnas.0707628104.

26. Qiu, W.; Baccarelli, A.; Carey, V. J.; Boutaoui, N.; Bacherman, H.; Klanderman, B.; *et al.* Variable DNA Methylation Is Associated with Chronic Obstructive Pulmonary Disease and Lung Function. *Am. J. Respir. Crit. Care Med.* **2012**, *185* (4), 373–381. https://doi.org/10.1164/rccm.201108-1382OC.

27. Hassan, F.; Nuovo, G. J.; Crawford, M.; Boyaka, P. N.; Kirkby, S.; Nana-Sinkam, S. P.; *et al.* MiR-101 and miR-144 Regulate the Expression of the CFTR Chloride Channel in the Lung. *PLoS One* **2012**, *7* (11), e50837. https://doi.org/10.1371/journal.pone.0050837.

28. Keller, A.; Leidinger, P.; Bauer, A.; ElSharawy, A.; Haas, J.; Backes, C.; *et al.* Toward the Blood-Borne miRNome of Human Diseases. *Nat. Methods* **2011**, *8* (10), 841–843. https://doi.org/10.1038/nmeth.1682.

29. Correia, C. N.; Nalpas, N. C.; McLoughlin, K. E.; Browne, J. A.; Gordon, S. V.; MacHugh, D. E.; *et al.* Circulating MicroRNAs as Potential Biomarkers of Infectious Disease. *Front. Immunol.* **2017**, *8*. https://doi.org/10.3389/fimmu.2017.00118.

30. de Souza, A. P.; Planello, A. C.; Marques, M. R.; de Carvalho, D. D.; Line, S. R. P. High-Throughput DNA Analysis Shows the Importance of Methylation in the Control of Immune Inflammatory Gene Transcription in Chronic Periodontitis. *Clin. Epigenet.* **2014**, *6* (1), 15. https://doi.org/10.1186/1868-7083-6-15.