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# Role of Mirnas in Pathogenesis of Common Kidney Diseases

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**Abstract**

MicroRNAs, or miRNAs, are endogenous short noncoding RNAs that regulate several vital physiological processes by inhibiting the expression of target genes. miRNAs have been associated with renal development, homeostasis, and physiological activities in the kidneys. Moreover, miRNAs have a substantial role in the progression of several renal illnesses, such as chronic kidney disease, diabetic nephropathy, acute kidney injury, hypertensive nephropathy, and other associated problems. Furthermore, miRNAs have substantial promise as biomarkers in several renal diseases. This review will clarify the participation of several microRNAs in contemporary cellular and animal models of various renal illnesses.

**Keywords:** MicroRNA, chronic kidney disease CKD, Acute kidney injury AKI, Diabetic nephropathy,Hypertensive nephropathy.

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## 1. Introduction

### *1.1 MiRNA: genetics and molecular aspects*

The mechanisms that govern gene regulation involve the involvement of a group of particles that have recently been identified. These particles can be classified according to their size, which can be classified as either short noncoding RNA (containing less than 200 nucleotides, such as miRNA, snoRNA, and piRNA) or long noncoding RNA (including lncRNA and circular RNAs, which contain more than 200 nucleotides) [1]. On the other hand, the microRNAs will be the primary focus of our specialized investigation. At the moment, there are more than two thousand microRNA molecules that have been found, and the genes that code for them make up around three percent of the genome [2]. These entities are noncoding RNAs that are intrinsic and relatively short (about 20–25 nucleotides) in length. They act as inhibitors of gene expression by either promoting the degradation of particular target messenger RNAs or suppressing the translation process of those messenger RNAs [3]. In the beginning, RNA polymerase II is responsible for the transcription of pri-miRNAs into longer RNA molecules. Following this, RNase III (Drosha) and DiGeorge syndrome critical region 8 (DGCR8) are responsible for cleaving the Pri-miRNAs inside the nucleus, which ultimately results in the maturation of miRNAs. Exportin is responsible for facilitating the movement of pre-miRNA hairpins, which are roughly sixty to seventy nucleotides in length, from the nucleus to the cytoplasm (cytoplasm). Through the action of the Dicer RNase III enzyme, these hairpins are cleaved in the cytoplasm, which ultimately leads to the production of a double-stranded miRNA/miRNA duplex that is roughly 22 base pairs in length. At the very end of the process, one strand is incorporated into the RNA-induced-silencing complex (RISC), which subsequently carries it to the messenger RNA (target mRNA) in order to decrease gene expression. During this time, the second strand is either undergoing fast degradation or transforming into miRNA, both of which result in unique biological consequences [1]. Despite the fact that changes are regularly reported beyond this region, the conserved sequence that is found in the seed region of mature miRNA is a remarkable trait. Because of this, a single microRNA has the ability to exert control over the expression of many target genes. This control may be exercised by either inhibiting the translation of target mRNA or facilitate the destruction of target mRNA. Several different developmental pathways are profoundly affected as a result of this event. During the process of translation, microRNAs (miRNAs) have the ability to delay the initiation and elongation processes of certain proteins, which ultimately results in a decrease in the expression of those proteins [4]. Their capacity to direct certain messenger RNAs to processing bodies in the cytoplasm, which ultimately leads to the

destruction of those messenger RNAs, is another one of their capabilities. In the end, they contribute to the silencing of transcriptional genes by specifically targeting the area of the promoter [5]. When it comes to the regulation of a large number of genes, the amount of complementarity between microRNA and its target mRNA, regardless of how strong or weak it may be, plays a significant effect. The expression of genes that are connected with microRNAs may result in the continuous activation of signaling pathways, which in turn influences the cellular phenotype under pathological settings and contributes to the course of illness. Despite the existence of considerable RNase activity, the ground-breaking work that was done by Mitchell and colleagues [6] was the first to uncover the presence of microRNAs in human plasma and to demonstrate their stability. It is possible for long noncoding RNAs, also known as lncRNAs, to influence the activity of microRNAs via two different mechanisms: either by serving as a sponge to decrease the action of certain miRNAs or by regulating the processes of chromatin remodeling [7]. There have been a great number of studies that have shed light on the major influence that the interaction between these two categories of noncoding RNAs has on the onset and progression of certain illnesses. It is possible to have a thorough understanding of the process of miRNA synthesis and its mechanism of action by referring to Figure 1. In recent times, microRNAs have garnered a lot of interest as possible biomarkers that might be of assistance in the diagnosis, evaluation, and monitoring of certain disorders [8].

### 1.2 MiRNA in common kidney disease

MicroRNAs has been implicated in the pathogenesis of common kidney diseases **[figure 2].** In this article, we will discuss some of them.

#### *1.2.1 MicroRNA in Acute Kidney Injury*

There are around 1500 microRNAs that have been discovered in humans. These microRNAs are involved in a variety of biological processes, such as the control of the cell cycle, apoptosis, hypoxia, metabolism, immunological response, and carcinogenesis. Over the course of the last decade, there has been a growing number of efforts made to assess the significance of microRNAs associated with acute kidney injury (AKI). This is evident from the fact that the number of articles published on this subject in PubMed has been steadily growing over the course of this time period, starting with four publications in the year 2010 and reaching an average of fifty to sixty papers each year over the course of the last five years [10]. In animal models of acute kidney injury (AKI), researchers have looked at a number of microRNAs, with miR-21 being the one that has been researched the most often. In order to investigate the patterns of expression, mechanisms of action, and possible therapeutic applications of these microRNAs, a substantial amount of research has been carried out about them. An example of this would be Song et al. [11], who conducted laboratory testing such as hypoxia/re-oxygenation and in vivo research utilizing animal models of ischemia-reperfusion injury (IRI) to investigate the effects of suppressing miR-21 on acute kidney damage (AKI). The results of the knockdown studies indicate that miR-21 provides protection against acute kidney injury (AKI) that is brought on by ischemia. The damage that was caused to renal epithelial cells by ischemia was made worse by the inhibition of miR-21 levels. Specifically, this was achieved by (1) boosting apoptosis via the PTEN/Akt/mTOR/HIF pathways and (2) increasing dendritic cell maturation, which ultimately led to an increase in inflammation [12]. The use of microRNAs as a potential therapy method for pre-clinical models of acute kidney injury (AKI) is now the subject of a comprehensive inquiry that is currently under progress. In order to bridge the gap between fundamental scientific knowledge and investigations involving humans, this study is very necessary. Although microRNAs have shown potential as therapeutic agents in preclinical models of acute kidney injury (AKI), there has not been a significant amount of research conducted on their efficacy and safety in the prevention or treatment of acute kidney injury in people [13]. In addition, the process of applying the findings of pre-clinical research to real-world situations has proven to be difficult, in part because shortcomings in the design of the study have been present. Studies that investigate IRI-AKI typically use male animals as the subjects of the majority of the studies. It has been demonstrated through the use of animal experimental models that the female gender offers protection against ischemia-reperfusion injury acute kidney injury (IRI-AKI). Additionally, this discovery has been supported by empirical investigations as well as a comprehensive analysis of other studies that have been conducted with human subjects [14]. The use of a number of microRNAs as potential indicators for acute kidney injury (AKI) and other renal disorders has been extensively researched. The levels of microRNAs in urine or plasma have been analyzed as a potential prognostic marker for acute kidney damage (AKI) in the context of preliminary research conducted in the field of cardiac surgery and on patients who are critically ill. In spite of this, a number of studies have reached contradictory conclusions, which highlights the complicated nature of miRNA pathways [15]. One example of this phenomenon is the microRNA known as miR-21, which has been demonstrated to have elevated levels in the urine and plasma of patients who are in a critical condition or who have undergone heart surgery and are suffering from acute kidney injury (AKI). A drop in pre-operative plasma levels of miR-21 was shown to be associated with an increased likelihood of developing acute kidney injury (AKI) in connection to the operation, according to the findings of an independent study that was carried out on patients who were due to undergo heart surgery. It has been shown that miR-10a, miR-192, and miR-194 have the potential to act as plasma biomarkers for

kidney damage that is caused by ischemia-reperfusion (I/R). With that being said, there was a significant amount of diversity in the outcomes among the individuals that were hospitalized. During the course of an investigation, it was discovered that the levels of plasma miR-16, miR-320, and miR-210 were altered in very unwell individuals who had suffered from acute kidney injury (AKI). This study was different from others that had been done in the past because it concentrated specifically on the prognosis of patients after 28 days and conducted a more in-depth analysis of the role that miRNAs play in predicting the prognosis. In order to resolve the inconsistencies that are brought about by the variability in studies, there are some academics who believe that aggregating a large number of samples could be a potential solution. In addition, research has demonstrated that the detection of microRNA in multiple types of samples, such as urine and plasma or plasma and kidney tissue, results in

significantly different findings when compared to the detection of miRNA in a single sample. Through the use of an animal model, a study was conducted to investigate the kidney damage that was brought about by ischemia/reperfusion (I/R). The study examined the levels of miRNA in both plasma and renal tissue. miRNAs displaying a link with the amount of the damage are considered promising biomarkers. The quantities of miR-714, miR-1188, miR-1897-3p, miR-877*, and miR-1224 were consistently raised in both plasma and renal tissue. An additional investigation comprising individuals who underwent heart surgery and suffered from acute kidney injury (AKI) discovered a link between heightened levels of miR-21 in both urine and plasma and the incidence of severe AKI, as well as unsatisfactory postoperative effects. These data imply that miR-21 may be employed as a prognostic marker in cardiac surgery circumstances. In addition, a research done on individuals who had kidney transplants and had acute tubular necrosis indicated that miR-142-3p has a different expression pattern, emphasizing its potential as a non-invasive diagnostic tool. The aforementioned research has revealed that the reliability of miRNAs as biomarkers, when validated by two or three independent sample types, is not higher than that of miRNAs found in only one sample type. On the other hand, it is predicted that more study will further elucidate these inconsistencies and anomalies [17]. This microRNA, which is uniquely expressed in endothelial cells, plays an important part in maintaining the structural integrity of blood arteries and is responsible for its expression. The presence of this substance is quite widespread in endothelial cells, however it is not seen in leukocyte cell lines or vascular smooth muscle cells. Mesangial cells and podocytes, on the other hand, have been responsible for the detection of trace levels of it. In addition to its advantages in vascular remodeling, miR-126-3p may also play a vital function in renal ischemia-reperfusion injury (IRI) [18]. The presence of miR-126-3p in the circulation has been established as a valid biomarker of acute kidney damage, while lower levels have been related with chronic rejection of donated kidneys. Biopsy samples taken from individuals with acute renal rejection also exhibited low levels of expression. Prior investigations have revealed that the usage of paeonol, a medicinal medication, promotes the expression of miR-126-3p. An increase in the expression of this gene has been shown to hinder the adhesion of monocytes and to obstruct the activation of the P12K/Akt/NF-κB signaling pathway, which plays a crucial role in the development of ischemia-reperfusion damage (IRI) [19].

### *1.2.2 MiRNA in Chronic Kidney Disease*

One of the ways in which microRNAs contribute to the progression of chronic kidney disease is by having an effect on the synthesis of microRNAs. MicroRNAs play a significant role in ensuring that renal homeostasis is maintained. Despite this, there is still a lack of comprehension about the degree to which they have an impact on the clinical outcome [20]. According to research that was conducted on animal models [21,22], it was discovered that microRNA has a significant role in the progression of glomerular and tubular damage from the beginning of the process. MicroRNA may play a part in the development of a broad range of diseases, including IgA nephropathy, lupus nephritis, and renal malignancies, according to these results, which indicate to the likelihood that microRNA has a function in the development of these diseases. MiR-200c, miR-141, miR-205, and miR-192 are all microRNAs that are expressed inside the kidney. There is a link between the expression of these microRNAs and the severity of IgA nephropathy as well as the development of the condition. The existence of distinct expression patterns of sixteen microRNAs in mononuclear cells of the peripheral circulation is a characteristic that distinguishes lupus-induced nephritis from other manifestations of the disease. The examination of microRNA has the potential to offer a more accurate categorization of kidney malignancies when compared to the analysis of mRNA. On the other hand, the expression of microRNA in individuals who have chronic renal illness has only been the subject of a limited amount of study [23]. Certain microRNAs are distinguished by their restricted location and have a preference for expression in the renal system that is characterized by their confined location. When compared to the levels of expression of miR-192, miR-194, miR-204, miR-215, and miR-216 in other organs, the kidney displays a significantly higher level of expression than the other organs under consideration. The kidney's particular production of essential proteins, which are required for kidney function, may be boosted by the relatively low levels or lack of certain miRNAs in comparison to other organs [24]. This is because the kidney is responsible for the production of these proteins. The reason for this is that essential proteins are involved in the functioning of the kidneys. MiR-30d, miR-140-3p, miR-532-3p, miR-194, miR-190, miR-204, and miR-206 were found to have lower levels in individuals who were diagnosed with progressive renal problems. These individuals also had lower levels of miR-206. Based on the findings of the inquiry into the patterns of expression of miRNA and mRNA in renal biopsy sections, this was revealed. Furthermore, it was shown that these microRNAs had the capacity to increase the expression of 29 target microRNAs, which are involved in intracellular signaling, inflammatory response, apoptosis, and cell-cell contact [20]. This was demonstrated by the experiments that were conducted.

During the course of the illness, it was observed that the level of miR-206 expression decreased. This was observed within the context of the progression of the illness. Additionally, there was a correlation between the decrease in the production of certain messenger RNAs (mRNAs) that are involved in inflammatory pathways and the increase in the production of these messenger RNAs. CCL19, CXCL1, IFNAR2, NCK2, PTK2B, PTPRC, RASGRP, and TNFRSF25 are some of the members of this group of messenger RNAs [25]. Additionally, the biopsies that were collected from patients whose health was deteriorating revealed a drop in the levels of miR-532-3p, which was followed by an increase in the levels of specific RNA molecules that are connected with the way of programmed cell death, which is also known as apoptosis. Mitogen-activated protein kinase kinase 14 (MAP3K14), tumor necrosis factor receptor superfamily member (TNFRSF10B)/TNF-related apoptosis-inducing ligand receptor 2 (TRAIL-R2), TNFR1-associated death domain protein (TRADD), and TNF-associated factor 2 (TRAF2) are the RNA molecules that are mentioned among those that are mentioned [9]. In accordance with the idea put out by the authors, there is a chance that the amounts of the miRNAs and target mRNAs that were described previously might be

associated to clinical parameters and histological damage indices. [26] In both acute and chronic models of renal injury, altered regulators of miR-21 have been shown to be present. This has been demonstrated by a number of distinct organizational studies. In the development of chronic kidney disease, renal fibrosis is a typical mechanism that plays a significant role in the evolution of the illness. The production of extracellular matrix to an excessive degree is the root cause of end-stage renal failure. The specific mix of molecular pathways that leads to renal fibrosis is still not completely understood according to the lack of clarity that exists. According to the results of scientific study, TGF β plays a significant part in this process. It achieves this by functioning as the principal regulator of matrix degradation inhibition, matrix synthesis, and myofibroblast activation (27). Within the context of the progression of diabetic kidney disease, it has been shown that TGF-β1 has an influence on a wide range of microRNAs, whereas microRNAs possess the capability to alter its expression. It is assumed that the epithelial to mesenchymal transition (EMT), which is the process by which cells move from an epithelial state to a mesenchymal one, plays a crucial role in the formation of renal fibrosis. It is probable that this process may result in the degeneration of the structure of the kidneys, which will finally lead to renal failure [28]. As a consequence of kidney injury, local fibroblasts get stimulated and go through a phenotypic shift, which finally culminates in the production of a considerable amount of extracellular matrix (ECM) components. The buildup of extracellular matrix (ECM) proteins in excessive numbers leads to the deterioration of renal tissue, which eventually results in the compromise of kidney function. The involvement of emergency medical technicians in renal fibrosis has been the subject of recent inquiries, which have given rise to concerns regarding this topic. The impact of the emergency medical treatment (EMT) procedure on renal fibrosis, on the other hand, is likely to vary depending on the specific illness and the circumstances [29]. This is the opinion of a number of specialists who argue that this is the case. It has been demonstrated through research that particular microRNAs, such as the miR-200 family and miR-205, have an effect on the regulation of the epithelial-mesenchymal transition (EMT) process. An investigation conducted by Li et al. [30] suggested that the activation of renal fibrosis by TGF-β takes place through the promotion of the expression of renal miR-433. The overproduction of miR-21, a molecule that plays a role in several biological processes including cell proliferation, differentiation, and apoptosis, is thought to have a significant impact on the progression of kidney fibrosis, according to research conducted by Gomez et al. [31] and Lai et al. [32]. It has been proven that miR-21 is responsible for encouraging the advancement of epithelial disease both in response to damage and the formation of fibrosis. This is accomplished via the control of a metabolic shift. The TGF-β/Smad pathway has been proposed as a possible explanation for the elevated expression of miR-21 in fibrotic tissues, which is recognized as one of the mechanisms responsible for this phenomenon. According to the hypothesis that was presented by Sun et al. [33], miR-21 plays a significant role in the process of promoting fibroblast activation in a variety of diseases that progress over time. There is a connection between the formation of a double negative autoregulatory loop that includes miR-21, PDCD4, and AP-1 and a high expression level of fibroblasts. This correlation is the result of a correlation between the two. In order to ensure that the hypothesis regarding the involvement of miR-21 in this pathological process is correct, it was found that the administration of antagomir-21 resulted in a reduction in the amount of kidney fibrosis. Because of these findings, the validity of the thesis was established. It is possible that targeting this feedback loop that is excessively stimulated could be beneficial in the treatment of fibrotic kidneys [9]. This is because of the fact that this feedback loop is excessively stimulated.

Furthermore, Zhong et al. [34] demonstrated that inhibiting miR-21 would slow the progression of renal fibrosis in experimental mouse models of kidney disease. This was in accordance with the findings of the previous discussion. Another piece of evidence supporting the hypothesis that miR-21 plays a part in the progression of renal fibrosis was provided by this discovery. Gomez et al. [35] demonstrated a significant protective effect on the kidneys by preventing the development of fibrosis in mice that were missing the miR-21 gene. This was done in a manner that was similar to the previous example. Studies have demonstrated that miR-21 plays a role in the promotion of renal fibrosis by targeting PPARα and Mpv171 in a selective manner. This is accomplished by inhibiting the fat metabolic pathway and enhancing the generation of reactive oxygen species (ROS), respectively. Moreover, the suppression of miR-21 was shown to augment the function of PPARα/retinoid X receptor and its subsequent pathways, leading to the maintenance of mitochondrial function and the decrease of inflammation and fibrogenesis in the renal tubule and glomeruli. Microarray profiling was performed on renal biopsy tissues obtained from three different clinical subtypes of CKD patients. In renal tissues that were affected by chronic kidney disease (CKD), the research showed that the expression of forty microRNAs showed an increase, while the expression of seventy-six microRNAs showed a decrease [36]. In a research undertaken by Yu et al. [37], three different types of renal diseases were examined, each exhibiting different degrees of fibrosis. A group of microRNAs that have the potential to be associated with the progression of renal fibrosis has been discovered. The authors postulated that the involvement of two recently identified miRNAs, hsa-miR-3607-3p and hsa-miR-4709-3p, in the fibrosis process linked to chronic kidney disease (CKD) is plausible. Hsa-miR-4709-3p increased the production of actin fibers and the movement of cells, while hsa-miR-3607-3p inhibited both of these activities. The precise roles of these two miRNA in human diseases are poorly characterized in the literature. According to pathway enrichment analysis conducted by Yu et al. [37], the mentioned miRNAs may have a role in regulating the actin cytoskeleton. This regulation could potentially contribute to kidney fibrosis by targeting ITGB8 (a member of the integrin beta chain family that encodes integrin αvβ8) and CALM3 (which encodes calmodulin-3, a crucial calcium sensor in the calcium signaling pathway). The heightened expression of ITGB8 is anticipated to lead to extended activation of TGF-β signaling, which is likely to have a role in the progression of renal fibrosis. Furthermore, several investigations have shown the significance of fluctuations in intracellular calcium levels in altering cellular shape and actin dynamics throughout the epithelial-mesenchymal transition (EMT) process. Yu et al. [37] revealed that the mTOR signaling pathway was the most enriched route for hsa-miR-4709-3p.

Moreover, the supplementary discoveries from their investigation correspond with other studies that recognize miR-21, miR-29, and miR-200 families as pivotal regulators in renal fibrosis. miR-126 has a high level of expression in endothelial cells (ECs) and has been widely investigated in the realm of vascular biology and diseases. Fish et al. [38] suggested that endogenous miR-126 may be associated with various vascular functions (angiogenesis, leukocyte adhesion, and inflammation) in atherosclerotic lesions by decreasing the expression of proteins involved in signaling pathways, such as Sprouty-related enabled/VASP homology domain-containing protein 1 and phosphatidyl inositol 3-kinase regulatory beta. During their discussion, decreases in these molecules initiate the rapid activation of fibrosarcoma in the mitogen-activated protein kinase signaling pathway, so promoting the synthesis of vascular endothelial growth factor and aiding the formation of new blood vessels. Harris et al. [39] found that increasing miR-126 levels in endothelial cells (ECs) not only stimulates angiogenesis but also inhibits the synthesis of vascular cell adhesion molecule 1, resulting in decreased adherence of leukocytes to ECs. Furthermore, miR-126 enhances the expression of sirtuin1 and superoxide dismutase-2, resulting to a reduction in oxidative stress in endothelial cells (ECs). Therefore, greater levels of circulating miR-126 may be connected to the preservation of vascular function and a lower risk of chronic kidney disease (CKD). In a mouse model of chronic kidney disease (CKD), there is a heightened expression of miR-126 in the aorta. This is followed by an increase in the synthesis of SDF-1, a chemokine protein that plays a critical function in the process of angiogenesis by recruiting endothelial progenitor cells from the bone marrow. During tissue healing, in a mouse model of atherosclerosis, endothelial cells generate miR-126 inside apoptotic bodies, which induces SDF-1-dependent vascular repair [40]. Furthermore, recent work has showed that the overexpression of miR-126 in bone marrow cells plays a key function in boosting the durability of blood vessels after kidney injury, hence supporting the repair of the kidney's microvasculature [41].

### *1.2.3 MiRNA in Hypertensive Nephropathy*

Through the use of gene and protein research, recent investigations have been effective in revealing putative pathways that contribute to hypertension (HTN). Dmitrieva and colleagues found substantial modifications in hepatocyte nuclear factor 1 by using different strains of spontaneously hypertensive rats. These variations had an effect on biological processes such as redox and other genes, which eventually resulted in kidney damage that is linked with high blood pressure. periostin, which is also known as osteoblast-specific factor 2, has substantial associations with plasma creatinine levels, proteinuria, and renal blood flow. As a result, it is an essential signal for both the beginning of hypertension and its reversal. Furthermore, it has been discovered that SMAD family member 7 possesses the capability to inhibit Ang II-induced hypertension. This is accomplished by regulating the nuclear factor kappa B (NF-κB)/miR-29b regulatory network through the Sp1/SMAD family member 3 pathways. This identifies it as a promising biomarker for the treatment of Ang II-induced hypertension. In a recent investigation on the relationship between micro-RNAs (miRNAs) and hypertension (HTN), it was shown that hypertensive nephrosclerosis is associated with increased expression levels of certain miRNAs. These miRNAs include miR-429, miR-200a, miR-205, miR-200b, miR-141, and miR-192. There is a clear correlation between the degree of their enhanced expression and the overall severity of the illness for most people. Hsa-miR-181a has an effect on the regulation of renin (REN) and apoptosis-inducing factor, mitochondrion-associated, 1 mRNA, which in turn has an effect on the expression of REN in hypertension (HTN). In addition, Berthier et al. analyzed the mRNA expression profiling dataset GSE37460 in order to determine the molecular pathways that are related with lupus nephritis. Among the processes that have been discovered are the activation or damage of endothelial cells, the infiltration or activation of immune cells, and the remodeling or fibrosis of tissue. It was revealed that both human individuals and mouse models exhibited activation of macrophages and dendritic cells. The researchers brought attention to the crucial functions that nuclear factor κB1 and peroxisome proliferator-activated receptor γ play in the regulation of tubule-interstitial and glomerular networks [42].

### *1.2.4 MiRNA in Diabetic Nephropathy*

microRNAs have been found in a variety of human tissues and body fluids, including blood, where they are found in a stable state that is shielded from the effects of endogenous RNase. The vast majority of microRNAs have sequences that are conserved across numerous species, and their expression is restricted to certain tissues or phases of development. A hypothesis has been developed as a result of this, which states that circulating microRNAs have the potential to function as efficient biomarkers for the diagnosis of a variety of disorders, including diabetes and cancer. The microRNA known as miR-126, which is found in very high concentrations in endothelial cells and is an essential component in the process of angiogenesis, is an example of a considerable interest. In the context of diabetes, microRNA miR-126 has emerged as the microRNA that has been investigated the most. In patients who have been diagnosed with type 2 diabetes (T2D), the amount of miR-126 in their circulation has been shown to decrease, according to a number of studies that have consistently documented this finding. Additionally, changes in the quantities of miR-126 in the circulatory system have been associated to diabetic nephropathy (DN) as well as the creation of microvascular structures seen in diabetic patients.

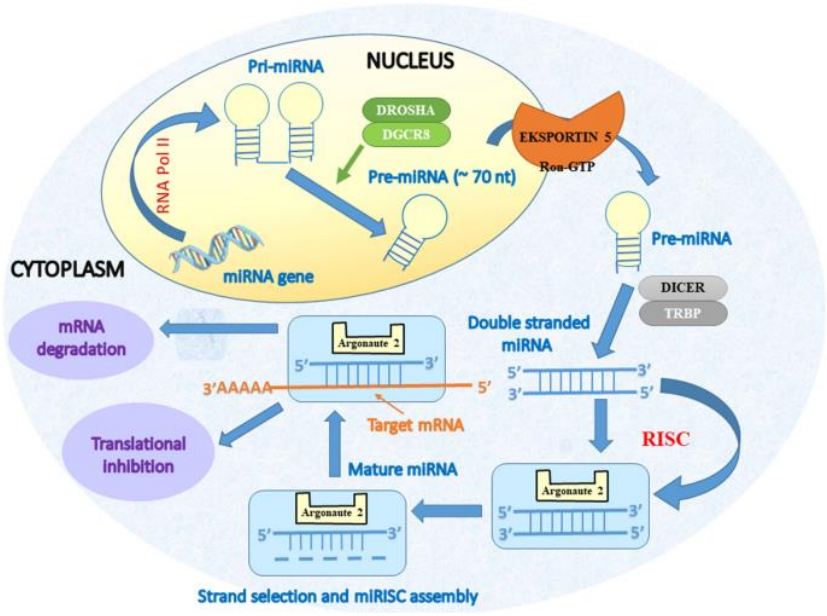


**Fig 1:** miRNA biogenesis and mechanism of action **[9]**
**RISC**: RNA-induced silencing complex
**TRBP**: Trans-activating response RNA binding protein
**pre-miRNA**: a precursor miRNA
**DGCR8**: DiGeorge syndrome critical region gene 8

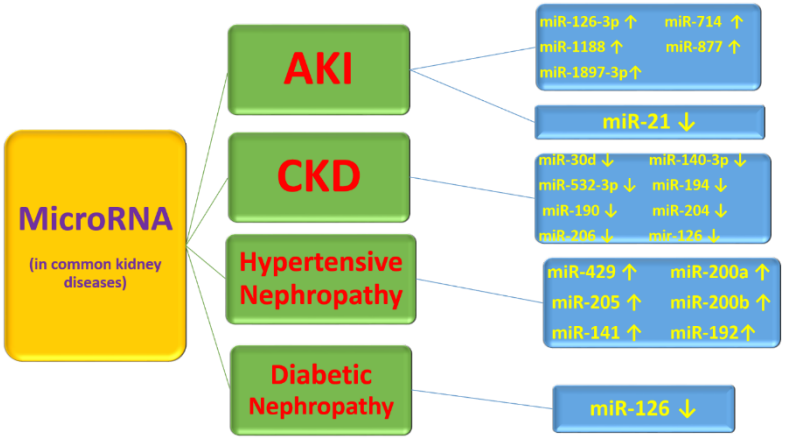


**Fig 2:** summery of affection of common kidney diseases on MiRNAs levels in blood
**AKI:** acute kidney injury
**CKD:** chronic kidney diseases

The crucial function that miR-126 plays in angiogenesis, which is the process of building new blood vessels, has been widely investigated in connection to diabetes on account of the fact that it is a microRNA that is mostly present in endothelial cells. Individuals who have type 2 diabetes have been shown to have lower amounts of miR-126 in their blood, according to the accumulation of studies. Particularly noteworthy is the fact that variations in the quantities of miR-126 in the blood have been linked to diabetic nephropathy (DN), vascular damage in diabetes [28], and the development to end-stage renal disease (ESRD) [43].

## 2. Conclusion and Future Recommendations

As a result of the substantial role that microRNAs play in the course of a number of kidney conditions, microRNAs offer a great deal of promise as new diagnostic and prognostic biomarkers for a broad variety of renal disorders. In spite of the fact that a number of microRNAs have been suggested as possible indicators for renal disorders, there is a dearth of clinical research that have been conducted to validate the use of these markers in a real-world setting at the present time. In addition, a number of research facilities have identified certain microRNAs that serve as biomarkers for a particular kidney illness. This finding lends credence to

the notion that a combination of various miRNAs may serve as a more effective diagnostic indication.

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