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The Contributory Mechanism of Alteration in Prorenin-Renin Homeostasis in the Pathogenesis of Diabetic Nephropathy

Kehinde Alare*, Oluwafemi Taiwo, Zainab Akindele, Peter Olaniyi and Rebecca Adeyemo

Abstract

Background: Diabetic nephropathy is part of the microvascular complication of diabetes mellitus along side neuropathy and retinopathy. Many mechanism has been presented as the pathophysiology of diabetic nephropathy but this could actually be attributed to the renin angiotensin system. The alteration in prorenin and renin homeostasis has been reported in patients with diabetes mellitus, it's noticed to reduction in conversion of prorenin to renin there by leading to accumulation of prorenin binding to (pro)renin.

Aim: This article is targeted at explaining the contributory roles of the alteration in the prorenin and renin homeostasis in the pathogenesis of diabetic nephropathy and to explain why some the drugs that act along renin angiotensin pathways especially angiotensin receptor blockers can be very helpful in the management of diabetic nephropathy.

Methods: A careful literature search was made on some scientifc databases such as PubMed, EMBase, Google Scholar, Research Gate and others using a very sensitive search strategy on researches that are related to efects of renin-angiotensin pathway on diabetic nephropathy focusing mainly on the use Handle Receptor Protein (HRP) and

and also that of Chu, which reported not only increase in the rate but also increase in the amount of prorenin converted to renin by the blockage of lysosomal glycosylation. ese actually suggested, presence of glucose moiety which are actually higher in diabetes; retarded the conversion of prorenin to renin thereby altering the homeostasis [4].

Researchers reported inhibitions of cathepsin B a proteolytic enzyme that catalyze cleavage of prosegment of prorenin to give active renin by high glucose concentration. is could also account for the increase in the level of prorenin seen in patient with diabetes [5].

Literature search of articles on reports the therapeutic importance of lowering the level or e ects of prorenin on diabetic nephropathy was made on di erent scienti c databases; which about 60 articles were collected and about 52 were exclude because they don't meet the inclusion criteria. Most of this articles are related directly to prorenin like articles which focus on the e ects of Handle Region Peptide (HRP) which is an inhibitor of prorenin or indirectly like those articles that looked into e ects of Angiotensin Receptor Blocker (ARB) on diabetic nephropathy. Inclusion criteria include that article is of statistically signi cance and shows the correlation of prorenin to diabetic nephropathy and that the article must be related to prorenin or renin-angiotensin system and also the methodology of the research must be involved mechanism in this path not in combination with others. Some of the articles were discarded because they were duplicate of others or had similar ndings to other selected articles [6].

e articles were reviewed under two categories, which are:

E ects of HRP on diabetic nephropathy

E ects of ARB on diabetic nephropathy

e Prisma ow chart showing the analysis of processes of articles selection is shown below (Figure 1).

A total of 60 articles were retrieved from di erent databases and only 8 articles were eventually used in this studies.

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Kökény compared the e ects of HRP, ACE inhibitor (Quinapril) and both on diabetic nephropathy in rats, it was observed that none has e ects on renal hypertrophy, HRP has no e ect on proteinuria but ACEI does and also ACEI + HRP does and Summary of their

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ree trials done on the e ects of Angiotensin II Receptor Blocker (ARB) were analyzed. In a trial, the Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) which was done on 1513 subjects reveals the e ectiveness of losartan in reducing the relative risk of primary composite end-point of nephritic death, serum creatinine, end stage renal disease and blood pressure regulation. Similarly, in the Irbesartan Diabetic Nephropathy Trial (IDNT) which

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