

Urinary Claudin-1 Level As a Marker of Podocyte Injury in Patients With Proteinuria

Thesis

Submitted For Partial Fulfillment of Master Degree in Internal Medicine

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2018

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لَسْبَدَانِكَ لَا نَعْلَمُ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢



Acknowledgement

First of all, thanks to *Allah* whose magnificent help was the main factor in completing this work.

No words can express my deep sincere feelings Towards *Prof Dr. Mohamed El-Tayeb Nasser* Professor of Internal Medicine and Nephrology Faculty of Medicine -Ain-Shams University for his continuous encouragement, guidance and support he gave me throughout the whole work. It has been a great honor for me to work under his generous supervision.

I would like to express my deepest appreciation, respect and thanks to *Prof. Dr .Sahar Mahmoud Shawky* Professor of Internal Medicine and Nephrology Faculty of Medicine -Ain-Shams University for her continuous guide in all aspects of life beside her great science, knowledge and information.

Last but not least, sincere gratitude to *My Family* for their continuous encouragement and spiritual support.

List of Contents

Title	Page No.
List of Tables	i
List of Figures.....	iv
List of Abbreviations	viii
Introduction	i
Aim of Work.....	4
Review of literature	
▪ Chapter (1): Claudins And Claudin-1	5
▪ Chapter (2): Podocytopathy In Diabetic	50
Patients and Methods.....	77
Results	81
Discussion.....	125
Summary.....	137
Conclusion.....	142
Recommendations	144
References	145

List of Tables

Table No.	Title	Page No.
Table (1):	Mechanisms leading to proteinuria following podocyte injury	31
Table (2):	Definition of the albuminuria in diabetic kidney disease.....	51
Table (3):	Pathologic Classification of Diabetic Nephropathy	54
Table (4):	Types of proteinuria	56
Table (5):	Causes of podocytes injury.....	75
Table (6):	The demographic & clinical characteristics of the studied groups.....	82
Table (7):	Etiology of Glomerulonephritis in GN group:	83
Table (8):	Comparison between the three studied groups regarding clinical and laboratory data:	85
Table (9):	Comparison between the studied groups as regard laboratory data	89
Table (10):	Comparison between the three studied groups regarding laboratory data:.....	91
Table (11):	Post Hoc analysis between the three studied groups as regard laboratory data:.....	92
Table (12):	Comparison between the three studied groups regarding urinary albumin / creatinine ratio (uACR)	95
Table (13):	Comparison between the three studied groups regarding urinary Claudin-1 level	96
Table (14):	Post Hoc analysis between the three studied groups as regared urinary alb/creat ratio (uACR) and urinary claudin-1	96
Table (15):	Roc curve (Diabetic group Vs Control group) regarding uACR & Urinary claudin-1	98
Table (16):	Roc curve (G.N. group Vs Control group) regarding Albumincreat & Urinaryclaudin.....	99

List of Tables

Table No.	Title	Page No.
Table (17):	Correlation between urinary albumin / creatinine ratio and other laboratory data in Diabetic group	100
Table (18):	Correlation between urinary claudin-1 and other laboratory data in diabetic group	101
Table (19):	Univariate linear regression analysis for predictors of urinary claudin-1 in diabetic group	102
Table (20):	Correlation between urinary albumin / creatinine ratio and other laboratory data in GN group	104
Table (21):	Univariate linear regression analysis for factors affecting the level of albumin/creat ratio among GN group	105
Table (22):	Multivariate linear regression analysis for factors affecting the level of albumin/creat ratio among GN group	105
Table (23):	Correlation between urinary claudin-1 and other laboratory data in GN group	106
Table (24):	Univariate linear regression analysis for factors affecting the level of urinary claudin-1 among GN group	107
Table (25):	Multivariate linear regression analysis for factors affecting the level of urinary claudin-1 among GN group	107
Table (26):	Correlation between urinary albumin /creat ratio and patients characteristics in Diabetic group:	113
Table (27):	Correlation between urinary claudin-1 and patients characteristics in diabetic group:	114
Table (28):	Correlation between uACR and patients characteristics in GN group	116

List of Tables

Table No.	Title	Page No.
Table (29):	Correlation between urinary claudin-1 and patients characteristics in GN group	119
Table (30):	Logistic regression analysis for predictors of diabetics group.....	121
Table (31):	Logistic regression analysis for predictors of GN group.....	122
Table (32):	Correlation between uACR and other laboratory data in control group	123
Table (33):	Correlation between urinary claudin-1 and other laboratory data in control group	124

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Schematic view of tight junction strands (lower part) and their major components, the claudins (top).	7
Figure (2):	Schematic representation of the claudin monomer.	9
Figure (3):	Phylogenetic tree for the full-length sequences of claudins.	10
Figure (4):	Tabulated interaction possibilities between claudins as, for example, reported for claudin-1 and -3.	12
Figure (5):	Localization of claudins along the adult mammalian renal tubule.	13
Figure (6):	Predominant claudin expression along the nephron.	13
Figure (7):	Physiologic roles of claudins in renal tubule epithelia.	16
Figure (8):	Structure of Claudin-1	24
Figure (9):	Schematic model of the molecular organisation of the slit diaphragm. Nephrin and NEPH1 are transmembrane proteins in the slit diaphragm.	27
Figure (10):	Generation and characterization of claudin-1–inducible animal model.	33
Figure (11):	Cellular localization of claudin-1 protein in mouse glomeruli.	34
Figure (12):	Urinary albumin levels in claudin-1–induced animals.	35
Figure (13):	Transmission electron microscopy imaging of mouse podocytes.	37
Figure (14):	Freeze-fracture deep-etching electron microscopy imaging of CON mouse glomeruli.	38
Figure (15):	Freeze-fracture deep-etching electron microscopy imaging of TG mouse glomeruli.	39
Figure (16):	Protein abundance levels of the indicated genes from isolated mouse glomeruli.	42
Figure (17):	Claudin-1 interacts with nephrin and podocin	43
Figure (18):	Claudin-1 gene expression in PAN	45

List of Figures

Fig. No.	Title	Page No.
Figure (19):	Immunostaining of nephrin and podocin in proteinuric state of puromycin aminonucleoside (PAN) nephropathy.	49
Figure (20):	Nature history and renal changes in type 1 diabetes mellitus.	52
Figure (21):	Schematic presentation of the glomerular basement membrane structure	58
Figure (22):	The podocyte and slit diaphragm	61
Figure (23):	Detailed electron tomograph of the slit diaphragm with wire frame representation of electron density.	62
Figure (24):	Description of the slit diaphragm in 1955, major breakthroughs in research have elucidated the contributions of the slit diaphragm to filtration and the response to injury.....	68
Figure (25):	Consequences of podocyte injury.....	69
Figure (26):	Podocytes and slit diaphragm.....	72
Figure (27):	Podocytes.....	74
Figure (28):	Comparison between the three studied groups regarding age (descriptive data of the study population).....	82
Figure (29):	Etiology of glomerulonephritis in GN group	83
Figure (30):	Comparison between different classes of cases with lupus nephritis showing that patients with lupus nephritis class II were 3 patients (17.6%) , lupus nephritis class III were 7 patients (41.2%) and lupus nephritis class IV were 7 patients (41.2%).....	84
Figure (31):	Comparison between the three studied groups as regard HbA1c	86
Figure (32):	Comparison between the three studied groups as regard FBS level.....	86
Figure (33):	Comparison between the three studied groups as regard 2hrs PP glucose level.....	87

List of Figures

Fig. No.	Title	Page No.
Figure (34):	Comparison between cases in diabetic group as regard using insulin or OHG.....	87
Figure (35):	Comparison between the three studied groups as regard HTN.....	88
Figure (36):	Comparison between diabetic and GN groups as regard antiproteinuric measures	88
Figure (37):	Comparison between the three studied groups as regard TLC	90
Figure (38):	Comparison between the three studied groups as regard.....	90
Figure (39):	Comparison between the three studied groups as regard BUN	93
Figure (40):	Comparison between the three studied groups as regard creatinine and K level.....	93
Figure (41):	Comparison between the three studied groups as regard Liver enzymes (AST, ALT).	94
Figure (42):	Comparison between the three studied groups as regard s. albumin.	94
Figure (43):	Comparison between Diabetic and GN groups as regard GFR.	95
Figure (44):	Comparison between the three studied groups as regard uACR.....	97
Figure (45):	Comparison between the three studied groups as regard urinary claudin-1.	97
Figure (46):	Correlation between uACR and urinary claudin-1 in Diabetic group.	102
Figure (47):	Correlation between urinary claudin-1 and HGB in diabetic group.	103
Figure (48):	Correlation between urinary claudin-1 and uACR in GN group.	108
Figure (49):	Correlation between uACR and BUN in GN group.....	108

List of Figures

Fig. No.	Title	Page No.
Figure (50):	Correlation between uACR and s.creatinine in GN group.....	109
Figure (51):	Correlation between uACR and s. albumin in GN group.....	109
Figure (52):	Correlation between uACR and GFR in GN group.....	110
Figure (53):	Correlation between urinary claudin-1 and s. creatinine in GN group.	110
Figure (54):	Correlation between urinary claudin-1 and s.albumin in GN group.....	111
Figure (55):	Correlation between urinary claudin-1 and age in GN group.....	111
Figure (56):	Correlation between urinary claudin-1 and HGB in GN group.....	112
Figure (57):	Correlation between antiproteinuric measures and urinary claudin-1 in Diabetic group	115
Figure (58):	Correlation between uACR and different types of GN	117
Figure (59):	Correlation between uACR and different classes of lupus nephritis in GN group	117
Figure (60):	Correlation between uACR and hypertension in GN group.....	118
Figure (61):	Correlation between uACR and antiproteinuric measures in GN group.....	118
Figure (62):	Correlation between urinary claudin-1 and different classes of lupus nephritis	120

List of Abbreviations

Abb.	Meaning
ASDN	Aldosterone sensitive distal nephron
CD.....	Collecting duct
CD2AP	CD2 adaptor protein
COIP	Co-immunoprecipitation
ECL.....	Extracellular loop
FHHNC.....	Familial hypomagnesemia with hypercalcuria and nephrocalcinosis
FPs	Foot processes
FSGS.....	Focal Segmental glomerulosclerosis
GBM	Glomerular basement membrane
HEK.....	Human embryonic kidney
IMCD.....	Inner medullary collecting duct
JAM	Junctional Adhesion Molecules
LLC-PK	Lilly laboratories cell - porcine kidney
MAGI-1	Membrane associated granulate kinase inverted-1
MAGUK.....	Membrane associated granulate kinase homologues
MCD	Minimal change disease
MCNS.....	Minimal change nephrotic syndrome
MDCK	Madin-Darby canine kidney
MUPP1	Multi PDZ domain protein 1
PAN	Puromycin aminonucleoside
PEC.....	Parietal epithelial cells
PT	Proximal tubule
SD	Slit diaphragm
TAL	Thick ascending limb

List of Abbreviations

Abb.	Meaning
tAL.....	Thin ascending limb
TALH	Thick ascending limb of Henle
tDL.....	Thin descending limb
TG.....	Transgenic
ZO-1	Zonula occludens-1
PGC	PPAR Gamma Co-activator

Abstract

Background: The biology of claudins is a rapidly evolving field, and many intriguing questions remain unanswered. Although it had been assumed that the reason there are ≥ 24 isoforms of claudin is that each one has distinct permeability properties. The nephron displays a wide spectrum of claudins, whose distribution varies in each tubular segment. In diabetic nephropathy and glomerulonephritis the gene expression of claudin-1, is markedly upregulated in the podocyte, accompanied by a tighter filtration slit diaphragm (cell-cell junction made by the glomerular podocytes) and the appearance of TJ-like structures between the foot processes causing further podocytes injury and proteinuria.

Aim of the work: to assess urinary claudin -1 level as a marker of podocyte injury in patients with proteinuria.

Patients and Methods: it is a case control study which was conducted upon 90 subjects who were divided into three groups: group I included 30 patients with type II DM, group II included 30 patients with glomerulonephritis and group III had 30 healthy subjects as controls. Urinary claudin-1 level was measured by Enzyme linked Immunosorbent Assay (ELISA)

Results: In this study, we found that urinary claudin-1 level was significantly higher in diabetics group and GN group than in control group. In comparison between GN group and diabetic group, we found that urinary claudin-1 level was higher in GN group than in diabetics group but with no statistically significant difference between the two groups.

Conclusion: urinary claudin-1 level was significantly higher in diabetics and GN group and has positive correlation with uACR. So it can be used as marker of podocytes injury and proteinuria.

Keywords: Thin descending limb, Transgenic, Zonula occludens-1, PPAR Gamma Co-activator

INTRODUCTION

Claudins were first purified and identified by Mikio Furuse in the tight junction laboratory of the late Shoichiro Tsukita. Their name was derived from the Latin word “claudere,” which means to close, because it was anticipated that these proteins might constitute the tight junctional barrier. It soon became apparent that the claudins are part of a large multigene family of 24 members of claudins (*Angelow et al., 2008*).

Claudins are tight-junction membrane proteins that function as both pores and barriers in the paracellular pathway in epithelial cells. In the kidney, claudins determine the permeability and selectivity of different nephron segments along the renal tubules (*Alan, 2014*).

The nephron displays a wide spectrum of claudins, whose distribution varies in each tubular segment; pore claudins are associated with leakier tubule segments, whereas barrier claudins are expressed in tighter distal segments (*Molina et al., 2014*).

Each claudin gene exhibits a unique nephron segment pattern of expression, and each nephron segment expresses multiple claudins. It is believed that the particular combination of claudins determines the unique paracellular permeability properties of each nephron segment.