



## ALBUMINURIA THE HIDDEN TRUTH: NEPHROTIC SYNDROME IS CAUSED BY "PATHOGEN"

### Nephrology

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### ABSTRACT

Nephrotic syndrome (Kidney injury) is complex disease which impairs the kidney functions dramatically. The classical features of Nephrotic syndrome are excessive loss of proteins through urine, Hyper cholesterolemia, Hyper lipidemia, Hypo albuminemia and edema. The exact underlying pathology (etiology) of this disease is not clear, however this is thought to be due to damage in kidney filtering units that is injury to podocyte or damage to Glomerular basement membrane (GBM). The condition exists as a Chronic or Acute based on the degree of kidney injury. Since the exact etiology of the disease is not well understood the management of the disease poses great challenge to medical field. It affects both the sexes and in all age groups. As the disease progresses further it leads to End stage renal disease (ESRD) where Dialysis or kidney transplant are the choice of management. My research revealed that this disease is caused by one specific "PATHOGEN" which remains "Hidden throughout the course of the disease. The "PATHOGEN" can be identified by specific simple and economic technology developed by me. If this "PATHOGEN" is targeted TOTAL CURE of this condition is possible.

### KEYWORDS

Nephrotic syndrome, Kidney injury, ARF, CRF, ESRD, Albuminuria, Biomarkers.

**Introduction :-** Kidney plays important role during the life span of an Individual. These organs are important as these are responsible to filter out metabolic waste products and retain important biomolecules to maintain health life and homeostasis in an individual. Apart from this important functions kidney's are also responsible for acid-base balance, water regulation and Hormone production. Kidney's consists of highly vascular bed (glomerulus) which is responsible for the selective ultrafiltration of plasma proteins and other biomolecules. Despite the Technical advancements in the critical care management, the onset of kidney failure is increasing at an alarming rate 1-4. Podocytes are tiny well differentiated filtering units which are like projections of outer epithelial cells of Glomerular Basement membrane (GBM) 5-8. Researcher's have demonstrated that podocyte can be vulnerable to Immune or non-Immune mediated response leading to kidney injury 9-11. Classical and characteristics feature of kidney injury is high level of proteinuria in which selective permeability of GBM increases and there is excessive loss of Albumin along with other plasma macromolecules. (12)

The exact cause of this injury is not yet understood clearly, however it is thought to be due to damage in podocyte structure and function, as well as damage to Glomerular basement membrane (GBM). The classical feature of this kidney injury is attributed to loss of excessive proteins (mainly Albumin) through Urine. Normally proteins are retained in host system and very negligible amount of these proteins are passed out of an individual through urine over period of 24 hrs. The excessive loss of Proteins leads to edema due to water retention and further results in low levels of Albumin in blood. The excessive loss of Proteins through urine results into Nephrotic syndrome and is usually detected by analyzing blood tests, urine tests and kidney biopsies. Nephrotic syndrome is a group of disease classified as minimal change disease (MCD), Membranous Nephropathy (MN), Focal Segmental Glomerulosclerosis (FSGS), Acute Glomerulonephritis (AGN), Mesangial Proliferative Glomerulonephritis (MPGN), and Rapidly progressive Glomerulonephritis (RPGN). So far various laboratory tests are used to diagnose, treat and monitor this clinical condition, however more prominently urine Albumin, Blood urea, Serum creatinine and GFR (glomerular filtration rate) are the choice of tests globally (13). The other kidney injury markers viz NGAL-Neutrophil gelatinase-associated Lipocalin, cystatin C, IL-18 Interleukin-18, KIM-1 kidney injury molecule 1 and L-FABP Liver-fatty acid binding protein have emerged however these biomarkers lack sensitivity and specificity. (14)

The specificity, sensitivity and the limitations of these tests poses challenge in the management of this clinical condition, BUL, serum creatinine and urine Albumin are the choice of tests however these tests as well lack sensitivity and specificity. The major limitation in this clinical condition is lack of good, sensitive and specific Biomarkers to detect the condition at its early stage. As quoted by Konder 2009

"There are no established guidelines on the diagnostic workup or management of Nephrotic Syndrome." (15)

BUL and serum creatinine do not show significant changes unless the disease progresses to 50% to 70% irreversible loss of kidney functions. The various stages in the disease process indicates clearly that the disease cannot be detected at its early stage and more over the cause of the disease can not be established based on the present diagnostic work up.

The disease exists as chronic condition (CRF) or Acute condition (ARF) based on the manifestation of the disease. Usually remission or relapsing cycle exist in this clinical condition which eventually leads to End stage renal disease (ESRD).

Hence identifying sensitive and specific Biomarkers in this condition is topmost research priority in this field. My research has shown that this disease is caused by one very specific "PATHOGEN" which remains "Hidden" throughout the course of the disease. (16). This "PATHOGEN" can be identified by employing specific Technology and protocol developed by me. This "PATHOGEN" is present in all the stages of Renal disease which suggests its strong association with disease condition (17). There is need to explore this further which will be useful to develop new diagnostic Biomarkers for kidney injury, new therapeutic drugs for total cure of the disease.

**Materials :-** 1) Sterile container  
2) 3% w/v sulphosalysylic Acid  
3) 0.2% w/v Ponceu'S stain  
4) Microscope  
5) Test Tubes

**Method :-** A simple, sensitive and highly economic method has been developed. Patients diagnosed as Nephrotic syndrome and Diabetic Nephropathy have been selected for This study. Following protocol has been followed:

- A] Collect fresh urine samples from these patients in clean sterile container by clean catch method.
- B] Approximately 3-5 ml of collected urine sample is centrifuged for 5 mins at 5000 rpm.
- C] Supernatant from step B is collected in another clean dry test tube.
- D] sediment is observed under highpower microscope and the findings are noted.
- E] The supernatant from step C is mixed with equal volume of 3% w/v sulphosalysylic Acid and mixed vigorously for a minute. This is allowed to settle at room temp.
- F] After few minutes once above mixture (step E) settles then transfer approximately 200 microliter of the supernatant from step E to another clean dry test tube. Add to it approximately 50-70 microliter of 0.2% w/v Ponceu'S stain and allow this to remain

- at room temperature for 10 mins with intermittent shaking.
- GJ** This mixture 10-20 microliter is then observed under high power microscope which will clearly show the motility of "PATHOGEN".
- HJ** Even if the wet mount gets dried up disturb the edges of cover slip and observe under high power microscope.

**Results and Discussion :-** Albumin is an important protein biomolecule of the blood which is responsible for various important biological functions. Almost 50 to 70 % of plasma protein consist of Albumin. Albumin is never filtered out through kidney's rather it is retained in blood. The presence of Albumin in urine has been recognized as sign of kidney damage since long time and in severe cases concentration more than 3.5 gms/L have been noted. The detection of Albumin in urine is very old Laboratory tests to understand the kidney functions.

Now the question arises why Albumin being such an important biomolecule is thrown out of host body when this molecule plays diverse physiological Functions? Since Albumin being globular protein and exists as dimer this made me to think whether it is carrying "something" which host wants to get rid off? And to my surprise after denaturing the Albumin structure the trapped "PATHOGEN" within Albumin molecule is released into the solution which can be observed under high power microscope. This indicates that Albumin molecule is capable of trapping "PATHOGEN" which may be forming "Cacoon" like structure for "PATHOGEN" hence host defense mechanism is unable to indentify this invader "PATHOGEN".

Whether Albumin entraps the "PATHOGEN" or "PATHOGEN" prefers to burrough itself in Albumin molecule and gets shield need to be explored further which will be useful to design the management strategies for the disease. The leaking of Albumin seems to be rather self defense mechanism by the host to get rid off these infectious organisms. This must be the "PATHOGEN" which is responsible for remission and relapsing cycle in host. This "PATHOGEN" is present almost in all samples including the pre and post dialysis patients. The excessive concentration of Albumin in urine may be causing excessive clogging of the filtering units leaving little or no place for fluid to flow through which results into ESRD. This must be the "PATHOGEN" which develops resistance to steroids manifesting as steroid Resistance Nephrotic Syndrom SRNS. This "PATHOGEN" can not be seen in untreated sample of patient however once the denaturation treatment is given to the samples, the trapped "PATHOGEN" is released into the solution which can be clearly seen under highpower microscope.18

This research would be certainly useful to develop new Diagnostic test, new therapeutic drugs and vaccines. The role of Albumin in other various chronic condition such as multiple sclerosis need to be established on similar principles. This would certainly be useful and helpful to have better quality life and decreased morbidity and mortality rate globally to have healthy and better life to human race.

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