International Journal of Healthcare Sciences ISSN 2348-5728 (Online)
Vol. 3, Issue 2, pp: (283-288), Month: October 2015 - March 2016, Available at: www.researchpublish.com

Nephrotic Syndrome

[1]Ibrahim Abdullak Alqurashi, [2]Mohammad Jaman Althaqafi, [3]Faris Ahmed Althomali, [4]Abdulaziz Ahmed Alzaher

Abstract: **Nephrotic syndrome is a condition of massive proteinuria (protein leaks from the blood to the urine through the glomeruli) that leads to hypoalbuminaemia and oedema. There are many specific causes of nephrotic syndrome. Nephrotic syndrome may affect adults and children, of both sexes and of any race. It may occur in typical form, or in association with nephritic syndrome. Objective: the propose of this study is to review and analysis previous based evidence studies that concerns with the classification, pathogensis, Etiology, , diagnosis and treatment outcomes of nephrotic syndrome, including all population of different ages and both sex. Methodology: we conducted systemic review with meta-analysis search through medical database online such as Medline; we include all those studies which were published in the last 15 years (2000-2015) about nephrotic syndrome. Conclusion: Patients with nephrotic syndrome can present to primary or secondary care with diverse symptoms that reflect the primary process or with one of the many systemic complications of the syndrome. For patients with nephrotic syndrome attributable to treatment-resistant glomerulonephritis, some benefits may be obtained with the new immunosuppressive drugs used in organ transplantation, such as cyclosporine, mycophenolate mofetil, and in some cases tacrolimus. For patients with diabetes mellitus or amyloidosis and for some patients with glomerulonephritis that does not respond to any immunosuppressive treatment, no causal treatment is currently possible.**

Keywords: **Nephrotic syndrome, adults and children, both sexes, cyclosporine.**

1. BACKGROUND

Classification of Nephrotic Syndrome:

Nephrotic syndrome can be classified as: a). Primary. b). Secondary.

- Idiopathic (primary) nephrotic syndrome Minimal change (80-90%).
- Secondary nephrotic syndrome.
- Congenital nephrotic syndrome .

Primary means the nephrotic syndorome is being the main disease affecting to the kidneys. But the secondary one means, it's a result of another primary disease, so it's secondary to that specific disease in both types; the main manifest is the damage of glomeruli.

There are several causes of **Primary nephrotic syndrome** which is showing as the following, regarding order of frequency:

- ***Membranous nephropathy:*** Membranous nephropathy is a condition in which the walls of the glomerular blood vessels become thickened from the accumulation of protein deposits.
- ***Minimal-change nephropathy:*** People with minimal change disease have normal or very mild abnormalities of the glomeruli.
- ***Focal segmental glomerulosclerosis:*** *FSGS* causes collapse and scarring of some glomeruli. *(Takehiko Wada and Masaomi Nangaku in 2015*) stated that , Primary focal segmental glomerulosclerosis (FSGS) is one of the major causes of steroid-resistant nephrotic syndrome, and renal prognosis in patients with steroid-resistant FSGS is poor. It has been long speculated that a circulating permeability factor should be implicated in the pathogenesis of the disease because a substantial portion of the patients with primary FSGS experience recurrence shortly after transplantation.

- ***Hereditary nephropathies:***

Secondary **nephrotic syndrome** caused secondry to the following diseases:

- Diabetes mellitus
- Lupus erythematosus
- Amyloidosis and paraproteinemias
- Viral infections

Pathogenesis:

Nephrotic syndrome develops when there is damage to the glomeruli, which are the structures in the kidneys that work to filter the blood. This damage allows Proteinuria and Hypoalbuminemia to happen.

Proteinuria is is the aftereffect of adjustments in the fuction of the glomerular filtration barriar junction. This barriar is made out of three layers in arrangement: the fenestrated endothelium, the glomerular cellar film, and the vascular glomerular epithelium, involved podocytes a. Podocyte is the name of the epithelial cell, and foot procedure is the section of the cell that stretches out into the urinary space. What happened is that in the nephrotic syndrome, there is destruction of the foot process, yet whatever remains of the cell as a rule is safeguarded.

Endothelial cells have very small diameter openings that are about 70 to 100 nm, which is called fenestrae that form a physical barrier for passage of macromolecules from plasma into the renal tubule. The dysfunction of this barrier has been investigated by electron microscopic which showed negatively charged particles in the glomerular basement membrane, which preclude the passage of anionic macromolecules, such as albumin.

Nephrotic Syndrome Symptoms:

Kidney failure: Some people with nephrotic syndrome have a decreased in kidney function, which causes no symptoms in the early stages. In any case, as the distrubtion in function of kidney worsening, that could be indications of developing kidney failure.

Hyperlipidiema: cholesterol and/or triglycerides parameters in blood can significantly elevated in nephrotic syndrome. (Vaziri ND, 2015 Nov 16).

Thrombsis: (*Hashmi M, Wasay M in 2011)*, stated People with nephrotic syndrome are at an increased risk of blood clots in the veins or arteries. thrombus may disattach as embolism and travel to the lungs.

2. INTRODUCTION

A glomerular disease that mostly affects children and adults, is classically defined by massive proteinuria (>40mg/m^2/hour), hypoalbuminemia (<2.5g/dL), generalized edema and hyperlipidemia. Membranous nephropathy (MN) is a major cause of nephrotic syndrome. However, the etiology of roughly 75% of MN cases is idiopathic. Auxiliary reasons for MN are immune system sicknesses, contamination, medications, and threat. The pathogenesis of MN includes development of safe complex in subepithelial destinations, yet the unequivocal system is still obscure. There are three speculations about the arrangement of insusceptible complex, including preformed invulnerable complex, in situ resistant complex development, and autoantibody against podocyte film antigen. The development of invulnerable complex starts supplement actuation, which therefore prompts glomerular harm.

Idiopathic nephrotic syndrome is the most frequent glomerular disease in children and in young adults. While hereditary examinations have given new of little of knowledge into malady pathogenesis through the revelation of a few podocyte qualities transformed in particular types of acquired nephrotic disorder, the sub-atomic bases of insignificant change nephrotic disorder and central and segmental glomerulosclerosis with backslides stay indistinct. Albeit resistant cell issues, which may include both inalienable and versatile insusceptibility, seem to assume a part in the pathogenesis of steroid touchy insignificant change nephrotic disorder, the components by which they impel podocyte brokenness stay uncertain. It was hypothesized that podocyte harm results from a coursing element emitted by anomalous T cells, however the likelihood that bipolarity of the ailment results from a practical issue shared by both insusceptible cells and the podocytes is not excluded.

There is increasing evidence that longer initial courses of prednisolone are associated with a lower incidence of relapse, and therefore a 12-week initial course is recommended. The dose of prednisolone is based on surface area.

• 60 mg/m^2/day for 4 weeks (maximim 80 mg)

• 40 mg/m^2/on alternate days for 4 weeks (maximum 60mg) Reduce dose by 5-10mg/m^2 each week for another 4 weeks then stop.

Twenty percent of idiopathic NS does not respond to steroid treatment. In addition to steroid resistance, frequent relapses and steroid dependence are concerns. Younger age, male gender, a history of atopy, longer time to first remission, a shorter time from remission to first relapse, and glucocorticoid receptor gene NR3C1 GR-9beta+TthIII-1 variants have been linked to frequent relapse and steroid dependence.

The treatment of edema in patients with nephrotic syndrome is generally managed by dietary sodium restriction and loop diuretics. On the other hand, edema does not enhance in a few patients in spite of sufficient sodium confinement and maximal dosage of diuretics. In such patients, blend of egg whites and a circle diuretic may enhance edema by diuresis and natriuresis. The reaction to this mix of egg whites and a diuretic has not been seen in all studies. The motivation behind this survey is to talk about the physiology of diuresis and natriuresis of this mix treatment, and give a brief synopsis of different studies that have utilized egg whites and a circle diuretic to enhance diuretic-safe edema. Additionally, the audit proposes different purposes behind not watching comparative results by different examiners.

3. OBJECTIVES

The aim of our study is to review and analysis previous based evidence studies that concerns with the classification, pathogenesis, Etiology, prognosis, diagnosis and treatment outcomes of nephrotic syndrome, including all population of different ages and both sex.

4. METHOD OF STUDY

Systemic review with meta-analysis searched was done through medical online database such as Medline; we include all those studies which were published in the last 15 years (2000-2015) about nephrotic syndrome.

5. ETIOLOGY

Nephrotic syndrome can be caused by diseases that affect only the kidneys, such as focal segmental glomerulosclerosis (FSGS) or membranous nephropathy. Diseases that affect only the kidneys are called primary causes of nephrotic syndrome. The glomeruli are usually the targets of these diseases for reasons that are not fully understood. In FSGS—the most common primary cause of nephrotic syndrome—scar tissue forms in parts of the glomeruli. In membranous nephropathy, immune molecules form harmful deposits on the glomeruli.

Nephrotic syndrome can also be caused by systemic diseases, which are diseases that affect many parts of the body, such as diabetes or lupus. Systemic diseases that affect the kidneys are called secondary causes of nephrotic syndrome. More than 50 percent of nephrotic syndrome cases in adults have secondary causes, with diabetes being the most common *(The Merck Manuals Online Medical Library*).

Childhood nephrotic syndromes are most commonly caused by one of two idiopathic diseases: minimal-change nephrotic syndrome (MCNS) and focal segmental glomerulosclerosis (FSGS). A third distinct type, membranous nephropathy, is rare in children. Other causes of isolated nephrotic syndrome can be subdivided into two major categories: rare genetic disorders and secondary diseases associated with drugs, infections, or neoplasia (*Eddy AA, Symons JM, 2003*). While initial evidence supported an imbalance of T helper responses, recent studies suggest alterations in both innate and adaptive immune responses, including evidence for impaired T regulatory function. The central role of the podocyte in causing proteinuria is confirmed by the observation of mutations in key podocyte proteins in steroid resistant nephrotic syndrome and experimental evidence of altered podocyte signaling and cytoskeletal organization. The outcome and management of idiopathic nephrotic syndrome in children is determined by the response to corticosteroids and the frequency of relapses. While patients with steroid sensitive nephrotic syndrome have a favorable long term outcome, almost half of them relapse frequently and are at risk of adverse effects of corticosteroids. Although various non-corticosteroid immunosuppressive agents are used to prolong disease remission, careful monitoring is required for the potential adverse effects *(Sinha A, Bagga A.,2012).*

6. DIAGNOSIS

1. Urine test:

Urine samples are taken to diagnose people suspected of having nephrotic syndrome.

Nephrotic syndrome is analyzed when a lot of protein are found in the urine. The blood protein egg whites makes up a great part of the protein that is lost, however numerous other critical proteins are additionally lost in nephrotic syndrome.

The vicinity of egg whites in the urine can be identified with a dipstick test performed on a urine test. The urine test is gathered in a unique compartment in a human services supplier's office or business office and can be tried in the same area or sent to a lab for investigation. For the test, a medical caretaker or specialist puts a portion of synthetically treated paper, called a dipstick, into the urine. Patches on the dipstick change shading when protein is available in urine.

A more exact estimation is generally expected to affirm the finding. Either a solitary urine test or a 24-hour accumulation of urine can be sent to a lab for investigation. With the single urine test, the lab measures both egg whites and creatinine, a waste result of ordinary muscle breakdown. The examination of the estimations is known as a urine egg whites to-creatinine proportion. A urine test containing more than 30 milligrams of egg whites for every gram of creatinine may signal a problem. With a 24-hour collection of urine, the lab measures only the amount of albumin present. The single urine sample is easier to collect than the 24-hour sample and is usually sufficient to confirm diagnosis, though the 24-hour collection may be used in some cases (*Papadakis MA, ed, et al. 2014*).

2. Blood test:

Once nephrotic syndrome is diagnosed, blood tests are usually needed to check for systemic diseases that may be causing the nephrotic syndrome and to find out how well the kidneys are working overall. A blood test includes drawing blood at a medicinal services supplier's office or business office and sending the example to a lab for examination.

Despite the fact that blood tests can indicate systemic ailments, a kidney biopsy is normally expected to analyze the particular basic illness creating the nephrotic syndrome and to determine the best treatment.

3. kidney biopsy:

A kidney biopsy is a methodology that includes taking a bit of kidney tissue for examination with a magnifying lens. Kidney biopsies are performed by a human services supplier in a healing facility with light sedation and nearby soporific. A biopsy is regularly not required for a man with diabetes on the grounds that the individual's therapeutic history and lab tests might be sufficient to analyze the issue just like a consequence of diabetes.

7. TREATMENT

The goals of treatment are to relieve symptoms, prevent complications, and delay kidney damage. To control nephrotic syndrome, you must treat the disorder that is causing it. You may need treatment for life.

Immunosuppressive Drugs:

The first controlled trial of immunosuppressive treatment in grown-up patients with glomerulonephritis and the nephrotic syndrome was embraced in 1970 with prednisone. That trial affirmed that a few sorts of glomerulonephritis reacted to immunosuppressive treatment superior to anything others and that patients with the inversion of proteinuria usually did not develop renal insufficiency *(Black DAK, Rose G,1979).* Consequently, other immunosuppressive drugs, such as azathioprine, cyclophosphamide, and chlorambucil, were tested for the treatment of glomerulonephritis; they improved and stabilized the outcome of treatment, especially for the poorly responding forms of glomerulonephritis [such as focal segmental glomerular sclerosis (FSGS) and membranous glomerulonephritis] (*Korbet SM, Schwartz MM,1994*). In recent years, immunosuppressive drugs used for organ transplantation have been increasingly tested for the treatment of resistant cases of glomerulonephritis.

Nonspecific Supportive Treatment:

Angiotensin-converting enzyme (ACE) inhibitors are known not proteinuria by lessening GFR and consequently affecting mesangial forms and additionally the sieving coefficient and size selectivity of the glomerular storm cellar film *(Maschio G, Alberti D, 1996)*. Angiotensin II receptor antagonists have the same effects on proteinuria and are as effective as ACE inhibitors *(Plum J, Bünten B,1998)*. The possibility of additive effects of the two types of compounds has not yet been tested.

Hydroxymethylglutaryl coenzyme A reductase inhibitors have strong lipid-lowering effects. It has been suggested that dyslipoproteinemia caused by renal disease, and especially by the nephrotic syndrome, may contribute not only to the accelerated development of atherosclerosis but also to the progression of renal disease *(Samuelsson O, Attman P-O,1998).* In addition to their lipid-lowering effects, statins improve endothelial function and alter the local fibrinolytic balance within the vessel wall, in a way that tends to increase fibrinolytic activity *(Katznelson S, Wilkinson AH,1996)*. However, the lipid-lowering effects of hydroxymethylglutaryl coenzyme A reductase inhibitors with respect to the extent of proteinuria in cases of nephrotic syndrome have not been proven *(Thomas ME, Harris KPG,1993).*

Nonsteroidal anti-inflammatory drugs have been shown to reduce proteinuria by reducing the GFR (*Donker AJM, Brentjens JRH, 1978*). The various renal reactions brought on by prostaglandin hindrance, for example, hemodynamic consequences for renal perfusion, edema arrangement, hyperkalemia, and renal danger, have prompted the limited utilization of these medications. Specific cyclooxygenase II inhibitors have been appeared to have the same advantageous impacts on proteinuria in rats, with less reactions, when managed in low measurements; at high dosages, cyclooxygenase II selectivity is lost and a greater amount of the regular previously stated symptoms of nonsteroidal anti-inflammatory drugs may be observed (*Blume C, Heise G, 1999*).

8. CONCLUSION

Nephrotic syndrome can be created by ailments that influence just the kidneys, for example, central segmental glomerulosclerosis (FSGS) or membranous nephropathy. Maladies that influence just the kidneys are called essential drivers of nephrotic syndrome. The glomeruli are typically the objectives of these illnesses for reasons that are not completely caught on. In FSGS—the most widely recognized essential driver of nephrotic syndrome scar tissue shapes in parts of the glomeruli. In membranous nephropathy, resistant atoms structure hurtful stores on the glomerThe nephrotic syndrome, brought about by glomerulonephritis, diabetes mellitus, or amyloidosis, is still a restorative test. More up to date remedial methodologies might be looked for in the fields of immunosuppression, nonspecific steady measures, heparinoid organization, and evacuation of an assumed glomerular basement membrane lethal variable. In immunosuppression, the more up to date sedates now utilized as a part of organ transplantation (cyclosporine, tacrolimus, and mycophenolate mofetil) can likewise be utilized as a part of the treatment of glomerulonephritis. In nonspecific steady treatment, angiotensin II receptor rivals are currently utilized as a part of expansion to angiotensin-changing over compound inhibitors. Constructive outcomes of hydroxymethylglutaryl coenzyme A reductase inhibitors on the nephrotic syndrome have not yet been demonstrated. Cyclooxygenase II inhibitors must be tried however likely have an excess of renal reactions, like those of nonsteroidal mitigating drugs. Heparinoids or glycosaminoglycans serve as polyanions and in this manner effectsly affect the negative charge of the glomerular basement membrane.

REFERENCES

[1] Hashmi M, Wasay M. Caring for cerebral venous sinus thrombosis in children. J Emerg Trauma Shock. 2011;4(3):389-94.

[2] atrakka J, Ruotsalainen V, Reponen P, et al. Recurrence of nephrotic syndrome in kidney grafts of patients with congenital nephrotic syndrome of the Finnish type: role of nephrin. Transplantation 2002;73:394-403.

[3] Vincenti F, Ghiggeri GM. New insights into the pathogenesis and the therapy of recurrent focal glomerulosclerosis. Am J Transplant 2005; 5: 1179–1185.

[4] Matalon A, Markowitz GS, Joseph RE, et al. Plasmapheresis treatment of recurrent FSGS in adult renal transplant recipients. Clin Nephrol 2001; 56: 271–278.

[5] Vaziri ND. HDL abnormalities in nephrotic syndrome and chronic kidney disease. 2015 Nov 16. doi: 10.1038/nrneph.2015.180

[6] Margaret Duffy, Shashank Jain, Nicholas Harrell, Neil Kothari and Alluru S. Reddi. Albumin and Furosemide Combination for Management of Edema in Nephrotic Syndrome: A Review of Clinical Studies. 2015, 4(4), 622-630; doi:10.3390/cells4040622.

[7] Hoyer PF. New lessons from randomized trials in steroid-sensitive nephrotic syndrome: clear evidence against long steroid therapy. Kidney Int. 2015;87:17–19.

[8] Tarshish P, Tobin JN, Bernstein J, Edelmann CM., Jr Prognostic significance of the early course of minimal change nephrotic syndrome: report of the International Study of Kidney Disease in Children. J Am Soc Nephrol. 1997;8:769–776.

[9] Giglio S, Provenzano A, Mazzinghi B, Becherucci F, Giunti L, Sansavini G, et al. Heterogeneous genetic alterations in sporadic nephrotic syndrome associate with resistance to immunosuppression. J Am Soc Nephrol. 2015;26:230–236.

[10] Sinha A, Bagga A. Nephrotic syndrome. • 2012Aug;79(8):1045-55.doi: 10.1007/s12098-012-0776-y. Epub 2012 May 30.

[11] Eddy AA1, Symons JM. Nephrotic syndrome in childhood. 2003 Aug 23;362(9384):629-39.

[12] Papadakis MA, ed., et al. Current Medical Diagnosis & Treatment 2014. 53rd ed. New York, N.Y.: The McGraw-Hill Companies; 2014.

[13] Nephrotic syndrome in adults. National Institute of Diabetes and Digestive and Kidney Diseases.

[14] Kong X, et al. Lipid-lowering agents for nephrotic syndrome (Review). Cochrane Database of Systematic Reviews.

[15] George BA, Zhou XJ, Toto R. Nephrotic syndrome after bevacizumab: case report and literature review. Am J Kidney Dis. 2007 Feb. 49 (2): e23-9.

[16] Ozkaya N, Cakar N, Ekim M, Kara N, Akkök N, Yalçinkaya F. Primary nephrotic syndrome during childhood in Turkey. Pediatr Int. 2004 Aug. 46(4):436-8.

[17] Black DAK, Rose G, Brewer DB: Controlled trial of prednisone in adult patients with the nephritic syndrome. Br Med J3 : 421-426,1979.

[18] Korbet SM, Schwartz MM, Lewis EJ: Primary focal segmental glomerulosclerosis: Clinical course and response to therapy. Am J Kidney Dis 23:773 -783, 1994.

[19] Maschio G, Alberti D, Janin G, Locatelli F, Mann IF, Motolese M, Ponticelli C, Ritz E, Zucchelli P: Effect of the angiotensin-converting-enzyme inhibitor benazepril on the progression of chronic renal insufficiency. *N Engl J Med* **334**:939 -945, 1996

[20] Plum J, Bünten B, Nemeth R, Grabensee B: Effect of the angiotensin II antagonist valsartan on blood pressure, proteinuria, and renal hemodynamics in patients with chronic renal failure and hypertension. *J Am Soc Nephrol***9** : 2223-2234,1998

[21] Wapstra FH, Navis G, De Jong PE, De Zeeuw D: Chronic angiotensin II infusion but not bradykinin blockade abolishes the antiproteinuric response to angiotensin-converting enzyme inhibition in established Adriamycin nephrosis. *J Am Soc Nephrol* **11**:490 -496, 2000

[22] Samuelsson O, Attman P-O, Knight-Gibson C, Larsson R, Mulec H, Weiss L, Alaupovic P: Complex apolipoprotein B-containing lipoprotein particles are associated with a higher rate of progression of human chronic renal insufficiency. *J Am Soc Nephrol***9** : 1482-1488,1998

[23] Kobashigawa JA, Katznelson S, Laks H, Johnson JA, Yeatman L, Wang XM, Chia D, Terasaki PL, Sabad A, Cogert GA, Trosian K, Hamilton MA, Moriguchi JD, Kawata N, Hage A, Drinkwater DC, Stevenson LW: Effect of pravastatin on outcomes after cardiac transplantation. *N Engl J Med***333** :621-627,1995

[24] Katznelson S, Wilkinson AH, Kobashigawa JA, Wang X-M, Chia D, Ozawa M, Zhong H-P, Hirata M, Cohen AH, Terasaki PI, Danovitch GM: The effect of pravastatin on acute rejection after kidney transplantation: A pilot study. *Transplantation* **61**:1469 -1474, 1996

[25] Thomas ME, Harris KPG, Ramaswamy C, Hattersley JM, Wheeler DC, Zac Varghese JD, Williams JW, Moorhead JF: Simvastatin therapy for hypercholesterinemic patients with nephrotic syndrome or significant proteinuria. *Kidney Int* **44**:1124 -1129, 1993

[26] Donker AJM, Brentjens JRH, van der Hem GK, Arisz L: Treatment of the nephrotic syndrome with indomethacin. *Nephron***22** : 374-381,1978

[27] Blume C, Heise G, Mühlfeld A, Bach D, Schrör K, Gerhardz D, Grabensee B, Heering P: Effect of flosulide, a selective cyclooxygenase 2 inhibitor, on passive Heymann nephritis in the rat. *Kidney Int***56** : 1770-1778,1999