FOCAL SEGMENTAL GLOMERULOSCLEROSIS AS ORIGINAL KIDNEY DISEASE FOR LIVING DONOR KIDNEY TRANSPLANTATION RECIPIENTS.

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Objectives:

- Focal segmental glomerulosclerosis (FSGS), a histologic pattern of glomerular injury, defines a number of clinicopathologic syndromes that may be primary (idiopathic) or secondary [1].
- Early in the disease process, the pattern of glomerulosclerosis is focal, involving a minority of glomeruli, and segmental, involving a portion of the glomerular tuft [1].
- Patients with primary FSGS present with asymptomatic proteinuria or full nephrotic syndrome. Hypertension is found in 30% to 50% of children and adults with FSGS at diagnosis. Microhematuria is found in 25% to 75% of these patients, and a decreased GFR is noted at presentation in 20% to30% [2].
- Kidney transplantation is a treatment, not a cure as it does not necessarily remove the cause of the original kidney disease. Glomerulonephritis (GN) and diabetes are the two leading causes of end-stage renal disease (ESRD) worldwide and both diseases may recur [3].
- Nowadays FSGS is the most common kidney disease known to recur after kidney transplantation. Recurrence rate of FSGS is 30% to 50% in adults. A reliable estimate is approximately 30% to 40% at a first graft, with an exponential increment of risk (up to 80%) at subsequent renal grafts [4].

Methods:

This retrospective single Centre study included 357 kidney transplant recipients who were transplanted at Mansoura urology & nephrology Centre, Egypt between June 1976 and December 2013.Patients divided into three groups according to the original kidney disease (OKD); group I all FSGS patients as OKD (88 patients),this group will be subdivided into 2 groups (non-recurrent FSGS group and recurrent FSGS group post-transplant, group II all glomerular disease other than FSGS (173 patients), group III Non-glomerular disease as OKD (96 patients).
In each visit recipients were subjected to: Thorough clinical examination, Laboratory investigations: Renal profile ;S creatinine., Urine analysis: microscopy and dipstick, CBC , Immunosuppressive drug level (each visit). CsA, Tacrolimus:, Sirolimus assay for whole blood trough level. Liver function test (every 6 ms).Total serum cholesterol (annually).Radiological and Histopathological examination of the graft biopsy in cases of graft dysfunction:

Statistical analysis:

The findings were recorded, tabulated and analyzed using SPSS for windows (SPSS inc. Chicago). T test was used to compare the continuous data between the two groups. Categorical data were compared using chi square test. The graft and patient survival were computed using the Kaplan-Meier technique. P-value < 0.05 was considered statistically significant.

I- Comparison between FSGS and non-glomerular diseases groups

Demographic and immunological data	FSGS (No=88)	Non-glomerular disease (No=96)	P-value
Recipient age(M ± SD) years	26.19 ± 9.5	28.46± 10.93	0.137
Recipient gender			0.802
Male	62(70.5%)	66(68.8%)	
Donor age(M ± SD) years	37.02 ± 11.02	37.66 ± 9.86	0.683
Donor gender			0.969
Male	41 (46.6%)	45(46.9%)	
Immunological workup:			
A) HLA class I matching			0.82
Four mismatch	8(9%)	7(7.3%)	
Three mismatch	8(9%)	8(8.3%)	
Two mismatch	52(59%)	50(52%)	
One mismatch	9(10.2%)	12(12.5%)	
Zero mismatch	4(4.5%)	7(7.3%)	
Inapplicable	7(8.3%)	12(12.6%)	
B) HLA class II (DR) matching			0.507
Zero mismatch	16(18.2%)	14(14.3%)	
One mismatch	72(81.8%)	82(85.4%)	
Prior blood transfusion	38(42.2%)	41(42.7%)	0.578

Induction of immunosuppressive therapy:	FSGS (No=88)	Non-glomerular disease (No=96)	P-value
ATG	10(11.5%)	9(9.5%)	0.260
Basiliximab	28(32%)	46(48.4%)	
NO INDUCTION	50(56.5%)	41(42.1%)	

Immunosuppressive therapy:	FSGS (No=88)	Other glomerular diseases (No=173)	P-value
Steroid-based	83(94.3%)	144(83.2%)	0.012
Tacrolimus-based	19(21.6%)	67(38.7%)	0.005
Cyclosporine-based	53(60.2%)	76(43.9%)	0.013
Mycophenolate mofetil-based	29(33%)	66(38.2%)	0.410
Azathioprine-based	50(56.8%)	86(49.7%)	0.277
Sirolimus-based	5(5.7%)	11(6.4%)	0.829

II- Comparison between FSGS and other glomerular diseases groups

Demographic and immunological data	FSGS (No=88)	Other glomerular diseases (No=173)	P-value
Recipient age(M ± SD) years	26.19 ± 9.5	25.8 ± 9.925	0.761
Recipient gender			0.268
Male	62(70.5%)	110(63.6%)	
Donor age(M ± SD) years	37.02 ± 111.02	36.47 ± 10.022	0.683
Donor gender			0.683
Male	41(46.6%)	77(44.8%)	
Immunological workup:			
A) HLA class I matching			0.483
Four mismatch	4(4.55%)	11(6.36%)	
Three mismatch	9(10.23%)	18(10.4%)	
Two mismatch	51(57.95%)	81(46.82%)	
One mismatch	8(9.09%)	25(14.45%)	
Zero mismatch	8(9.09%)	14(8.1%)	
Inapplicable	8(9.09%)	24(13.87%)	
B) HLA class II (DR) matching			0.396
Zero mismatch	16(18.2%)	24(13.87%)	
One mismatch	72(81.8%)	149(86.13%)	
Prior blood transfusion	38(42.2%)	76(43.9%)	0.229

Induction of immunosuppressive therapy:	FSGS (No=88)	Other glomerular diseases (No=173)	P-value
ATG	10(11.5%)	19(11%)	0.399
Basiliximab	2832%)	78(45.3%)	
NO INDUCTION	50(56.5%)	76(43.7%)	

Immunosuppressive therapy:	FSGS (No=88)	Other glomerular diseases (No=173)	P-value
Steroid-based	83(94.3%)	144(83.2%)	0.012
Tacrolimus-based	19(21.6%)	67(38.7%)	0.005
Cyclosporine-based	53(60.2%)	76(43.9%)	0.013
Mycophenolate mofetil-based	29(33%)	66(38.2%)	0.410
Azathioprine-based	50(56.8%)	86(49.7%)	0.277
Sirolimus-based	5(5.7%)	11(6.4%)	0.829

Comparison between recurrent FSGS and non-recurrent FSGS groups

Demographic and immunological data	Recurrent FSGS (No=35)	Non-recurrent FSGS (No=53)	P-value
Recipient age(M ± SD) years	23.74 ± 8.4	27.8 ± 9.87	0.042
Recipient gender			0.871
Male	25(71.4%)	37(69.8%)	
Donor age(M ± SD) years	34.46 ± 11.18	38.7 ± 10.68	0.076
Donor gender			0.314
Male	14(40%)	27(50.9%)	
Age at diagnosis of FSGS	19.13 ± 10.5	24.028± 10.22	0.03
Immunological workup:			
A) HLA class I matching			0.173
Four mismatch	3(8.6%)	1(2%)	
Three mismatch	5(14.3%)	4(7.8%)	
Two mismatch	19(54.3%)	33(62.7%)	
One mismatch	4(11.4%)	4(7.8%)	
Zero mismatch	4(11.4%)	4(7.8%)	
Inapplicable	0	7(11.9%)	
B) HLA class II (DR) matching			0.417
One mismatch	30(85.7%)	42(78.8%)	
Zero mismatch	5(14.3%)	11(21.2%)	

Pre-transplant medical disorders	Recurrent FSGS (No=35)	Non-recurrent FSGS (No=53)	P-value
Pre-transplant hypertension	20(57.1%)	26(49.1%)	0.457
Pre-transplant diabetes mellitus	3(8.6%)	4(7.6%)	0.882
Pre-transplant HCV infection	1(2.9%)	2(3.8%)	0.804
Mesangial proliferation in native kidney biopsy (36 patients)	13(86%)	12(63%)	0.23
Pre-transplant dialysis	35(100%)	51(96.2%)	0.245
Dialysis duration (months) Median, range	21(1, 48)	12(0, 96)	0.831
Duration between FSGS diagnosis and starting dialysis (months) Median, range	24(2, 168)	18 (2, 120)	0.224

Induction of immunosuppressive therapy:	Recurrent FSGS (No=35)	Non-recurrent FSGS (No=53)	P-value
ATG	3(8.8%)	7(13.8%)	0.106
Basiliximab	12(34.3%)	16(31.4%)	
NO INDUCTION	20(56.9%)	30(54.9%)	
Pre-transplant plasma exchange	8(22.9%)	7(13.2%)	0.239

Immunosuppressive therapy:	Recurrent FSGS (No=35)	Non-recurrent FSGS (No=53)	P-value
Steroid-based	35(100%)	48(90.6%)	0.061
Tacrolimus-based	7(20%)	12(22.6%)	0.768
Cyclosporine-based	26(74.3%)	27(50.9%)	0.029
Mycophenolate mofetil-based	10(28.6%)	19(35.8%)	0.477
Azathioprine-based	19(54.3%)	31(58.5%)	0.697
Sirolimus-based	2(5.7%)	3(5.7%)	0.991

Number and types of rejection episodes:	Recurrent FSGS (No=35)	Non-recurrent FSGS (No=53)	P-value
Number of acute rejection			
No rejection	13(36.4%)	23(43.4%)	0.711
One episode	14(40%)	17(32%)	
Two episodes	6(17.7%)	9(17.1%)	
Three episodes	2(5.9%)	2(3.75%)	
Four episodes	0	2(3.75%)	
Chronic rejection	13(37.1%)	13(25%)	0.155

Response to treatment modalities of FSGS recurrence post-transplant:	No response	Partial remission	Complete remission
ACEI`s & lipid lowering drugs (17 patients)	8	9	0
I.V pulse steroid (3 patients)	0	1	2
I.V Cyclophosphamide (3 patients)	2	0	1
Plasmapharesis (9 patients)*	0	4	5
Anti-CD20 (3 patients)**	0	1	2

*Protocol of 10 sessions every other day then monthly for 6 to 12 months
**375mg/m^2 weekly for 4 weeks

Figure (1): Graft survival among the three groups

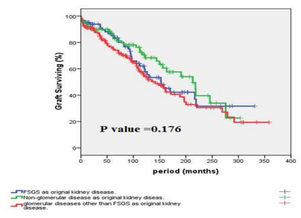
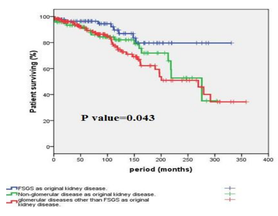


Figure (2): Patient survival among the three groups



Results:

- FSGS group and non-glomerular diseases groups were comparable regarding demographic data, pre-transplant immunological data, pre-transplant medical disorders and frequency of acute rejection episodes. Post-transplant medical complications as hypertension, diabetes mellitus and 5- year graft function and survival were also comparable.
- The use of steroids was significantly more frequent among FSGS group than the non-glomerular group. This could be explained by the more attention and precautions of FSGS recurrence by giving more steroids in such cases.
- Graft survival was comparable between both groups with no clinically and statistically significant difference. At last follow up, 50 out of 88 patients with FSGS were living with functioning graft at while 64 out of 96 patients with non-glomerular diseases were living with functioning graft.
- When the outcome of FSGS group was compared with other glomerular diseases group; demographic data, pre-transplant immunological data, pre-transplant medical disorders and frequency of acute rejection episodes were comparable. Likewise, post-transplant medical complications hypertension, diabetes mellitus, bacterial infection and CMV disease and 5-year graft survival and function were comparable.
- On the other hand, there was a significant difference in the type of calcineurin inhibitors used in both groups. Cyclosporine was more frequently used among FSGS group while tacrolimus was more frequently used among the group of other glomerular diseases.
- The data that was obtained from the last 2 comparison underline the fact that patients affected by FSGS can obtain a good graft survival even in the long term. Even if recurrence occurred, plasmapharesis and anti-CD 20 use improved the outcome.

Conclusions:

- We could conclude from this study that a good graft outcome could be obtained when kidney transplantation to FSGS patients and FSGS patients shouldn`t be excluded from transplantation.
- Younger recipient age and younger onset of FSGS are the only risk factors have been proved in this study.
- Pre-transplant plasmapharesis didn`t statistically affect the graft outcome but clinically, evaluation upon more patients is needed.
- We recommend:
  - Performing pre-transplant plasmapharesis even only for high risk patients.
  - Strict follow up for proteinuria after kidney transplantation. Once recurrence is suspected, we recommend starting plasmapharesis sessions and/or anti-CD 20.
  - Genetic analysis is important and should be done especially for recurrent FSGS patient to determine whether to re-transplant or not on the base that recurrence occurs more frequently in patients with no NPHS2 gene mutation while no recurrence occur in patients with mutations particularly if homozygous.
  - Urinary podocyte specific mRNA P.C.R should be done as screen tests for all FSGS patients after kidney transplantation as early recurrence detector. Plasmapharesis should be started immediately if +ve results were obtained.
  - Protocol for prophylactic post-transplant plamapharesis for high risk patients is controversial.

References:

1-D'Agati VD (2011): "Podocyte injury can be catching". J Am Soc Nephrol. 22: 1181- 1183.
2-Johnson JR., Feehally J and Floege R (2014): "Primary and secondary causes of FSGS". Comprehensive clinical nephrology. 18: 220-222.
3-Cole EH., Johnston O., Rose CL and Gill JS (2008): "Impact of acute rejection and new- onset diabetes on long-term transplant graft and patient survival". Clin J Am Soc Nephrol.3: 814-821.
4-Hickson LJ., Gera M., Amer H., Iqbal CW., Moore TB., Milliner DS., Cosio FG., Larson TS., Stegall MD., Ishitani MB., Gloor JM and Griffin MD (2009): "Kidney transplantation for primary focal segmental glomerulosclerosis: Outcomes and response to therapy for recurrence". Transplantation. 87: 1232-1239.

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