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Histological Pattern of IgA Nephropathy (IgAN) by Oxford Classification by MEST Scoring

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Abstract

IgAN is one of the commonest biopsy proven primary glomerular diseases with diverse histological patterns based on the geographic location. This is a study was done by including all consecutive cases of biopsy proven IgAN(native kidney) performed at EMS Memorial Cooperative Hospital, Perinthalmanna, Kerala, India, from September 2009 to February 2016. We had 62 (Females: 36, Males: 26) cases of biopsy proven IgAN. The mean age of the patients was 37.71 years and male: female ratio was 1.38:1. The IgAN was classified according to the Oxford classification (MEST scoring). Majority of the patients had mesangial hypercellularity (91.94%) and tubular atrophy (69.36%; T1-43.55%, T2-25.81%). Only few patients had endocapillary proliferation (20.97 %), and segmental sclerosis (39.68 %). Glomerular crescents (involving 5-20% of glomeruli) were found in 4.84 % of patients with IgAN. The commonest combinations of MEST scoring were M1, E0, S0, T1 (25.81%), followed by M, E0, S1, T1 (14.52%) and M0, E0, S0, T0, was seen only in 6.45% of cases. This study confirms the aggressive nature of IgAN in Indian subcontinent, unlike western literature.

Keywords: IgAN; Oxford-MEST Classification.

Introduction

Immunoglobulin A nephropathy (IgAN) is one the most common glomerulonephritis worldwide [1-6]. The bulk of the disease burden is borne by Asian countries [2-6]. The Oxford classification (MEST) of IgAN was proposed in 2009; found that mesangialcellularity, endocapillary proliferation, segmental sclerosis and tubular atrophy/interstitial fibrosis, to have independent predictive value on clinical outcome [7] Recent trials from Europe and North America have validated its utility [8-10]. However, its clinicopathologic spectrum in Asian and South American countries is not well documented except for few studies [11-14].

Aims and Objectives

To classify the patients of biopsy proven IgAN based on MEST Oxford- classification.

To analyze the histological combinations of MEST scoring in IgAN.

Meterials and Methods

This is a retrospective study which included all consecutive patients with diagnosis of IgAN on light and immunofluorescence microscopy. The biopsies performed at EMS Memorial Cooperative Hospital and Research Centre, Perinthalmanna, Kerala, from September 2009 to April 2016, under guidance of ultrasound using Bard® Max-Core® disposable core biopsy instrument, CR Bard Inc., USA. All the biopsies were analyzed by light microscopy using hematoxylin and eosin (H&E), periodic acid Schiff (PAS), Jone's silver methaneamine and Gomori's trichrome stains (MT) and immunofluorescence studies were performed using anti-human IgG, IgA, IgM, C3, C1q, kappa and lambda light chains. The IgAN was diagnosed in presence of IgA-dominant mesangial or immune deposits (> 2+ and the absence of C1q deposition) through immune fluorescence (IF) microscopy. The data was analyzed by SPSS 17 for Windows, by SPSS Inc. IL, USA. Two-sided p value of < 0.05 was considered as statistically significant.

The IgAN was classified according to the Oxford-MEST classification [mesangial hypercellularity score (M; M0 < 0.5, M1 >0.5), the presence of endocapillary proliferation (E; E0: absent, E1: present) and segmental glomerulosclerosis/adhesion (S; S0: absent, S1: present), and the severity of tubular atrophy/interstitial fibrosis (T; T0 <25%, T1: 26–50%, T2 >50%) [7].

Results

A total of 271 patients underwent renal biopsy during the study period. The IgAN was diagnosed in 62 out of 271 (22.88%) patients, and was most common biopsy proven renal disease in the study. Among those with IgAN, 36 were males and 26 were females; with M: F ratio of 1.38:1. The age of subjects ranged from 12-75 years (Mean:37.71, SD: 14.21) and majority (62.90%) were of < 40 years of age. Both males and females were of similar age (Table 1); the difference was statistically insignificant (p:0.20).

The indications of renal biopsies in the study were; microhematuria in 3, subnephrotic protienuria in 3, subnephrotic proteinuria with haematuria in 13, nephrotic syndrome in 4 and renal insufficiency (serum creatinine >1.4mg/dl) with proteinuria and haematuria in 39 subjects. Among those with renal insufficiency 28.21 % (11 out of 39) had severe failure (eGFR < 30 ml/min/1.73m2), 69.23 % (27 out of 39) had moderate renal insufficiency (eGFR 30 to 59 ml/

min/1.73m2) and 2.56 % (1 out of 39) had mid renal insufficiency.

The patients were categorised based on indication for renal biopsies and results of MEST scoring are represented in figures 1 to 6. Frequencies of MEST score combinations in the study are listed in Table 2. Overall prevalence of M1, E1, S1, T1 and T2 was noted in 91.94, 20.97, 39.68, 43.55 and 25.81% of renal biopsies respectively. The commonest combinations of MEST scoring were M1, E0, S0, T1 (25.81%), followed by M, E0, S1, T1 (14.52%) and M0, E0, S0, T0, was seen only in 6.45% of cases. 3 out of 62 (4.84 %) patients also had associated extracapillary proliferation in the form of fibrocellular crescents in renal biopsy. There was statistically significant correlation of indication of biopsy with presence of M1 (p:0.008) and TA (tubular atrophy T1 or T2) (p:0.018) on univariate analysis, however, it was insignificant with E1 (p:0.374) or S1 (p:0.295).

Multivariate analysis of indication of biopsy with MEST scoring showed a statistically significant correlation with presence of TA (p:0.003); whereas, it was not significant with M1 (0.689), E1 (0.272) or S1 (0.30). There was no statistically significant effect of gender or age on MEST score on multivariate analysis.

Mesangial Hypercellularity

The majority of the subjects had mesangial hypercellularity (M1) in the study.The majority of patients who underwent renal biopsy for microhematuria (66.67%), subnephrotic protienuria (100%), subnephrotic proteinuria with haematuria (92.31%), nephrotic syndrome (50%) and renal insufficiency with proteinuria and haematuria (97.44 %) had M1.

Endocapillary Proliferation

Only minority of patients had endocapillary proliferation (E1) in the study. The E1 was found in 38.46% of subjects with subnephrotic proteinuria with haematuria, 25% with nephrotic syndrome and 17.95% with renal insufficiency with proteinuria and haematuria. None of the subjects with isolated microhematuria orsubnephrotic protienuria had E1.

Segmental Glomerulosclerosis

The segmental glomerulosclerosis (S1) was found 39.68 % in the study. The S1 was found in 33.33% of subjects with isolated microhematuria, 66.67% with subnephrotic protienuria, 23.07 % with

subnephrotic proteinuria with haematuria, 75% with nephrotic syndrome and 48.72% with renal insufficiency with proteinuria and haematuria.

Tubular Atrophy

Tubular atrophy (TA) of grade either T1 or T2 was found in 69.36% of biopsies. The presence of TA was found in 33.33% of subjects with isolated microhematuria, 33.33% with subnephrotic protienuria, 56.16% with subnephrotic proteinuria with haematuria, 50% with nephrotic syndrome and 84.62% with renal insufficiency with proteinuria and haematuria.

Table 1: The demographic data of subjects with IgAN (age)

Gender	N	Mean	Std, Deviation	Std. Error
Females	26	35.96	13.55	2.66
Males	36	38.97	14.73	2.45
Total	62	37.71	14.21	0.95

Table 2: Frequencies of MEST score combinations

- M1 E0 S0 T1: 25.81 %
- M1 E0 S0 T0: 9.68 %
- M1 E0 S1 T1: 0.1 %
- M1 E0 S0 T2: 0.1 %
- M1 E0 S1 T0: 9.68 %
- M1 E0 S1 T1: 9.68 %
- M1 E0 S1 T2: 14.52 %
- M1 E1 S0 T0: 0.3 %
- M1 E1 S0 T1: 0.1 %
- M1 E1 S0 T2: 6.45 %
- M1 E1 S1 T0: 0.1 %
- M1 E1 S1 T1: 4.76 %
- M1 E1 S1 T2: 0.3 %
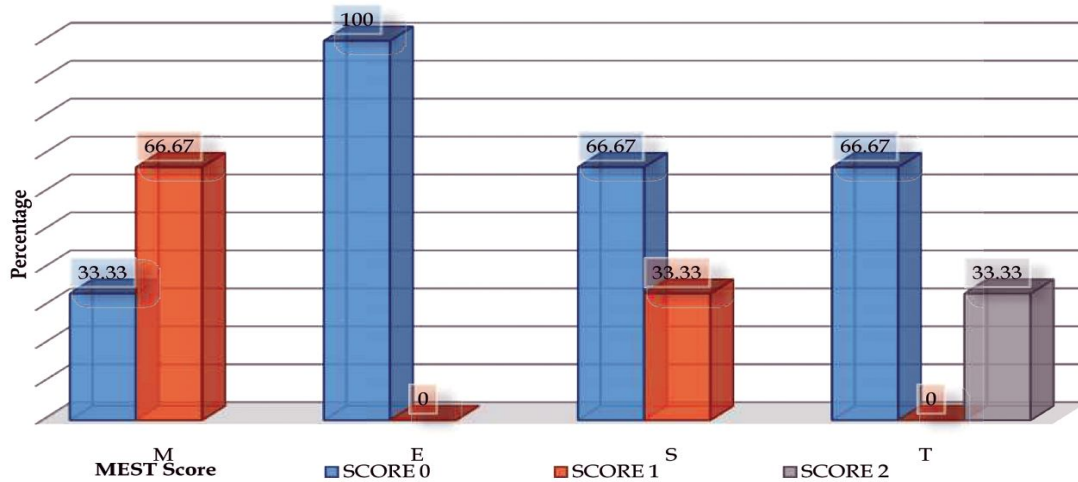- M0 E0 S0 T0: 6.45 %

Fig. 1: Mest score in those microhematuria
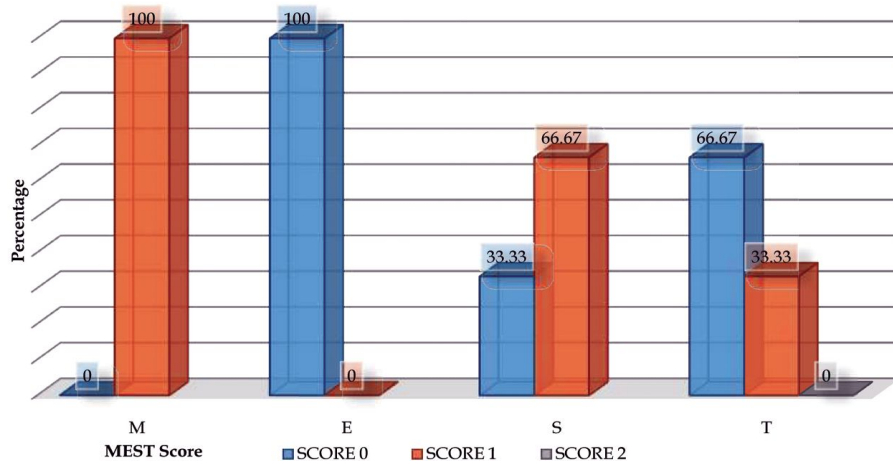

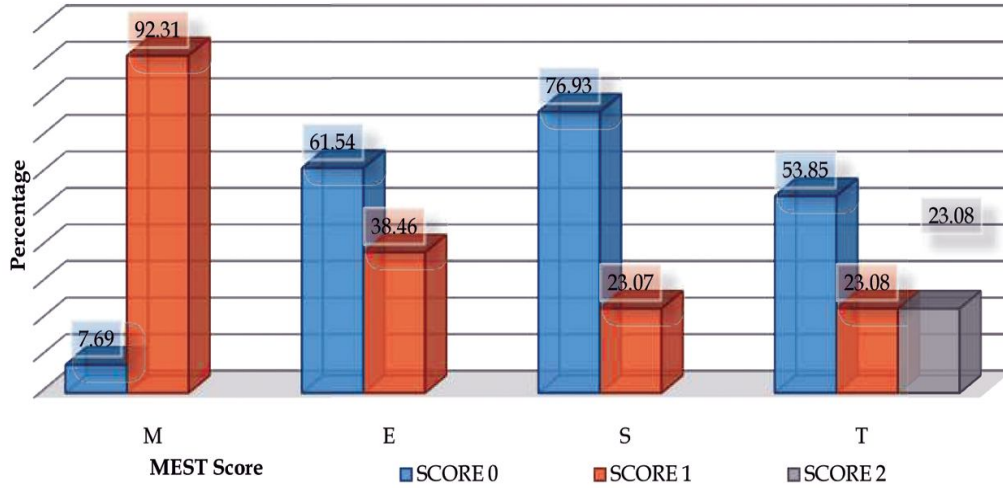**Fig. 2:** MEST in those with proteinuria

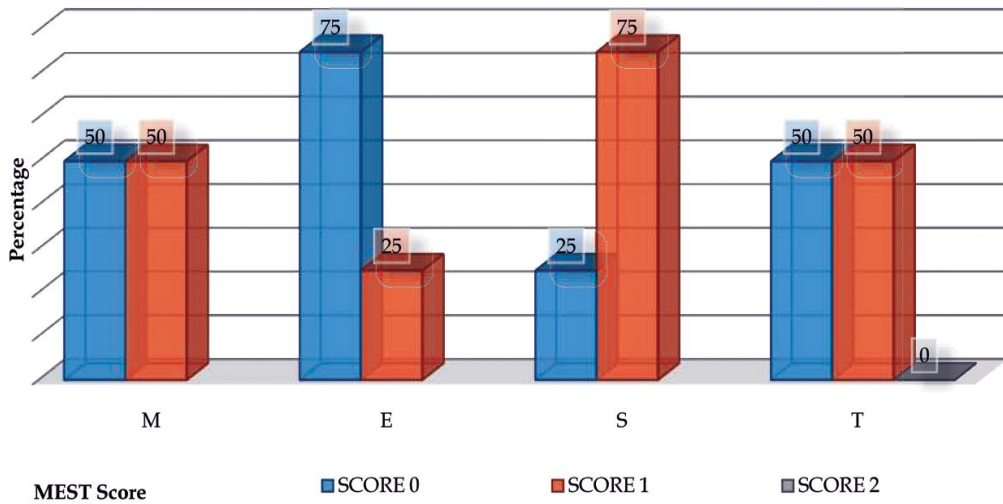**Fig. 3:** MEST score in those with protienuria and microhematuria

Fig. 4: Mest score in those with nephrotic syndrome
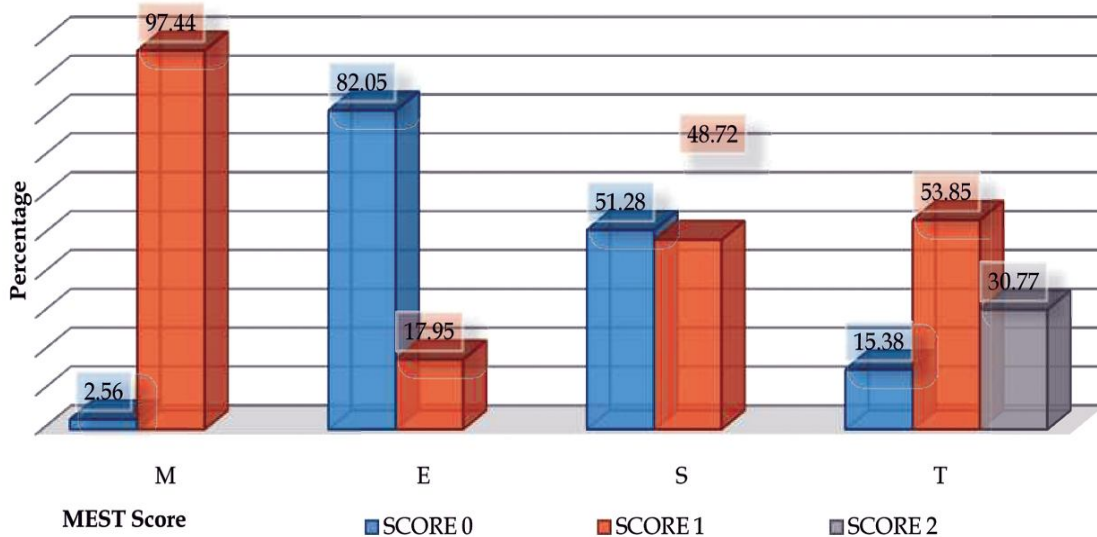

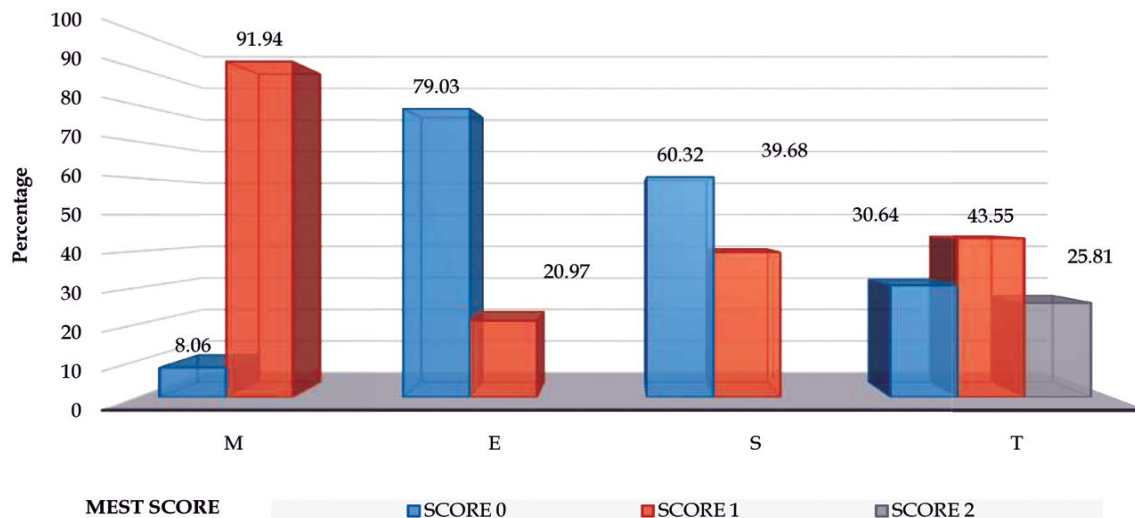**Fig. 5:** Mest score in those with Renal Insufficiency

Fig. 6: Mest score of the all subjects study

Discussion

IgAN is among the most common glomerular diseases worldwide, with varying histological patterns [1-6]. Oxford classification of IgAN by MEST scoring, is an important step for classification as it will serve to achieve for uniformity in classification, initiation, monitoring of treatment [7]. It will also aid easier design of multicentre trials and analysis.

In our study the IgAN was the most common biopsy proven renal disease; more common in males than females and majority of the subjects were of age < 40 years. The presence of renal insufficiency with proteinuria and haematuria was the commonest indication for renal biopsy (62.90%) followed by subnephrotic proteinuria with haematuria (20.97%), nephrotic syndrome (6.45%),microhematuria (4.84%) and subnephrotic protienuria in 4.84 % of subjects. Overall prevalence of M1, E1, S1, T1 and T2 was noted in 91.94, 20.97, 39.68, 43.55 and 25.81% of renal biopsies respectively.

In of the earlier studies from India; involving 66 patients (male: female ratio of 4.4:1; mean age: 29.9 years), the prevalence of MEST scores M1, E1, S1, T1 and T2 were observed in 68.18%, 24.24%, 48.48%, 30.30% and 43.93% in respectively [11].

In a study from Iran (102 patients,72% males, mean age: 37.7 ± 13.6 years) the rates MEST variables were; M1: 90.2 %, E: 32 %, S: 67 %, T in grades 1 and 2 were in 30% and 19% respectively [12].

In a Brazilian study (600 patients; Male to female ratio: 1.24:1; mean age of 32.76 ± 15.12 years); M1 and S1 were the main glomerular findings (47.6 and 46.2 %). T1 or T2 was observed in 32.2% of the cases.

Segmental sclerosis (S1) showed a stronger tendency of association with the presence of tubulointerstitial lesions (T1 and T2) than other glomerular variables.Tubular atrophy and interstitial fibrosis were more strongly associated with higher 24-h proteinuria and serum creatinine levels [13].

The findings of the present study are consistent with first two studies and patients in Brazilian had milder form of disease with mean serum creatinine level of 1.5 mg/dl with lesser of them having mesangial hypercellularity and tubular atrophy [11, 12, 13].

Most patients in the present study presented with renal failure similar to profile of earlier studies [11, 12] and except that a significant percentage (23%) also had nephrotic range proteinuria in one of them [11]. The present study being a hospital based one, might led to the bias in selection for biopsies towards those with renal insufficiency similar to other studies. [11, 12].

The commonest combinations of MEST scoring in the study were M1, E0, S0, T1 (25.81%), followed by M, E0, S1, T1 (14.52%) and M0, E0, S0, T0, was seen only in 6.45% of cases. Whereas; the commonest combination was M0 E0 S0 T0 (22.4%) in Brazilian study, expectedly as patients had milder form of disease [13].

In the present study, of the MEST variables presence of M1, TA (T1 or T2) had a statistically significant correlation with indication for biopsy on univariate analysis, however; only on TA showed a statistically significant correlation on multivariate analysis. There was no statistically significant effect of gender or age on indication for renal biopsy or MEST score on multivariate analysis.

In one of the earlier study; gender had a significant effect (males > females) was on presence of segmental glomerulosclerosis and interstitial fibrosis/tubularatrophy. The possible reason for this difference being a higher serum creatinine and protienuria in males in that study [12].

Conclusions

IgAN is more common in males and affects those of younger age.Majority of patients who underwent biopsy had renal insufficiency; majority of those presenting with renal insufficiency had M1 and T1 or T2. Among the MEST score combinations M1 E0 S0 T1, was the commonestand M0 E0 S0 T0 was one the least common patterns, implying a severe disease at presentation in our population. The presence of M1, TA (T1 or T2) had a statistically significant correlation with indication for biopsy on univariate analysis, however; only on TA showed a statistically significant correlation on multivariate analysis. There was no statistically significant effect of gender or age on MEST score on multivariate analysis.

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