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Control of Diabetes Mellitus

Notification Rate and Counseling

Highlights

Diagnosis and Control

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Discovering Thoughts, Inventing Future

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Correlation Between Glycosylated Haemoglob in and Plasma Glucose Levels for the Diagnosis and Control of Diabetes Mellitus at a Tertiary Care Hospital in Western Rajasthan

By Ankur Kumar, Manju Bohra, Kheemraj, Ankesh Kumar, Chandra Prakash Sharma & Sandeep Kumar Uppadhaya

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Background- Conventional methods are inadequate, unreliable, cumbersome and impractical to monitor continuous 24 hours blood glucose level, to overcome this problem development of new test detecting Glycosylated Haemoglobin (HbA1c), indicates plasma glucose level in last 3 months duration hence it is satisfactory tool for assessment of diabetic control. Therefore the present study is planned to know about the glycaemic control of diabetic patient by HbA1c and to know about the various complications. Objectives: To find correlation of Glycosylated Haemoglobin with fasting and post-prandial plasma glucose levels for the diagnosis and control of Diabetes Mellitus.

Keywords: glycosylated haemoglobin, plasma glucose, correlation.

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Correlation between Glycosylated Haemoglobin and Plasma Glucose Levels for the Diagnosis and Control of Diabetes Mellitus at a Tertiary Care Hospital in Western Rajasthan

Ankur Kumar [α], Manju Bohra [σ], Kheemraj [ρ], Ankesh Kumar [ω], Chandra Prakash Sharma [¥] & Sandeep Kumar Uppadhaya [§]

Background- Conventional methods are inadequate, unreliable, cumbersome and impractical to monitor continuous 24 hours blood glucose level, to overcome this problem development of new test detecting Glycosylated Haemoglobin (HbA1c), indicates plasma glucose level in last 3 months duration hence it is satisfactory tool for assessment of diabetic control. Therefore the present study is planned to know about the glycaemic control of diabetic patient by HbA1c and to know about the various complications. Objectives: To find correlation of Glycosylated Haemoglobin with fasting and post-prandial plasma glucose levels for the diagnosis and control of Diabetes Mellitus. Material and Methods: A hospital based Cross sectional study was conducted at chemical pathology section of Department of Pathology, Mahatma Gandhi and Mathura Das Mathur Hospital, affiliated to Dr. S. N. Medical College, Jodhpur. One hundred diabetic patients attending medical outpatient department of the same institution were included in the study. Results: Total one hundred confirmed diabetic patients with mean age 55.7±12.9 years and sex ratio of 1.85 in favor of males, were included in the study. Among both type of diabetics we found that fasting and post prandial plasma glucose levels had linear relationship with level of glycosylated Haemoglobin and on regression analysis this result was found statistically significant($p<0.001$). Patients with greater duration of illness had greater burden of complications. Conclusion: In most of diabetics there was linear correlation between glycosylated Haemoglobin and fasting plasma glucose as well as post prandial plasma glucose.

Keywords : glycosylated haemoglobin, plasma glucose, correlation.

I. Introduction

Diabetes mellitus (DM) is a clinical syndrome characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiencies in insulin secretion and/or insulin action.[1]

As the incidence and prevalence of diabetes is increasing day by day so the world is facing an escalating epidemic of diabetes. The prevalence of diabetes in adults worldwide, estimated to be 4% in 1995, is supposed to rise to 5.4% by the year 2025, and is higher in developed countries than in developing countries. The major part of this increase will occur in developing countries so by the year 2025, more than 75% of people with diabetes will reside in developing countries like India, China and U.S.[1]

Continuous research work has been done in this area of internal medicine, but lack of infirmity and standardization of screening procedure accounts for difficulty in evaluation of prevalence rates of Diabetes. Diabetes is itself a complex disease, moreover variation in diagnostic techniques used all over world makes this task more difficult, but inspite of that a good deal of progress has been made worldwide. In India specially, Western Rajasthan still lots of worked has to be done. One of the main reason for difficulty in resolving this problem is lack of satisfactory method for quantitative assessment of Diabetes control. This problem is not solved by routinely used methods like random blood sugar estimation and intermittent measurement of daily urinary glucose excretions. These methods are inadequate, unreliable, cumbersome and impractical to monitor continuous 24 hours blood glucose levels specially in out-patient setting. The answer to this problem is development of new test detecting Haemoglobin A_1C, indicates plasma glucose level in last 3 months duration hence it is satisfactory tool for assessment of diabetic control. This method is helpful not only for conducting long term studies on the course and effect relationship between diabetic control and late complications but also for day to day management of diabetic patient.

Haemoglobin A_1C, a fast moving minor Haemoglobin component is present in normal persons, but increases in presence of hyperglycemia. HbA_1 is fractionated into HbA_1a,b,c by ion exchange column chromatography. Most of these are HbA1C and are most susceptible to the effects of fluctuation in glucose levels. That is why it is most suitable as an indicator of blood glucose control.[2,3]

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Synthesis of increased amounts of HbA_1C has been shown to correlate with glucose control in diabetics.[4]

As the number of studies done about screening the glycaemic control and early detection of complications are very less specially in western zone of Rajasthan, therefore the present study is planned to know about the glycaemic control of diabetic patient by HbA1C and to know about the various complications.

II. Materials and Methods

a) Study design

A hospital based Cross sectional study design was adopted for the study.

b) Study Area

Study was conducted at chemical pathology section of Department of Pathology, Mahatma Gandhi and Mathura Das Mathur Hospital, affiliated to Dr. S. N. Medical College, Jodhpur.

c) Sample size

One hundred diabetic patients attending medical outpatient department of Mahatma Gandhi and Mathura Das Mathur Hospital, Jodhpur were included in the study.

d) Tool and Techniques

Patients attending medical outpatient department of Mahatma Gandhi and Mathura Das Mathur Hospital, Jodhpur were scruted for diabetes mellitus.

Prior consent was taken of all patients included in the study. A self preparedsemistructuredProforma was used to obtain complete clinical picture of patients. The Proforma comprised of three parts, part one consisting of epidemiological profile and detailed history regarding diabetes mellitus, part two consisting of complete physical examination and part three consisting of complete investigations regarding diabetes mellitus as well as other body system functions.

The diagnostic criteria were based on WHO study group criteria (i.e. fasting plasma glucose ≥126 mg/dl or 2 hours post glucose level ≥200 mg/dl).[5]

Quantitative estimation of glycosylated Haemoglobin (HbA1) in blood by cation exchange resin chromatography method. From the value of HbA1, HbA1c was calculated using the formula [HbA1c = (HbA1 – 6.14) / 1.23].

e) Exclusion Criteria

1. Patients with recent onset diabetes (<6 months).
2. Patients within 1 month of any coronary vascular event.
3. Patients with recent acute illness (<3 months).
4. Patients of liver disease, gout and hypothyroidism.
5. Alcoholic patients.
6. Patients on lipid lowering agents, niacin, neomycin, estrogen, HRT, corticosteroids and stanozolol.
7. Pregnancy.

f) Data Analysis

Data was entered and analyzed by using Microsoft Exel and SPSS Version 16.0 and appropriate statistical tests were applied to find out statistically significant difference.

III. Results

Total one hundred confirmed diabetic patients were included in the study. Patients belonged to 14 -85 years age group (mean age 55.7±12.9 years). Majority 65(65%) of patients were males and patients between 41-60 years were most commonly (49%) affected. Majority 86(86%) of the patients belong to diabetes mellitus type-2.*(Table 1)*

Table 1: Distribution of type of diabetes according to age group

Age	Type of Diabetes		Total
	Type 1 Diabetes Mellitus	Type 2 Diabetes Mellitus	
0-20	1 (7.14)	0 (0)	1 (1)
21-40	9 (64.28)	2 (2.32)	11 (11)
41-60	3 (21.43)	46 (53.49)	49 (49)
61-80	1 (7.14)	37 (43.02)	38 (39)
>80	0 (0)	1 (1.17)	1 (1)
	14 (100)	86 (100)	100 (100)

Among Both Type-1 DM and Type-2 DM patients most common presenting symptoms was polyuria (92.85% in Type-1 and 95.34% in Type-2) followed by Polyphasia (85.71% in Type-1 and 91.86% in Type-2), Polydypsia (85.71% in Type-1 and 86.04% in Type-2), Weakness (64.28 in Type-1 and 61.62% in Type-2) and Weight loss (57.14% in Type-1 and 61.62% Type-2).

Majority of 8(57.12%) Type-1 diabetics and 43(50%) of Type-2 diabetics were having more than 9% glycosylated Haemoglobin.*(Table 2)*

Table 2: Distribution of levels of glycosylated Haemoglobin according to presence of clinical presentations

Clinical Presentation	Glycosylated Haemoglobin							Total
	≤7.0	7.1-8.0	8.1-9.0	9.1-10.0	10.1-11.0	11.1-12.0	>12.0	
Polyphagia	15 (16.49)	21 (23.08)	7 (7.69)	14 (15.38)	7 (7.69)	7 (7.69)	20 (21.98)	91 (100)
Polydipsia	16 (18.39)	20 (22.99)	5 (5.75)	13 (14.94)	8 (9.19)	7 (8.04)	18 (20.69)	87 (100)
Polyuria	18 (18.95)	23 (24.21)	5 (5.26)	15 (15.79)	8 (8.42)	8 (8.42)	18 (18.95)	95 (100)
Weight Loss	12 (19.67)	10 (16.39)	5 (8.19)	10 (16.39)	5 (8.19)	8 (13.11)	11 (18.03)	61 (100)
Weakness	8 (12.91)	12 (19.35)	4 (6.45)	9 (14.52)	7 (11.29)	6 (9.68)	16 (25.81)	62 (100)

Among both type of diabetes with increasing fasting plasma glucose, level of glycosylated Haemoglobin increases and on regression analysis this result was found statistically significant($p<0.001$). In case of Type-1 diabetes mellitus only 2(14.28%) patients having fasting plasma glucose level below 140 mg/dl and their glycosylated Haemoglobin was less than 7.0%. While only 3(21.42%) patients having fasting plasma glucose level more than 300 mg/dl and their glycosylated Haemoglobin was more than 11.0%. In case of Type-2 diabetes mellitus only 12(13.95%) patients having fasting plasma glucose level below 140 mg/dl and their glycosylated Haemoglobin was less than 7.0%. While only 7(8.14%) patients having fasting plasma glucose level more than 300 mg/dl and their glycosylated Haemoglobin was more than 11.0%. *(Figure 1)*

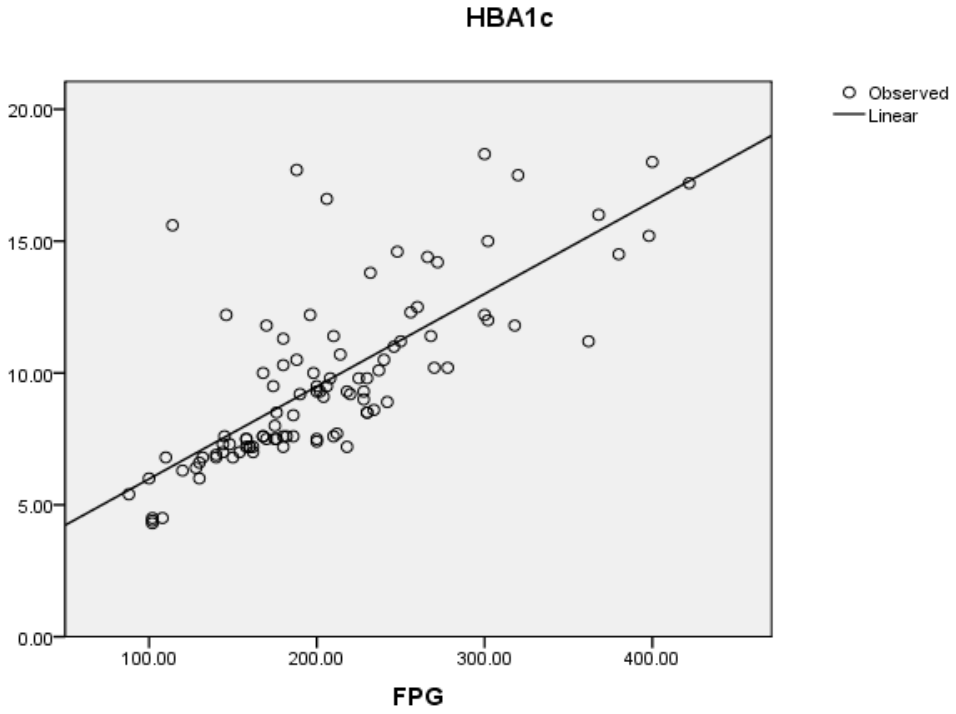

Figure 1 : Showing linear relationship between fasting plasma glucose and glycosylated Haemoglobin level

Among both type of diabetes with increasing post prandial plasma glucose, level of glycosylated Haemoglobin increases and on regression analysis this result was found statistically significant($p<0.001$). In case of Type-1 diabetes mellitus 6(42.95%) patients having post prandial plasma glucose level below 220 mg/dl and their glycosylated Haemoglobin was less than 8.0%. While 4(28.57%) patients having post prandial plasma glucose level more than 300 mg/dl and their glycosylated Haemoglobin was more than 11.0%. In case of Type-2 diabetes mellitus 27(31.4%) patients having post prandial plasma glucose level below 220

mg/dl and their glycosylated Haemoglobin was less than 9.0%. While only 13(15.12%) patients having post prandial plasma glucose level more than 300 mg/dl and their glycosylated Haemoglobin was more than 11.0%. *(Figure 2)*

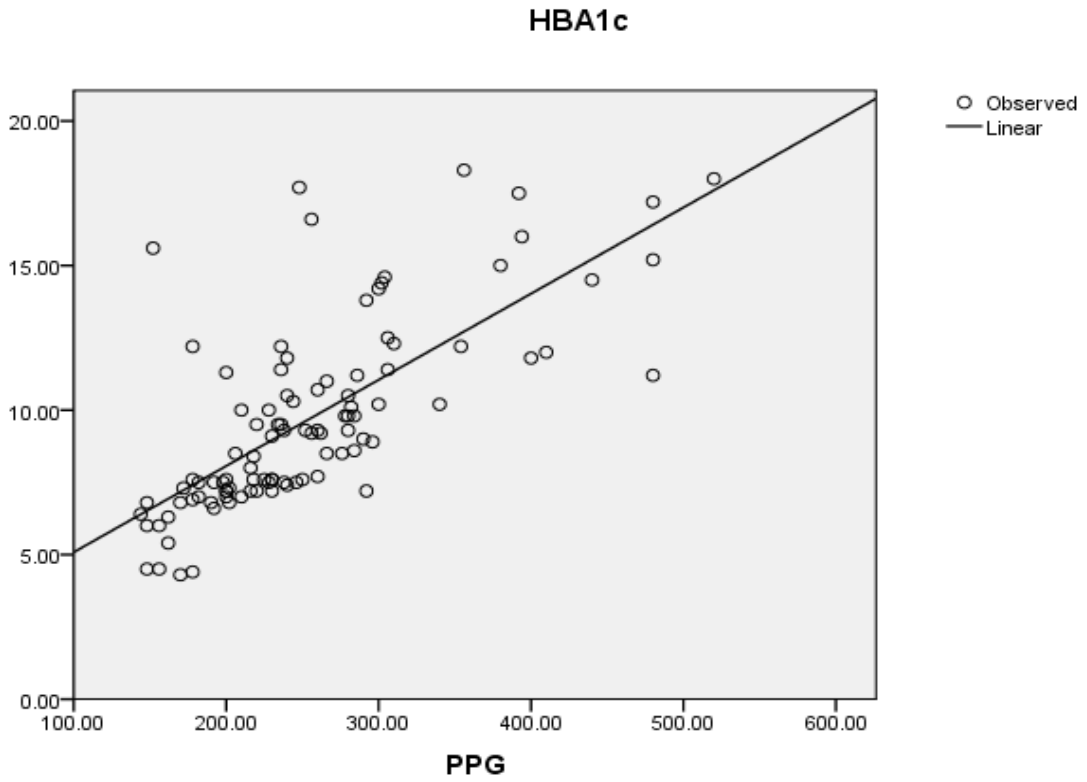

Figure 2: Showing linear relationship between post prandial plasma glucose and glycosylated Haemoglobin level

In case of diabetes mellitus type-1 majority 10(71.42%) of patients had complications. Among these 3(21.42%) patients had Retinopathy followed by Nephropathy, Neuropathy and Cardiovascular diseases in 2(14.28%) patients and Skin related complications in 1(7.14%) patients. Among these patients with complications, majority 6(60%) of patients had duration of illness more than 5 years.

In case of diabetes mellitus type-2 majority 56(65.11%) of patients had complications. Among these 33(38.37%) patients had Nephropathy followed by Cardiovascular diseases in 27(31.4%) patients, Skin related complications in 20(23.56%) patients, Neuropathy in 18(20.93%) patients, Retinopathy in 16(18.6%) patients and cerebrovascular accident in 1(1.16%) patients. Among these patients with complications, majority 40(70.46%) of patients had duration of illness more than 5 years.

Most common complication among diabetes mellitus was nephropathy (38%) and least common complication was cerebrovascular accident (2%). As greater the duration of diabetes, the burden of complications also increases. *(Table 3)*

Table 3: Status of complications in diabetes mellitus patients according to duration

Complications	Duration		
	≤5	>5	Total
Neuropathy	10 (17.85%)	14 (31.81%)	24 (24%)
Nephropathy	18 (32.14%)	20 (45.45%)	38 (38%)
Retinopathy	10 (17.85%)	15 (34.09%)	25 (25%)
CVA	2 (3.57%)	0 (0%)	2 (2%)
CVD	13 (23.21%)	20 (45.45%)	33 (33%)
Skin	13 (23.21%)	13 (29.54%)	26 (26%)

Note: Figures are overlapping.

In case of type-1 diabetes mellitus, all type of complications except CVA were found in patients with Glycosylated Haemoglobin level more than 11.0%.

In case of type-2 diabetes mellitus, majority of the patients having Glycosylated Haemoglobin level more than 9.0% presented with complications.

Among all cases majority 57(57%) patients did not had albuminuria, while 43(43%) patients had albuminuria either microalbuminuria and /ormacroalbuminuria . *(Table4)*

Table 4: Status of albuminuria according to Glycosylated Haemoglobin levels

Albuminuria	Glycosylated Haemoglobin							
	≤7.0	7.1-8.0	8.1-9.0	9.1-10.0	10.1-11.0	11.1-12.0	>12.0	Total
Nonalbuminuric	17	19	4	10	1	2	4	57(57%)
Microalbuminuric	0	5	2	5	7	5	12	36(36%)
Macroalbuminuric	0	1	1	0	0	1	4	7(7%)
Total	17	25	7	15	8	8	20	100(100%)

IV. Discussion

Present study was conducted at chemical pathology section of Department of Pathology, Mahatma Gandhi and Mathura Das Mathur Hospital, affiliated to Dr. S. N. Medical College, Jodhpur and One hundred diabetic patients attending medical outpatient department of Mahatma Gandhi and Mathura Das Mathur Hospital, Jodhpur were included in the study.

In our study majority 67(67%) of patients belong to 45-65 years age group, while only 16(16%) patients were of more than 65 year of age. In congruence to our results study conducted by *King et al*[1] found that majority of the patients belonged to middle age (45-65 years) group in developing countries like india and majority of diabetic patients are in the older age category (≥ 65 years) in developed countries. So in developing countries, these patients will have more years of life to develop chronic complications of diabetes, which undoubtedly will have major implications with respect to health care needs, resource utilization and cost.

Age of 10(71.44%) Type-1 Diabetic patients were below 40 years of age while only 2(2.32%) of Type-2 diabetics were belonging to this group and 84(97.68%) Type-2 diabetics were more than 40 years age group. Similar to our findings, study conducted by *La Porte R.E. et al.*[6]found that majority (85-89%) of the patients belong to Type-2 diabetes mellitus and usually occurs in adults over 35 years of age while Type-1 diabetes accounts for 0.2 to 1.5 percent of patients and especially afflicts children and young adults.

Among both type of diabetes there was strong correlation between levels of glycosylated Haemoglobin and fasting plasma glucose($p<0.001$) and with increasing fasting plasma glucose, level of glycosylated Haemoglobin increases and on regression analysis this result was found statistically significant($p<0.001$). Similar to our results *Tossapornpong et al*[7-10]. Also found significant correlation between glycosylated Haemoglobin level and fasting plasma glucose ($p<0.1$), but in contrast to our result their correlation was poor.

In present study majority (28.57%) of type-1 DM patients had fasting plasma glucose level between 141-180 mg/dl. Similar to our results *Masram S. W. et al*[11] also observed mean fasting plasma glucose level 169.47 mg/dl. In our study majority (28.57%) of type-1 DM patients had HbA1c level more than 12%. In contrast to our result *Masram S. W. et al*[11] observed mean HbA1c level 9.1%.

In present study majority (27.90%) of type-2 DM patients had fasting plasma glucose level between 181-220 mg/dl. Similar to our results *Masram S. W. etal*[11] also observed mean fasting plasma glucose level 223.82 mg/dl. In our study majority (25.58%) of type-2 DM patients had HbA1c level more than 7.1-8.0%. In contrast to our result *Masram S. W. et al*[11] observed mean HbA1c level 11.06%.

There was strong correlation between post prandial plasma glucose and level of glycosylated Haemoglobin ($p<0.001$) in both types of diabetic patients in the present study and similar to our results *Masram S. W. et al*[11] also found strong correlation between post prandial plasma glucose and level of glycosylated Haemoglobin ($p<0.001$).

In present study majority (28.57%) of type-1 DM patients had post meal plasma glucose level between 180-220 mg/dl. Similar to our results *Masram S. W.* et *al*[11] also observed mean fasting plasma glucose level 243.93 mg/dl. In our study majority (28.57%) of type-1 DM patients had HbA1c level more than 12%. In contrast to our result *Masram S. W. et al*[11] observed mean HbA1c level 9.1%.

In present study majority (30.23%) of type-2 DM patients had fasting plasma glucose level between 221-260 mg/dl. Similar to our results *Masram S. W. et al*[10] also observed mean fasting plasma glucose level 269.94 mg/dl. In our study majority (25.58%) of type-2 DM patients had HbA1c level more than 7.1-8.0%. In contrast to our result *Masram S. W. et al*[11]observed mean HbA1c level 11.06%.

Most common complication was nephropathy (38%) followed by cardiovascular disease (33%), skin diseases(26%), retinopathy(25%), neuropathy(24%) and cerebrovascular accident(2%) in present study and similar to our result *Masram S. W. et al*[11] also found CVD in 33% and CVA in only 6.9% diabetics. In contrary to our finding *Masram S. W. et al*[11] found neuropathy in 60% and retinopathy in 15.4% diabetics.

Present study showed 43% of diabetic had albuminuria either microalbuminuria or macroal buminuria. Similar to our result *Deepak Parchwani et al*[12] also found microalbuminuria in 30% of diabetics.

V. Conclusion

In most of diabetics there was linear correlation between glycosylated Haemoglobin and fasting plasma glucose as well as post prandial plasma glucose. With increased duration of illness burden of complications also increases. We concluded that most of diabetic patients having high level of glycosylated Haemoglobin, also had one or more diabetic complications. Glycosylated Haemoglobin did not correlate well with blood glucose level estimated at one point of time. Glycosylated Haemoglobin is a better index for diagnosis and control of diabetes and for early detection of complications.

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Celiac Disease: An Assessment of Subjective Variation and Diagnostic Reproducibility of the Various Classification Systems

By Manas Madan, Sanjay Piplani, Manisha Sharma, Tejinder Singh Bhasin, Mridu Manjari, Harjot Kaur, Jasmeet Kaur & Saumil Garg

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Abstract- *Introduction:* Celiac disease (CD) is a chronic immune mediated disorder occurring in genetically predisposed individuals with intolerance to gluten, particularly its protein gliadin. The histological examination still remains the gold standard for its diagnosis. Marsh-Oberhuber classification is very widely used by pathologists for the diagnosis of CD and is valid under optimal clinical conditions. However, due to the presence of greater diagnostic categories, it lends itself to greater subjective variability and lower interobserver and intraobserver agreement and hence lower reproducibility of the diagnosis. Recently, Corazza and Villanacci introduced a classification that reduces the number of categories and the interobserver variation. This study was undertaken to observe the reproducibility of the Marsh-Oberhuber classification in comparison to the newer Corazza and Villanacci classification and determine the intra and interobserver variation in both the classifications.

Keywords: *celiac disease, gluten, histopathology.*

GJMR-C Classification : *NLMC Code: WD 175*

Celiac Disease: An Assessment of Subjective Variation and Diagnostic Reproducibility of the Various Classification Systems

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Abstract- *Introduction:* Celiac disease (CD) is a chronic immune mediated disorder occurring in genetically predisposed individuals with intolerance to gluten, particularly its protein gliadin. The histological examination still remains the gold standard for its diagnosis. Marsh-Oberhuber classification is very widely used by pathologists for the diagnosis of CD and is valid under optimal clinical conditions. However, due to the presence of greater diagnostic categories, it lends itself to greater subjective variability and lower interobserver and intraobserver agreement and hence lower reproducibility of the diagnosis. Recently, Corazza and Villanacci introduced a classification that reduces the number of categories and the interobserver variation. This study was undertaken to observe the reproducibility of the Marsh-Oberhuber classification in comparison to the newer Corazza and Villanacci classification and determine the intra and interobserver variation in both the classifications.

Materials And Methods: The present study was a retrospective one and comprised of 86 patients who were already diagnosed as CD according to Marsh Oberhuber classification at Sri Guru Ramdass Institute of Medical Sciences and research, Amritsar, Punjab. The slides were retrieved from the archives and reexamined independently by two pathologists and re classified according to Marsh Oberhuber classification without either of them knowing the initial diagnosis. The slides were then shuffled and again classified according to Corazza and Villanacci classification by the same two pathologists. Then the initial diagnosis reported as per the Marsh Oberhuber classification was also noted. The intraobserver and interobserver variation among the two classification systems was then determined.

Conclusion: There is immense histological variation in CD and the spectrum is increasing along with the number of tests involved in its diagnosis. Histopathology is considered as the gold standard in its diagnosis along with the clinical history and serological findings. The classification systems are also ever evolving each with its merits and demerits. The modified Marsh classification system although efficacious and widely used lends itself to a greater subjective variation due to the large number of categories involved. The new classification system proposed by Corazza and Villanacci simplifies the above classification, reduces the number of categories and hence greater diagnostic reproducibility. Our study further corroborates this fact although it is limited by small sample size. More studies should be undertaken with a larger sample size to determine its validity, accuracy and reproducibility.

Keywords: *celiac disease, gluten, histopathology.*

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I. Introduction

The term celiac was first used in the first century AD by the physician Celsius when he used the term Celiac for a diarrhea like disease. The understanding of Celiac disease (CD), also known as gluten induced enteropathy has come a long way since with regards to its etiology, pathogenesis and the various modalities of diagnosis. Now we are clear that this disease is a chronic immune mediated disorder occurring in genetically predisposed individuals with intolerance to gluten, particularly its protein gliadin. This elicits an abnormal immune mediated response characterized by chronic inflammation of small intestinal villi and associated with progressive disappearance of intestinal villi.(1,2)

The histological examination remains the gold standard for its diagnosis. (1,3,4) The diagnosis is based on biopsy showing the presence of characteristic histological changes in duodenum and jejunum that improve after gluten free diet. (2,3)

Histological abnormalities characteristic of CD were described in 1954 by Paulley. Marsh in 1990 classified the various histologic patterns seen in CD which were further modified by Oberhuber in 1999. This classified the histology into 5 categories (Type 0-4).(2,3,4)

Type 0: Preinfiltrative, Normal small intestinal architecture, < 30 Intraepithelial lymphocytes (IEL)/100 enterocytes.

Type I: Infiltrative type, normal villous:crypt ratio >3:1, > 30 IEL enterocytes.

Type II: Infiltrative hyperplastic: Normal villi, Crypt hyperplasia, increased IELs

Type III: Destructive CD further subdivided into 3 sub categories.

- Type IIIa: Mild villous atrophy, villi:crypt ratio <3:1, increased IELs.
- Type IIIb: Marked villous atrophy, villi:crypt ratio <1:1, increased IELs.

- Type IIIc: Total villous atrophy (flat mucosa), increased IELs.

Type IV : Atrophic type (hypoplastic)

The above classification is very widely used by pathologists for the diagnosis of CD and is valid under optimal clinical conditions. However, due to the presence of greater diagnostic categories, it lends itself to greater subjective variability and lower interobserver and intraobserver agreement and hence lower reproducibility of the diagnosis. (1,3,5)

Recently, Corazza and Villanacci modified the above classification. This newer classification reduces the number of categories. Type 1 and 2 have been clubbed into Grade A, 3a and 3b into Grade B1, 3c into grade B2. Type 4 category of Marsh Oberhuber has been deleted. This classification system further simplifies the criteria and reduces the number of categories and hence the interobserver variation. (1,2,3,5)

Table 1

Criteria	Type A (Non Atrophic)	Type B1 (Atrophic)	Type B2 (Atrophic)
Intraepithelial Lymphocytosis	Present	Present	Present
Villi	Normal	Still detectable	Undetectable
Marsh Oberhuber Equivalent	**Type 1 and 2**	**Type 3a and 3b**	**Type 3c**

This study was undertaken to observe the reproducibility of the Marsh-Oberhuber classification in comparison to the newer Corazza and Villanacci classification and determine the intra and interobserver variation in both the classifications.

II. Materials and Methods

The aim of the study was to observe the reproducibility of the classification systems in patients of CD and to assess the interobserver and intraobserver variation among these.

The present study was a retrospective one and comprised of 86 patients who were already diagnosed as CD according to Marsh Oberhuber classification at Sri Guru Ramdass Institute of Medical Sciences and research, Amritsar, Punjab.

The slides were retrieved from the archives and reexamined independently by two pathologists and re classified according to Marsh Oberhuber classification without either of them knowing the initial diagnosis. The slides were then shuffled and again classified according to Corazza and Villanacci classification by the same two pathologists. Then the initial diagnosis reported as per the Marsh Oberhuber classification was also noted.

- The intraobserver variation (among each of the two pathologists) was then noted among the two diagnosis (initial diagnosis and the diagnosis made after reexamination, both according to Marsh Oberhuber classification)
- The interobserver variation was then determined among the two pathologists for the diagnosis made after reexamination according to Marsh Oberhuber classification
- Also, the interobserver variation was determined among the two pathologists for the diagnosis made after reexamination according to Corazza and Villanacci classification.

III. Results

86 patients were included in this study group.

Histological Examination: The histology was classified first according Marsh Oberhuber and then according to Corazza staging.

Results of initially reported diagnosis: The initial diagnoses for the 86 cases according to Marsh Oberhuber classification were as follows:

Table 2

Category	Type I	Type II	Type IIIa	Type IIIb	Type IIIc	Type IV
Total	18	03	13	17	35	00

When reclassified according to the same classification, following were the results of both the pathologists.

Table 3

Pathologist 1:

Category	Type I	Type II	Type IIIa	Type IIIb	Type IIIc	Type IV
Total	17	02	16	14	37	00

Table 4

Pathologist 2:

Category	Type I	Type II	Type IIIa	Type IIIb	Type IIIc	Type IV
Total	18	04	12	18	34	00

Thus, there was a significant intraobserver and interobserver difference in categories type IIIa and IIIb of Marsh-Oberhuber classification whereas the difference was much less in the categories types I and IIIc. No case was diagnosed as CD type IV in all the three instances.

The results of both pathologists when classified according to the Corazza and Villanacci classification were as follows.

Table 5

Pathologist 1:

Category	Type A	Type B1	Type B2
Total	21	30	35

Table 6

Pathologist 2:

Category	Type A	Type B1	Type B2
Total	22	30	34

Thus, much lesser interobserver variation was found when CD was classified according to Corazza and Villanacci classification.

IV. Discussion

This study was undertaken in 86 already diagnosed cases of CD according to Marsh Oberhuber classification which were then reexamined by two pathologists independently and reclassified according to Marsh Oberhuber and Corazza Villanacci classification to assess the intraobserver and interobserver variation among the two classification systems.

CD is a highly variable disease histologically and can exhibit many microscopic patterns. Although histopathology is considered as the gold standard for its diagnosis, the correct diagnosis of CD depends on a combination of clinical features, serology and histopathological features to give a presumptive diagnosis of CD. The final diagnosis rests on the improvement of the symptoms/serological values/biopsy findings after gluten free diet.(2,3,5,6,7)

Due to a variety of histological patterns, many classification systems have been proposed in the past to categorize the various patterns that this disease exhibits. Initially proposed by Marsh and then modified by Oberhuber, the modified Marsh classification system has been widely used for the classification of CD. This system is no doubt efficacious and is valid under optimal clinical conditions.(2,3,4,6,7,8)

However, there are concerns about its validity and efficacy in daily clinical practice and with respect to an individual's clinical presentation. Due to the large number of diagnostic categories, there tends to be lower intraobserver and interobserver agreement therefore leading to a lower reproducibility of the diagnosis.(1,2,3,4,5,6,8,9) The same was found in our study where there was both intraobserver and interobserver variation when CD was classified according to this classification. This variation was negligible in type I (Corazza type A) (Fig 1), and IIIc categories whereas it was much more pronounced in type IIIa and IIIb categories. This could be due to the fact that recognition of lesser degrees of villous abnormalities lends itself to a greater intraobserver and interobserver variability because of subjective differences in the recognition of these changes. The new classification system by Corazza groups these two categories into a single one (Type B1) (Table 2) (FIG 2). Due to the reduction of the categories and hence a consequent reduction in the subjective variation (in seeing whether the villi are mildly atrophic or markedly atrophic but not yet completely flat), there tends to be better agreement among the various pathologists.(1,2,3,4,5,6,8,9) Our study further corroborated this as there was significantly improved intraobserver and interobserver agreement in type B1 category of Corazza when independently examined by two pathologists. (Table 2,3,4,5,6)

Figure 1

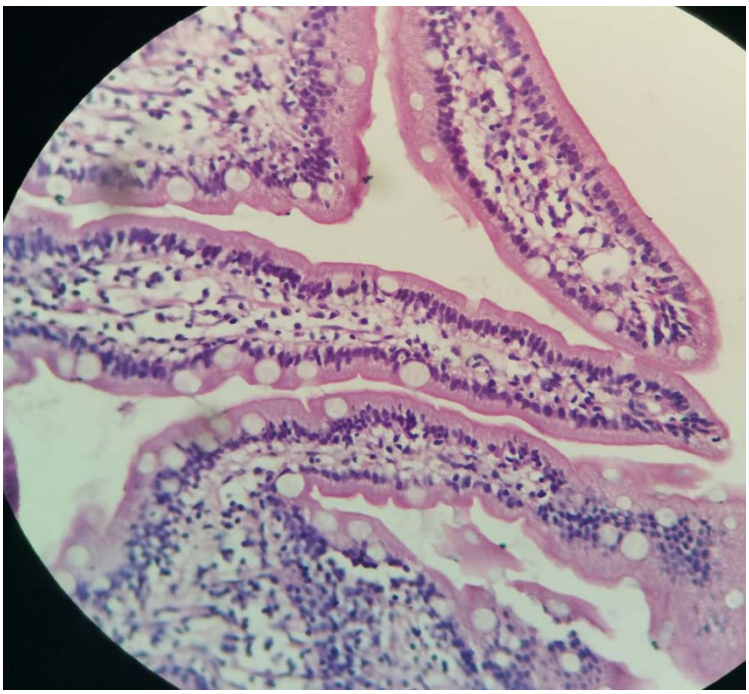

Figure 1: Type A CD: Normal villi with increase in intraepithelial lymphocytes (H&E x 400)

Figure 2

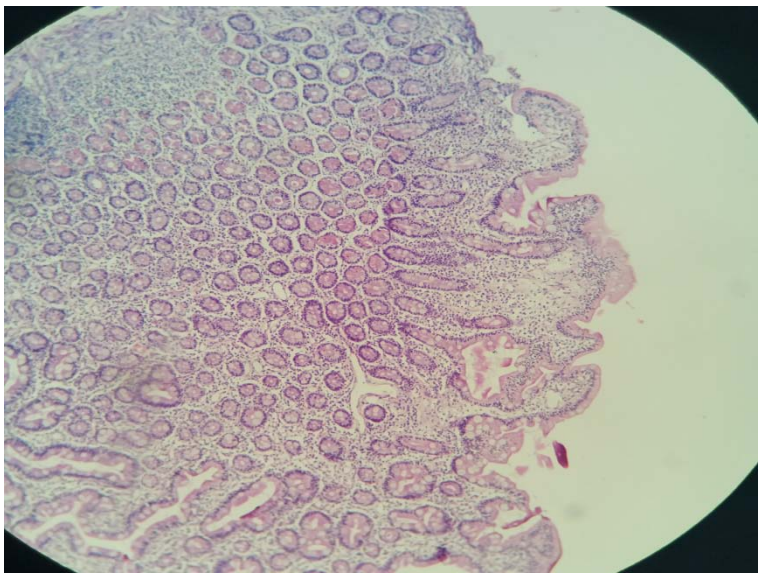

Figure 2 : Type B1 CD: Partial atrophy of villi with increase in intraepithelial lymphocytes (H&E x 100)

The type 2 hyperplastic lesions category according to modified marsh classification has been omitted in the new Corazza classification due to the doubts in its usefulness and efficacy. The new patients would already be diagnosed by increased IELs and hence this category does not impart any useful information about the disease although it definitely represents a spectrum of the histological stage.(2,3,5) In our study, a very minor number of cases were classified into this category. (Table 2)

Type 3c category of Marsh classification has been re designated as B2 and these are the very commonly encountered lesions in CD. This category lends itself to very less subjective variation as the histological changes are very marked and striking leading to a greater diagnostic reproducibility.(2,3,4,5,7,8,9,10) In our study too, very good intraobserver and interobserver agreement as found in this category. (Table 2,3,4,5,6) (FIG 3)

Figure 3

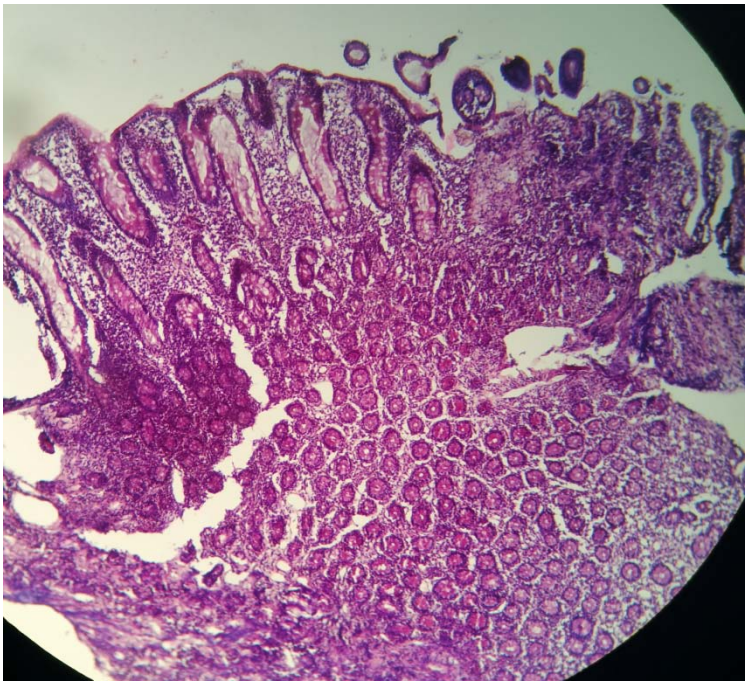

Figure 3 : Type B2 CD: Complete atrophy of villi (H&E x 100)

The last category of Marsh classification (type IV) has been omitted as it is virtually never seen in practice and has aloes been made obsolete by a recent finding of an aberrant IEL clone characteristically seen in refractory sprue, ulcerative jejunoileitis and enteropathy type intestinal T cell lymphoma.(2,3,6) No case was reported as type IV in our study too. (Table 2)

V. Conclusion

There is immense histological variation in CD and the spectrum is increasing along with the number of tests involved in its diagnosis. Histopathology is considered as the gold standard in its diagnosis along with the clinical history and serological findings. The classification systems are also ever evolving each with its merits and demerits. The modified Marsh classification system although efficacious and widely used lends itself to a greater subjective variation due to the large number of categories involved. The new classification system proposed by Corazza and Villanacci simplifies the above classification, reduces the number of categories leading to more intraobserver and interobserver agreement and hence greater diagnostic reproducibility. Our study further corroborates this fact although it is limited by small sample size. More studies should be undertaken with a larger sample size to determine its validity, accuracy and reproducibility.

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"Notification Rate and Counseling for Seropositive Donors in a Tertiary Care Teaching Hospital at Amritsar (Punjab), India"

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Abstract- *Introduction:* Screening for Transfusion transmitted infections (TTI's) is done to provide safe blood. Very often donors are found to be seropositive for one or more of the TTI's. The present study was undertaken in a blood bank of a tertiary care hospital to determine the response rate of the blood donors after they were notified about their reactive status.

Materials and Methods: The one year observational study was done in a prospective manner from January 2013 – December 2013 taking in account of all the registered donors coming to the blood bank after notification.

Keywords: *donor, notification rate, seropositivity, screening , transfusion transmitted infection.*

GJMR-C Classification : *NLMC Code: QZ 4*

Strictly as per the compliance and regulations of:

"Notification Rate and Counseling for Seropositive Donors in a Tertiary Care Teaching Hospital at Amritsar (Punjab), India"

Harjot Kaur [α], Rahul Mannan [σ], Mridu Manjari [ρ], Sanjay Piplani [ω] & Swati Arora[¥]

Abstract- *Introduction:* Screening for Transfusion transmitted infections (TTI's) is done to provide safe blood. Very often donors are found to be seropositive for one or more of the TTI's. The present study was undertaken in a blood bank of a tertiary care hospital to determine the response rate of the blood donors after they were notified about their reactive status.

Materials and Methods: The one year observational study was done in a prospective manner from January 2013 – December 2013 taking in account of all the registered donors coming to the blood bank after notification.

Results : Seropositivity in the present study was 3.36% with HCV being the most common TTI recorded followed by HBV, syphilis HIV respectively. No case of Malaria was recorded.

Of the 204 seropositive cases only 181 (88.73%) could be contacted. Of these 56(27.45 %) were responders with rest being non responders..

Discussion: Seroprevalence rate in the present study was comparable to the study done previously in the same city and elsewhere in India.

The notification rate in the present study was towards the lower side (27.45 %) in comparison to various India and international studies. The notification rate was maximum in donors positive for HBV followed by HCV. The response rate amongst donors positive for HIV were low in contrast to the studies done elsewhere.

Keywords : donor, notification rate, seropositivity, screening , transfusion transmitted infection.

I. Introduction

Blood donation is life saving if the blood is safe for recipient. HIV I and HIV II , Hepatitis B(HBV) , Hepatitis C (HCV), syphilis and malaria are the five major Transfusion transmitted infections (TTI's) for which screening is done.[1]

In present scenario it is realized that to prevent TTI's, the role of blood donor education along with notification and counseling of donors about their seroreactivity is of major importance for blood safety. As per objective 4.16 of the Indian action plan for blood safety, the blood donors are counseled about TTIs prior to donation and are offered the option of knowing (notify) their sero -reactive status provided they give their consent.[2] The concept of notification and counseling is important in today's setting because as there is development of more sensitive methods to detect TTI's; the prevalence of false-positive cases has increased manifold .This in turn leads to unnecessary anxiety in donors who are notified about their reactive results.

Despite the benefits of the concept of notification, it has been noted that most donors who are notified of their results either do not respond at all or do not follow up their first visit to the blood centre. Some donors with deferrable risk behaviors continue to donate blood (at other blood donation centers) despite being notified about the infectious disease test results on their blood samples. This study was undertaken in a blood bank of a teaching hospital in north India to determine the response of voluntary blood donors after they were notified of their reactive status by telephone calls or letters and to analyze the reasons regarding the non compliance of defaulters.

II. Materials and Methods

The one year study was conducted in a prospective observational way from January 2013 – December 2013 in a blood bank of a teaching hospital catering to a rural and urban population in and around Amritsar (Punjab), India. All the blood donors (voluntary and replacement) were registered to fill up the donor screening cum registration card formulated as per the guidelines.[3] All the donors were taken up for pre donation counseling and screened for TTI's. In all the cases a written consent was taken, procedure explained and also told about the sequence of events in case an abnormal /reactive test is obtained in blood bank TTI lab. They were reassured about the maintenance of confidentiality at each step and even encouraged to themselves enquire about their screening tests results.

After the donation, if a donor was identified reactive for a screening test, the donor registration record was retrieved and a telephone call was made and letter was posted by the counselor to the donor to revisit the blood bank. If the intended donor did not respond , a second call after 10 days was repeated with a positive encouragement offered to them to visit the

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blood bank assuring them the confidentiality. Finally if the donor did not respond even on 2nd call after another 10 days then he/she was considered non responder.

The reactive donors immunoreactive for HIV who returned back to blood bank were again tested and in event of a repeat reactive result were counseled for the health status and high risk behavior of patient. They were then referred to an integrated counseling and testing center (ICTC) where the testing and counseling was done according to the ICTC guidelines.

On the other hand the donor who were reactive to VDRL were referred to sexually transmitted diseases (STD) clinics for proper counseling and management of the same.

The donor who were reactive to HBsAg and HCV were counseled about the etiology and referred to the gastroenterology unit of medicine department for confirmation of the viral status by polymerase chain reaction (PCR).Subsequently, these patients also underwent viral load assays. The results of TTI prevalence and response rate amongst the reactive donors were recorded and tabulated for simple statistical analysis.

III. Results

Out of 6065 donors , who came to the blood bank during the one year period of the study . 204 donors were found to be seropositive for either one or more than one TTI's. In the present study HCV(79; 38.72%) was the commonest TTI recorded followed by HBV (58; 28.43%). No case of malarial parasite was recorded in the present study (Table -1).

Table 1 : Comparison studies of Reactive Donors

TTI's	Number of Reactive donors			
	Present study	Aggarwal [4]	Roshan et al[5]	Patel et al [1]
HIV	11(5.39%)	17(4.08%)	87(14.8%)	15(15.09%)
HBsAg	58(28.43%)	225(54.08%)	209(35.5%)	176(45.01%)
HCV	79(38.72%)	76(18.26%)	208(35.5%)	28(7.16%)
Syphilis	56(27.45%)	98(23.55%)	85(14.4%)	128(32.74%)
Malaria	00	00	00	00
Total	204(100%)	416(100%)	589(100%)	391(100%)

Of the 204 seroreactive only 181 (88.75%) could be contacted over phone or by means of letter from the office of blood bank through blood bank counselor. Amongst these; while 56 (27.45%) donors returned back to blood bank for post donation counseling (hence categorized as responders), 125 (61.27%) of the same donors did not turn up despite giving 2 more reminder calls (hence categorized as non responders).The commonest reason for not coming back to blood bank was expressed unwillingness and personal reasons. Later on of these 56 seropositive patients who responded to blood bank were retested. The most common response rate was noted in reactive HBV donors followed by HCV reactive donors.(Table-2)

Table 2 : Responders among TTI's Reactive Donors

TTI	No of Responders		
	Present study	Roshan et al[5]	Patel et al[1]
HIV	18.18%	54%	52.54%
HBsAg	32.75%	58.9%	19%
HCV	25.31%	70.7%	20%
VDRL	26.7%	32.9%	15%
Malaria	00	00	00
Average	27.45%	63.5%	60.36%

IV. Discussion

The notification of blood donors represents a setting in which asymptomatic individuals are informed of abnormal test results .Despite pre donation counseling by counselor, screening and examination by blood bank staff; 204 donors (3.36 %)out of all donations were found positive for one of the TTI's. This rate is comparable to the studies done previously from the same city [6] and elsewhere in India. [7,8] A 3.36 % seropositive rate may be attributed to the socio economic and socio cultural background of donors especially the prevalence of intravenous drug abuse amongst the young Punjabi population. [6]

Of all the TTI's hepatitis group (Hepatitis B & Hepatitis C) form the most common infectious agent against which seropositivity rate was 3.36%. This is in concordance with other major studies done in different regions of India (Table-1). However the prevalence of Hepatitis C if taken separately, it was more than Hepatitis B in difference to other studies conducted in India where reverse is true. [1,4,5]

In the present study, only 56 donors out of 204 reactive donors (27.45%) responded and were counseled during the study period and 125/204 (72.54%) donors did not turn up at blood bank despite initial willingness of them to report for counseling. Low response rate in the present study was attributed to poor health care knowledge and poor understanding of screening results of the population under study. While low response rates (21% -67%)have also been reported outside India by Moyer et al[9], Sanchez et al[10] and Kleinman et al [11], but most western studies show a higher response rate. [12] On comparing the result of the study conducted with the response rate response rate in other Indian studies by Patel et al [1], Aggarwal [4] and Battacharaya et al [5] (60.36%, 68.4 % and 34 %) the response rate were found to be on a lower side.

The principle of repeated notification is also necessary as many researchers such as Kleinman et al [11], have reported that upto 10% of donors either did not open or read the letter or did not understand the content and even refused to receive the primary contact letter. Advent of telecommunication has led to negation of all the above stated facts provided that the correct phone number are provided by the donors on their donor registration form which is often not the case as many phone numbers provided are either factitious or found not in existence when tried.

A study by Sharma et al [13] found an unusual behavioral pattern of many donors (who did not know about the window period) indulging in high risk behavior and continued to donate blood as they knew that the donated blood would be tested for the infectious agents anyway and would be discarded if found sero positive. .

Another study by Roshan et al [5] also suggest that test seekers who use blood donation as the testing also contribute to such a pool of donors .

Disease wise categorization showed that the response rate amongst donors positive for HIV I & II was the lowest 18.81% (2/11) which points towards social taboo, self denial and possibility of being a social outcast which is associated with AIDS as a possible explanation. This is in contrast with studies done elsewhere where the rate of response is a little higher on notification. [1,5]

In the present study response rate in Hepatitis B were slightly more than Hepatitis C although Hepatitis C per se was a more prevalent TTI than Hepatitis B. Comparison with other studies have been done in (Table-2) with a glaring finding of a very low average response rate of 27.45% in contrast to other studies.

Notification of the abnormal results is important as although the demand for blood & blood components is showing an exponential growth pattern in today' s hi tech medical world but the availability of safe blood as a basic therapeutic tool for patients remain a distant dream especially in developing and recourse challenged countries of the third world. Many ultra sensitive tests (such as universal NAT screening) are not economical feasible in such countries.

Donors who come for counseling are benefitted in various ways over those who do not turn up after notification. During counseling donors are encouraged to ask questions about their status and their myths and anxieties are taken care of. The responsibilities of these donors towards society and their partners and the various treatment options available for the disease in question are also discussed in detail. In comparison, donors who do not seek counseling continue to be a threat to the public , their families and blood transfusion services.

A higher response rate is beneficial as a lower response rate has a definite impact on transmission and prevalence of infection in the community.

Research suggests that the it should be mandatory for all blood banks to follow up greater risk to community reactive donors as these "asymptomatic donors'' pose greater risk to community at large. Also it has been suggested that the process of notification , disclosure of results should be standardized with mandatory submission of identity proof with some unique identification number at the time of donation as this can help to search the non responder afterwards.
The reactive respondent donor should be referred with a referral slip mentioning the TTI test result as well as detailed address of the concerned physician to get better response out of notification.

Sustained efforts of a trained counselor as well as close communication with treating physician/ dermatologist in for all reactive cases along with better community health education programs can bring a lot of change in donor notification which is great social concern of today time.

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Clinical Characteristics and Histopathological Findings in Renal Parenchymal Disease Patients: our Single Centre Experience from Northern Plains of India

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Abstract- *Introduction:* For renal diseases, renal biopsy is considered gold standard to reach a diagnosis. The present study was undertaken to understand and analyze clinical symptoms, lab findings and final histological diagnosis for clinico-pathological correlation.

Material and Methods: The present prospective study comprised of 127 patients who underwent per-cutaneous renal biopsies over a period of three years. Before undertaking renal biopsies the clinical findings along with biochemical and urinary investigations were done.

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GJMR-C Classification : *NLMC Code: QZ 4*

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Clinical Characteristics and Histopathological Findings in Renal Parenchymal Disease Patients:our Single Centre Experience from Northern Plains of India

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Material and Methods: The present prospective study comprised of 127 patients who underwent per-cutaneous renal biopsies over a period of three years. Before undertaking renal biopsies the clinical findings along with biochemical and urinary investigations were done.

Specimens were subjected to light microscopic studies (with Hematoxylin and Eosin, periodic Schiff, Massons Trichrome and periodic methenamine silver). Autoimmune panel was employed in 79 cases. All the findings were noted and tabulated.

Results: Most of the patients who underwent renal biopsy were of nephrotic range proteinuria (40.15%). End stage renal disease (ESRD) was the most common glomerulopathy. Lupus nephritis was the most common secondary glomerulopathy recorded. 12.5 % cases were also sero-positive for anti-neutrophilic cytoplasmic antibody (ANCA). Of the clinical symptoms oliguria/anuria with anasarca were the commonest recorded followed by fever, loss of appetite and malaise

Conclusion: The present study which was truly a clinico-pathological study not only adds on to the available Indian literature about spectrum of glomerulopathies in a region of poor human developmental indices but also stresses on the very innocuous sounding symptoms of urinary disturbance and anasarca presenting with fever and weight loss as important pointers towards renal diseases. The finding of ESRD as the most common glomerulopahy in the region under investigation should prompt both the practising physicians and the pathologist in this region to be ever vigilant against a possibility of glomerulopathy in patients attending outpatients so that early action can be initiated to preserve kidney function.

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I. Introduction

Kidney diseases manifest in many ways. A patient may be asymptomatic or may be suffering with a life threatening emergency. Apart from the clinical history, ancillary investigations, including urine examination and radiological investigations; renal biopsy is considered gold standard in reaching a diagnosis in many conditions especially in cases of acute renal failure (ARF). Renal biopsy is also the most definitive method of differentiating acute from chronic kidney disease and various renal/tubule-interstitial disorders. The underlying cause of most glomerular diseases remains an enigma. Infectious agents, autoimmunity, drugs, inherited disorders and environmental agents have been implicated as the cause of certain glomerular diseases.[1]

The present study was undertaken over a period of three years in a single tertiary care center in the northern part of India so as to take a glimpse of the pattern of disease in an area which is highly resource challenged. A comparison was also drawn with areas in and around Indian subcontinent. A major part of the present study was to understand and analyze clinical symptoms and findings with laboratory investigations and final histopathological diagnosis (clinico-pathological correlation). The biopsies were also tabulated according to auto-immune serological panel as well.

II. Materials and Methods

The present prospective study comprised of 127 patients who underwent percutaneous renal biopsies over a period of three years (2005- 2007) pertaining to renal parenchymal disease. The study was

done in conjunction with department of pathology and nephrology MLN medical college with SRN hospital, Allahabad, Uttar Pradesh (India). Most of the patients included in the biopsy were of adult age group with very few pediatric samples. The study was conducted after obtaining approval from the ethical committee of the institute. In all the cases informed consent was obtained.

Four per-cutaneous core (specimen) biopsies were retrieved after ultra-sonographic localization of the kidneys in each individual case. The patients complain and complications post procedures were noted.

Specimens were subjected to light microscopic studies (with Hematoxylin and Eosin, periodic Schiff, Massons Trichrome and periodic methenamine silver). Due to economic constraints immunofluoresence studies were done wherever possible. Biopsy samples were considered satisfactory for diagnosis if they contained five or more glomeruli. Biopsies were categorized as inadequate for diagnosis if glomeruli were less than 5. A total of 3 pathologists reviewed and reported the histopathological slides over this period to limit the interpersonal bias. The final diagnoses were then tabulated to ascertain the spectrum of glomerular diseases.

The indications for performing the biopsies were nephrotic syndrome, nephritic syndrome, acute and chronic renal failure of known/unknown etiology, persistent or recurrent asymptomatic hematuria or proteinuria. The biopsies were tabulated according to age, sex, clinical complaints and findings and lab investigation findings (notably urine examination and biochemical examination). The final histopathological diagnoses were then extrapolated on the clinical presentation and laboratory findings for clinico-pathological deductions.

Autoimmune panel was employed in 79 cases which included- complement levels (C3/C4), anti nuclear antibody (ANA), double stranded DNA (dsDNA), peri-nuclear anti neutrophilic cytoplasmic antibody (P-ANCA), cytoplasmic anti neutrophilic cytoplasmic antibody (C-ANCA), anti glomerular basement memberane (Anti-GBM) and cryoglobulins detection.

III. Results

a) *Glomeruolopathy Spectrum*

A total of 127 renal biopsies were performed at our centre during the study of which 7 were considered inadequate. There were 86 (67.71%) males and 41 (32.28%) females with male to female ratio being 2:1. The male predominance was virtually present in every lesion except for those seen in lupus nephritis, renal cortical necrosis and in a single recorded case of focal global glomerulosclerosis. The average age of the patients who underwent the procedure was 34 years. (Table-1)

Table 1 : Subdivision Of Various Renal Lesions According To The Frequency, Age And Sex Distribution

SN	GLOMERULONEPHRITIS (GLN.)	TOTAL	% OF ALL LESIONS	% OF GLN.	MALE	FEMALE	NO.OF GLO/ BIOPSY	AVG. AGE
1	End Stage Renal Disease (ESRD)	21	13.04	16.53	15	06	12.81	37.91
2	Membranous	16	09.93	12.59	12	04	08.50	34.75
3	Mesangial Proliferative	11	06.83	08.66	07	04	12.08	31.77
4	Diffuse Proliferative	10	06.21	07.87	08	02	13.22	36.66
5	Focal Segmental/ Proliferative	10	06.21	07.87	07	03	15.40	49.33
6	Membrano Proliferative (MPGN)	08	04.96	06.29	04	04	13.87	27.64
7	Systemic Lupus Erythematosus (SLE)	08	04.96	06.29	01	07	14.42	33.56
8	Diabetic Nephropathy	07	04.34	05.51	04	03	16.57	48.20
9	Focal Segmental Glomerulosclerosis (FSGS)	07	04.34	05.51	06	01	09.57	17.57
10	Inadequate	07	04.34	05.51	06	01	00.00	34.66
11	Crescentic	05	03.10	03.93	05	00	05.80	27.00
12	Minimal Change Disease	05	03.10	03.93	03	02	08.40	14.40
13	Amyloid Nephropathy	04	02.48	03.14	04	00	18.75	33.75
14	Normal	03	01.86	02.36	03	00	03.66	37.00
15	Renal Cortical Necrosis	02	01.24	01.57	00	02	11.50	37.00
16	Benign Nephrosclerosis	01	00.62	00.78	01	00	10.00	60.00
17	Focal Necrotizing	01	00.62	00.78	01	00	04.00	60.00
18	Focal Global Glomerulosclerosis	01	00.62	00.78	00	01	40.00	07.00
	TOTAL	127	78.39		87	40	12.14	34.90

The overall complication rate in this study was 2.0%. Local pain at the biopsy site was noted in 1.5% with gross/ microscopic hematuria was noted in 0.5% patients.

Most of the cases who underwent biopsy were of nephrotic range proteinuria (51 patients; 40.15 %) followed by nephritic syndrome (30 patients; 23.62 %) and sub-nephrotic range proteinuria (21 patients; 16.53%). A few cases also underwent renal biopsy having presenting complains of renal failure of uncertain etiology (15 patients; 11.81%) and asymptomatic hematuria (10 patients; 7.87%). (Table-2)

Table 2 : Indication for per-cutaneous renal biopsies

SN	Indication	Total	Incidence
1	Nephrotic Syndrome	51	40.15%
2	Nephritic Syndrome	30	23.62%
3	Sub-Nephrotic Proteinuria	21	16.53%
4	Renal Failure of uncertain etiology	15	11.81%
4	Asymptomatic hematuria	10	07.87%

Of all the glomerulopathies, primary glomerulonephropathy was observed in 108 patients (85.0%) with end stage renal disease (ESRD) was the commonest recorded lesion followed by membranous glomerulonephritis (MGN) and Mesangioproliferative (MeGN) glomerulonephritis (MPGN) respectively. (Table-1)

Secondary glomerulopathy was found in 19 cases (15.0%); most common pathology was lupus nephritis (4.96%) followed by diabetic nephropathy (4.34%) and amyloid nephropathy (2.48%).

Serological studies concluded that 15 cases (12.5 %) were serologically P-ANCA, C-ANCA or both positive and were categorized as ANCA positive biopsies. P-ANCA positivity accounted for the maximum number of ANCA cases (80.00%) whereas C-ANCA positivity was seen in 13.33% of all ANCA cases. Rest of the cases (20.00%) on serology were showed positivity for both C-ANCA and P-ANCA.

Of all the serologically ANCA positive cases; the maximum number of cases were of end stage renal disease (ESRD) (26.66 %). Focal and segmental mesangial proliferative and crescentic glomerulonephritis without fibrinoid necrosis were the next most common category (20.00 %) followed by necrotizing crescentic glomerulonephritis (13.33 %). Necrotizing glomerulonephritis, focal proliferative and membranous with foci of fibrinoid necrosis were the least commonly seen (6.66 %).(Table-3)

Table 3 : Histopathological diagnosis rendered in various ANCA positive cases

SN	AGE	SEX	P-ANCA	C-ANCA	HISTOLOGICAL DIAGNOSIS
1	19	M	+	_	Crescentic Necrotizing Glomerulonephritis
2	25	M	+	_	Crescentic Glomerulonephritis
3	22	F	+	_	End Stage Renal Disease (ESRD)
4	35	F	+	_	Necrotizing Focal And Segmental Glomerulonephritis
5	43	M	+	_	Crescentic Necrotizing Glomerulonephritis
6	40	F	+	_	Necrotizing Focal proliferative Glomerulonephritis
8	10	M	+	+	Focal Necrotizing Glomerulonephritis
9	22	F	_	+	Necrotizing Focal proliferative glomerulonephritis
10	70	M	+	+	Diffuse Proliferative And Sclerosing Glomerulonephritis (ESRD)
11	45	F	+	_	End Stage Renal Disease (ESRD)
12	42	M			Diffuse global and Segmental Mesangioproliferative glomerulonephritis
13	45	F	+	+	Diffuse Global Glomerular Sclerosis with Advanced Diabetic Glomerulopathy (ESRD)
14	21	M	+	-	Crescentic Glomerulonephritis
15	29	M	-	+	Membranous with foci of fibrinoid change

b) Clinico-pathological correlation

A major part of present study dealt with correlation of clinical presentation according to the histopathological diagnosis. All the signs and symptomswere recorded and later on tabulated according to histopathological diagnosis in 114 cases with detailed patient history and physical examination. (Table-4 and 5)

In the present study oliguria/ anuria and anasarca were the commonest clinical symptoms recorded (77.19 %) followed by anorexia/weight loss and malaise (72.80%) and fever (55.26%). Palpable purpura was the least common clinical symptom recorded in cases of ANCA positive focal segmental glomerulonephritis.

Clinical signs and symptoms with individual glomerulonephritis have been discussed under Table-4.

Table 4 : Distribution of the clinical symptoms according to the various glomerulopathies as recorded in different patients at initial presentation

	RCN (n=2)	MPGN (n=8)	DPGN (n=10)	MEM (n=16)	ESRD (n=21)	MCD (n=5)	DN (n=7)	LN (n=8)	CGN (n=5)	FSGS (n=10)	FOS (n=10)	FON (n=1)	MEGN (n=11)
Fever	01 (50)	04 (50)	07 (70)	02 (12.5)	15 (71.4)	01 (20)	04 (57.1)	08 (100)	04 (80)	04 (40)	06 (60)	01 (100)	06 (54.5)
Oliguria/ Anuria	02 (100)	02 (25)	07 (70)	16 (100)	21 (100)	05 (100)	07 (100)	06 (75)	05 (100)	05 (50)	07 (70)	01 (100)	04 (36.6)
Cola coloured urine	-	05 (62.5)	08 (80)	-	-	-	-	06 (75)	05 (100)	02 (20)	04 (40)	01 (100)	04 (36.6)
Anasarca	02 (100)	07 (87.5)	05 (50)	16 (100)	21 (100)	05 (100)	07 (100)	04 (50)	05 (100)	06 (60)	07 (70)	01 (100)	02 (18.1)
Persist.nausea, vomiting >3 months	02 (100)	04 (50)	04 (40)	-	21 (100)	-	05 (71.4)	03 (37.5)	-	03 (30)	03 (30)	-	-
Anaemia, weakness and malaise	02 (100)	06 (75)	08 (80)	11 (68.7)	21 (100)	02 (40)	06 (85.7)	08 (100)	-	05 (50)	09 (90)	-	05 (45.5)
Pain abdomen/ lump	02 (100)	04 (50)	03 (30)	-	10 (47.6)	01 (20)	04 (57.1)	03 (37.5)	03 (60)	01 (10)	01 (10)	-	-
Altered sensorium, confusion and seizures	01 (50)	-	04 (40)	-	08 (38)	-	01 (14.2)	-	03 (60)	-	02 (20)	-	-
Signs of LVF	01 (50)	-	-	-	07 (33.3)	-	04 (57.1)	01 (12.5)	01 (20)	-	01 (10)	-	-
B.P (Average)	110/ 80	128/ 96	148/ 100	124/ 96	210/ 150	106/ 90	200/ 120	160/ 100	160/ 100	142/ 96	146/ 96	210/ 168	126/ 86
Small joint pain, alopecia, rash	-	-	-	-	02 (9.5)	-	-	06 (75)	02 (40)	-	-	-	01 (9.9)
Palpable purpura/ petechiae	-	-	-	-	01 (4.7)	-	-	01 (12.5)	01 (20)	-	03 (30)	01 (100)	-

RCN= Renal cortical necrosis; MPGN= Membranoproliferative glomerulonephritis; DPGN= Diffuse proliferative glomerulonephritis, MEM= Membranous; ESRD= End stage renal disease; MCD= Minimal change disease; DN= Diabetic nephropathy; LN= lupus nephritis; CGN= Crescentic glomerulonephritis; FSGS= Focal segmental glomerulosclerosis; FOS= Focal segmental/proliferative glomerulonephritis; FON= Focal necrotizing glomerulonephritis; MEGN= Mesangioproliferative glomerulonephritis.

Study also recorded the various biochemical and urinary findings in all the cases at the time of the biopsy which are discussed in details according to individual glomerulopathies under Table-5.

Table 5 : Various Laboratory And Biochemical Parameters Recorded In Different Patients Of Glomerulopathies At The Time Of Biopsy

Urine Examination	RCN	MPGN	DPGN	MEM	ESRD	MCD	DN	LN	CGN	FSGS	FOS	FON	MEGN
CHEMICAL EXAMINATION													
Protein	2+	2+	1+	3+	3+	4+	1+	2+	1+	3+	1+	1+	2+
Sugar	-	-	-	1+	1+	-	3+	1+	1+	-	-	-	-
MICROSCOPIC EXAMINATION													
Pus cells/hpf	0-3	0-4	5-10	0-5	20-30	0-5	20-30	5-8	5-10	1-5	1-5	1-2	1-2
RBC's /hpf	40-60	5-10	20-50	0-3	5-10	0-2	0-3	8-10	20-30	2-4	8-10	20-30	5-8
Granular casts/lpf	1-2	1-2	5-9	-	-	-	-	2-5	2-3	-	1-2	1-2	2-4
Hyaline casts/lpf	5-9	1-2	1-2	2-3	5-8	1-2	1-2	2-3	3-5	2-4	1-4	2-5	2-3
RBC casts/lpf	5-9	1-2	10-20	-	-	-	-	2-3	8-10	-	3-6	5-8	-
Broad waxy casts/lpf	-	-	-	-	5-9	-	-	-	-	-	-	-	<1
BIOCHEMICAL INVESTIGATIONS													
Serum Urea (mg/dl)	168.9	59.9	122.6	34.8	210.8	23.0	77.7	78.9	198.9	39.9	67.8	112.0	80.0
Serum Creatinine (mg/dl)	5.1	1.2	3.1	0.8	6.9	0.5	2.3	1.9	7.10	1.2	1.9	4.7	1.8

RCN= Renal cortical necrosis; MPGN= Membranoproliferative glomerulonephritis; DPGN= Diffuse proliferative glomerulonephritis, MEM= Membranous; ESRD= End stage renal disease; MCD= Minimal change disease; DN= Diabetic nephropathy; LN= lupus nephritis; CGN= Crescentic glomerulonephritis; FSGS= Focal segmental glomerulosclerosis; FOS= Focal segmental/proliferative glomerulonephritis; FON= Focal necrotizing glomerulonephritis; MEGN= mesangioproliferative glomerulonephritis

IV. Discussion

In the present study, nephrotic range proteinuria, was detected in majority of patients who underwent renal biopsy at our centre. This is comparable to the study by Balakrishnan et al [2] and Narasimhan et al [3] who also reported nephrotic syndrome (proteinuria >3.5 g/24 hr) as the major clinical presentation in Indian adults undergoing renal biopsy.

The predominant primary glomerular pathology in our study was ESRD followed by MGN and MPGN. The present study was conducted in a tertiary care hospital in North Indian state of eastern Uttar Pradesh and hence represents data analysis from this region. This is in contrast to other Indian studies which have recorded MEGN as the commonest injury pattern followed by MGN. [4, 5] In a few studies from north India MCD is the commonest recorded injury pattern. [6]

Asian studies done in Saudi Arabia and China have reported MPGN as the most common glomerulaopathy followed by FSGS. [7, 8, 9] The spectrum of glomerular disease is a little different in European and American context where Ig A nephropathy is the most common patern of glomerular injury. [5]

Also it was noted in the present study that ESRD was not only the most common injury pattern noted overall but also in the cases of systemic vasculitis.

Thus in contrast to the documented finding of most common histological findings of cresenteric type glomerulonephritis in cases of systemic vasculitis [10] and MEGN in non systemic vasculitis cases by various researchers, diffuse global glomerulosclerosis/ ESRD was the most common histological finding in our group. This in turn points towards a poor socio-economic indicators in patients from in and around north gangectic plains of Allahabad region and reflects delayed presentation and patient ignorance about and complications of renal diseases as a great challenge to nephrologists practising in this region. This is in turn the larger scenario noted in many developing countries of Asia and Africa which are highly resource challenged.

The probable reasons for having a different spectrum of renal diseases in different regions of same country and internationally is attributed to the multiple factors such as environmental (infectious as well as non-infectious), human developmental indices, facilities and access to health facilities, degree of health education,

competence of para-medical and medical staff and calculated time lag (disease presentation to presentation of patient in physician OPD to final diagnosis). [11]

The second part of study which studied in details the clinical features with renal diseases overall and with specific glomerulopathies also detail presence of urinary disturbances (anuria/oliguria) and anasarca if presenting with fever and weight loss as the lower most common denominators in screening out all patients who would eventually be diagnosed to be suffering from glomerulopathies.

This becomes important in educating patients as well as physicians as pyuria and hematuria are often thought as red –herrings by both as the features associated with glomerulopathies. But as noted in the study conducted this is often not the case in these patients as despite high urea and creatinine levels and discordance in various other urinary parameters, patients with glomerular diseases present late when only possible therapy is renal replacement either dialysis or renal transpalnation.

Comparing the biochemical and urinary findings with other studies, it was found that nephrotic range proteinuria of 4+ was seen in minimal change disease only with 3+ proteinuria noted in FSGS, ESRD and MeM glomerulonephritis. The proteinuria in rest of the glomerulonephritis was sub-nephritic to minimal. [Table-3]

Similary very exuberatnt hematuria was noted in renal cortical necrosis and diffuse proliferative glomerulonephritis. Pyuria was seen in cases of secondary glomerulonephritis especially associated with diabetic nephropathy and ESRD. Often in these cases the patients were in higher grade of renal failure with features consistent with those of uremia. In the present study the range of increased urea levels was from 80-210.8 mg/dl with higher values recorded in ESRD. Very high creatinine values were seen in two ends of spectrum of renal failure with an average creatinine value of 7.10 in cases of acute renal failure associated with cresentic glomerulonephritis and chronic renal failure associated with ESRD. These findings are also corroborated with work done previously by various researches. [12, 13, 14]

V. Conclusion

The present study which was truly a clinico-pathological study not only adds on to the available Indian literature about spectrum of glomerulopathies in a region of poor human developmental indices but also stresses on the very innocuous sounding symptoms of urinary disturabce and anasarca presenting with fever and weight loss as important pointers towards renal diseases. The finding of ESRD as the most common glomerulopahy in the region under investigation should prompt both the practising physicians and the pathologist in this region to be ever vigilant against a possibility of glomerulopathy in patients attending outpatients so that early action can be initiated to preserve kidney function and to avoid renal replacement therapies which add on to the morbidity and economic burden to the patients. In this regard work by government and non government organization to educate masses in this region can also go a long way to prevent kidney failure and reduce the prevalence of ESRD.

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Legends to Figures

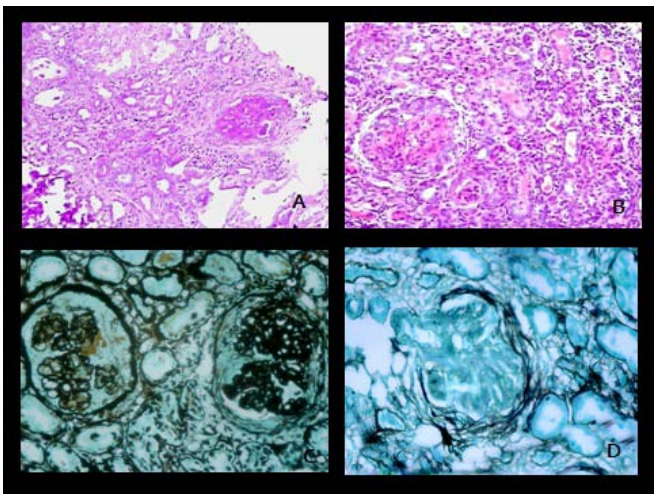

Figure 1 : Morphological spectrum of various crescentic glomerulonephritis

Figure1 A : A cellular crescent showing central fibrinoid necrosis in a case of ANCA positive case. (H & E 200 X)
Figure1B: A cellular crescent in a case of rapidly progressing glomerulonephritis (RPGN). (H & E 200 X)
Figure1 C : Negative shadow of a cellular crescent and sclerozed capillary loops on silver stain in a case of RPGN (PMS 400 X)
Figure1 D : Few reticulin positive fibres noted in a fibro-cellular crescent on silver stain in a case of RPGN (PMS 400 X)

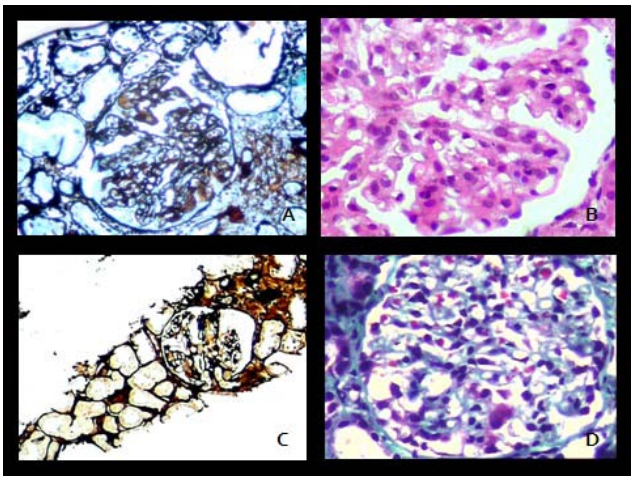

Figure 2 : Histopathological spectrum of various primary glomerulopathies

Figure 2 A : Double contouring of basement menbranes in a case of membranous glomerulopathy (PMS 200 X)
Figure 2 B : Splitting of basement membrane with increased mesangial cellularity in a case of membr - anoproliferative (MPGN) glomerulopathy. (H & E 400 X)
Figure 2 C : A focally sclerozed glomeruli highlighted on silver stain in a case of focal segmental glomerulosclerosis (FSGS). (Reticulin 200 X)
Figure 2 D : Increased mesangial cells and expansion of mesangial matrix highlighted by trichrome staining in a case of Mesangial glomerulopathy. (MT 400 X)

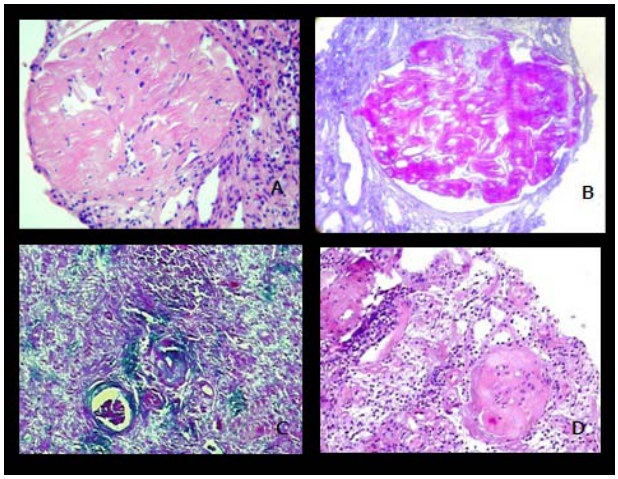

Figure 3 : Histopathological spectrum of various secondary glomerulopathies

Figure 3 A : Obsolescent glomeruli filled with homoge - neous eosinophilic amyloid like material in a case of Amyloid nephropathy. (H & E 400 X)
Figure 3 B : Glomeruli showing amyloid positivity on metachromatic stain in the same case (Fig 3A). (Toluidine blue 400 X)
Figure 3 C : Increased fibrosis (collagenisation) highlight -ted by trichrome stain in a case of end stage renal disease (ESRD). (MT 200 X)
Figure 3 D : Exudative lesion and nodular glomerulos-clerosis in diabetic nephropathy. (H & E 200 X)

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FELLOWS

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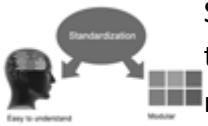

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3. Submission of Manuscripts,

4. Manuscript's Category,

5. Structure and Format of Manuscript,

6. After Acceptance.

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Before start writing a good quality Computer Science Research Paper, let us first understand what is Computer Science Research Paper? So, Computer Science Research Paper is the paper which is written by professionals or scientists who are associated to Computer Science and Information Technology, or doing research study in these areas. If you are novel to this field then you can consult about this field from your supervisor or guide.

TECHNIQUES FOR WRITING A GOOD QUALITY RESEARCH PAPER:

1. Choosing the topic: In most cases, the topic is searched by the interest of author but it can be also suggested by the guides. You can have several topics and then you can judge that in which topic or subject you are finding yourself most comfortable. This can be done by asking several questions to yourself, like Will I be able to carry our search in this area? Will I find all necessary recourses to accomplish the search? Will I be able to find all information in this field area? If the answer of these types of questions will be "Yes" then you can choose that topic. In most of the cases, you may have to conduct the surveys and have to visit several places because this field is related to Computer Science and Information Technology. Also, you may have to do a lot of work to find all rise and falls regarding the various data of that subject. Sometimes, detailed information plays a vital role, instead of short information.

2. Evaluators are human: First thing to remember that evaluators are also human being. They are not only meant for rejecting a paper. They are here to evaluate your paper. So, present your Best.

3. Think Like Evaluators: If you are in a confusion or getting demotivated that your paper will be accepted by evaluators or not, then think and try to evaluate your paper like an Evaluator. Try to understand that what an evaluator wants in your research paper and automatically you will have your answer.

4. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

5. Ask your Guides: If you are having any difficulty in your research, then do not hesitate to share your difficulty to your guide (if you have any). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work then ask the supervisor to help you with the alternative. He might also provide you the list of essential readings.

6. Use of computer is recommended: As you are doing research in the field of Computer Science, then this point is quite obvious.

7. Use right software: Always use good quality software packages. If you are not capable to judge good software then you can lose quality of your paper unknowingly. There are various software programs available to help you, which you can get through Internet.

8. Use the Internet for help: An excellent start for your paper can be by using the Google. It is an excellent search engine, where you can have your doubts resolved. You may also read some answers for the frequent question how to write my research paper or find model research paper. From the internet library you can download books. If you have all required books make important reading selecting and analyzing the specified information. Then put together research paper sketch out.

9. Use and get big pictures: Always use encyclopedias, Wikipedia to get pictures so that you can go into the depth.

10. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right! It is a good habit, which helps to not to lose your continuity. You should always use bookmarks while searching on Internet also, which will make your search easier.

11. Revise what you wrote: When you write anything, always read it, summarize it and then finalize it.

12. Make all efforts: Make all efforts to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in introduction, that what is the need of a particular research paper. Polish your work by good skill of writing and always give an evaluator, what he wants.

13. Have backups: When you are going to do any important thing like making research paper, you should always have backup copies of it either in your computer or in paper. This will help you to not to lose any of your important.

14. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several and unnecessary diagrams will degrade the quality of your paper by creating "hotchpotch." So always, try to make and include those diagrams, which are made by your own to improve readability and understandability of your paper.

15. Use of direct quotes: When you do research relevant to literature, history or current affairs then use of quotes become essential but if study is relevant to science then use of quotes is not preferable.

16. Use proper verb tense: Use proper verb tenses in your paper. Use past tense, to present those events that happened. Use present tense to indicate events that are going on. Use future tense to indicate future happening events. Use of improper and wrong tenses will confuse the evaluator. Avoid the sentences that are incomplete.

17. Never use online paper: If you are getting any paper on Internet, then never use it as your research paper because it might be possible that evaluator has already seen it or maybe it is outdated version.

18. Pick a good study spot: To do your research studies always try to pick a spot, which is quiet. Every spot is not for studies. Spot that suits you choose it and proceed further.

19. Know what you know: Always try to know, what you know by making objectives. Else, you will be confused and cannot achieve your target.

20. Use good quality grammar: Always use a good quality grammar and use words that will throw positive impact on evaluator. Use of good quality grammar does not mean to use tough words, that for each word the evaluator has to go through dictionary. Do not start sentence with a conjunction. Do not fragment sentences. Eliminate one-word sentences. Ignore passive voice. Do not ever use a big word when a diminutive one would suffice. Verbs have to be in agreement with their subjects. Prepositions are not expressions to finish sentences with. It is incorrect to ever divide an infinitive. Avoid clichés like the disease. Also, always shun irritating alliteration. Use language that is simple and straight forward. put together a neat summary.

21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. Think technically: Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

31. Adding unnecessary information: Do not add unnecessary information, like, I have used MS Excel to draw graph. Do not add irrelevant and inappropriate material. These all will create superfluous. Foreign terminology and phrases are not apropos. One should NEVER take a broad view. Analogy in script is like feathers on a snake. Not at all use a large word when a very small one would be sufficient. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Amplification is a billion times of inferior quality than sarcasm.

32. Never oversimplify everything: To add material in your research paper, never go for oversimplification. This will definitely irritate the evaluator. Be more or less specific. Also too, by no means, ever use rhythmic redundancies. Contractions aren't essential and shouldn't be there used. Comparisons are as terrible as clichés. Give up ampersands and abbreviations, and so on. Remove commas, that are, not necessary. Parenthetical words however should be together with this in commas. Understatement is all the time the complete best way to put onward earth-shaking thoughts. Give a detailed literary review.

33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.

Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear

· Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page
- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

· Use standard writing style including articles ("a", "the," etc.)

· Keep on paying attention on the research topic of the paper

· Use paragraphs to split each significant point (excluding for the abstract)

· Align the primary line of each section

· Present your points in sound order

· Use present tense to report well accepted

· Use past tense to describe specific results

· Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives

· Shun use of extra pictures - include only those figures essential to presenting results

Title Page:

Choose a revealing title. It should be short. It should not have non-standard acronyms or abbreviations. It should not exceed two printed lines. It should include the name(s) and address (es) of all authors.

Abstract:

The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript--must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

- Reason of the study - theory, overall issue, purpose
- Fundamental goal
- To the point depiction of the research
- Consequences, including definite statistics - if the consequences are quantitative in nature, account quantitative data; results of any numerical analysis should be reported
- Significant conclusions or questions that track from the research(es)

Approach:

- Single section, and succinct
- As a outline of job done, it is always written in past tense
- A conceptual should situate on its own, and not submit to any other part of the paper such as a form or table
- Center on shortening results - bound background information to a verdict or two, if completely necessary
- What you account in an conceptual must be regular with what you reported in the manuscript
- Exact spelling, clearness of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else

Introduction:

The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

- Explain the value (significance) of the study
- Shield the model - why did you employ this particular system or method? What is its compensation? You strength remark on its appropriateness from a abstract point of vision as well as point out sensible reasons for using it.
- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
- Very for a short time explain the tentative propose and how it skilled the declared objectives.

Approach:

- Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done.
- Sort out your thoughts; manufacture one key point with every section. If you make the four points listed above, you will need a least of four paragraphs.

- Present surroundings information only as desirable in order hold up a situation. The reviewer does not desire to read the whole thing you know about a topic.
- Shape the theory/purpose specifically - do not take a broad view.
- As always, give awareness to spelling, simplicity and correctness of sentences and phrases.

Procedures (Methods and Materials):

This part is supposed to be the easiest to carve if you have good skills. A sound written Procedures segment allows a capable scientist to replacement your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt for the least amount of information that would permit another capable scientist to spare your outcome but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section. When a technique is used that has been well described in another object, mention the specific item describing a way but draw the basic principle while stating the situation. The purpose is to text all particular resources and broad procedures, so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step by step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

- Explain materials individually only if the study is so complex that it saves liberty this way.
- Embrace particular materials, and any tools or provisions that are not frequently found in laboratories.
- Do not take in frequently found.
- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

Methods:

- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

Approach:

- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

What to keep away from

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings - save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently.You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.

Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or in manuscript form.

What to stay away from

- Do not discuss or infer your outcome, report surroundings information, or try to explain anything.
- Not at all, take in raw data or intermediate calculations in a research manuscript.
- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

Figures and tables

- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
- Despite of position, each figure must be numbered one after the other and complete with subtitle
- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

Discussion:

The Discussion is expected the trickiest segment to write and describe. A lot of papers submitted for journal are discarded based on problems with the Discussion. There is no head of state for how long a argument should be. Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implication of the study. The purpose here is to offer an understanding of your results and hold up for all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of result should be visibly described. Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved with prospect, and let it drop at that.

- Make a decision if each premise is supported, discarded, or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
- Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work
- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
- Submit to work done by specific persons (including you) in past tense.
- Submit to generally acknowledged facts and main beliefs in present tense.

Please carefully note down following rules and regulation before submitting your Research Paper to Global Journals Inc. (US):

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- To guard yourself and others from possible illegal use please do not permit anyone right to use to your paper and files.

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Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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