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EDITORIAL

ACUTE ON CHRONIC LIVER DISEASE: A PREDICTOR OF POOR PROGNOSIS IN PATIENTS WITH VARICEAL BLEEDING

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Acute on chronic liver failure (ACLF) is associated with acute hepatic decompensation in patient with cirrhosis leading to jaundice and prolongation of the international normalized ratio, along with one or more organ failure with high risk of mortality from 28th day to 3 months of onset. Therefore it is not surprising that ACLF is also leading to high mortality in patients with variceal bleeding. (1)

In patients with variceal bleeding the prevalence of ACLF is about 13% that leading to acute detoriation of chronic liver disease. The survival rate is also lower in patients with ACLF than that of without ACLF patients, and higher grade of acute on chronic liver disease has lower survival rate. Recently, A study conducted by Trebicka et al . reported that the incidence of ACLF in patients with variceal bleeding is about 17.8% at hospital admission and the presence of ACLF were independently related to risk of rebreeding and mortality. (2)

According to Shin et al, the 28 days cumulative mortality in patients with variceal bleeding and ACLF is high as much as 41%. However the mortality rate in patients with decompensated cirrhosis is much higher than the former study. This study also indicated that patients with ACLF grade 3 had poor survival <10 in 90 days. Therefore, in such circumstances we need to consider liver transplantation imperative same as similar to aggravated decompensated cirrhosis. But, this study does not includes the patients with optimal management of variceal bleeding likes TIPS, that may change clinical course if TIPS is used in acute varicel bleeding or in case of re-bleeding, as many studies are suggested that TIPS improved survival of variceal bleed patients even in ACLF patients. A study conducted by Lv et al. reported that higher transplant free survival in patients with acute variceal bleeding in advanced cirrhosis compared to that of standard care including beta blocker or band ligation but the proportion of ACLF in this study is unknown. (3-4)

Finally as in both the situations, hepatic pressure venous gradient is elevated. It is unclear that ACLF induce variceal bleeding or not. Also, in case of variceal bleeding, subsequent hypoxic hepatitis may induce liver and renal failure and hepatic encephalopathy in chronic liver disease. (5)

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Both studies by Shin et al.[1] and Trebicka et al.[2] did not reveal the temporal relationship between variceal bleeding and ACLF. Therefore, we could not compare the survival according to the order of the two pathologic conditions. Generally, the baseline characteristics of patients with underlying ACLF followed by variceal bleeding might be poorer than those of patients manifesting ACLF after variceal bleeding. However, the precise prognosis of both groups remains unknown, and requires further analysis.

ACLF is probably a predictive factor of poor prognosis after variceal bleeding, based on the results of recent and current studies. Regardless of the order of events, it is possible that ACLF and variceal bleeding may influence each other with negative synergism, which facilitates the clinical monitoring of patients for possible multi-organ failure or bleeding events.

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COMMENTARY

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DIAGNOSTIC TESTS FOR COVID-19 (SARS-COV-2) – ILLUSTRATIVE VIEW

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ABSTRACT

Awareness of SARS CoV-2 diagnostic testing is still in hit-and-trial phases all over the world. Usage for SARS-CoV-2 infections Reverse Transcriptase - Polymerase Chain Reaction (rT-PCR) and IgM/IgG serology by Enzyme Linked Immunosorbent Assay (ELISA) or Electro-Chemiluminescent Immunoassay remains the main diagnosis stay, advancing day by day through ongoing study and comprehensive trials. However, in both children and adults, the time course for PCR positivity and seroconversion continues to differ, which often involves a large population of asymptomatic individuals that are theoretically considered negative, posing a significant threat to the local group.

KEYWORDS:

COVID-19, SARS - CoV - 19, Polymerase chain reaction, Enzyme linked immunosorbant assay, antibodies, immunoglobulins.

BACKGROUND

COVID-19, i.e. Coronavirus disease abbreviation 2019, is now a global health concern for a day. On 11 March 2020, its spread was announced by the Director of the World Health Organization as a pandemic disease. [1] The viral pathogen that causes this disease belongs to the family of Coronaviridae and is ultimately described as Corona Virus 2 Severe Acute Respiratory Syndrome (SARS-CoV-2). The sequence closely matches the homologous virus (SARS-CoV-1) that previously triggered the outbreak of SARS in 2003. [2] Awareness of SARS CoV-2 diagnostic testing is still at an initial stage and is improving day by day through studies and comprehensive patient and exposed population trials. It is really important to have a good and simple understanding of the essence of tests and the interpretation of their results, which can contribute a great deal with patient care.

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Therefore, this commentary describes how the two types of diagnostic tests widely used for SARS-CoV-2 infections are interpreted: Reverse Transcriptase Polymerase Chain Reaction (rt-PCR) and IgM/IgG serology by Enzyme Linked Immunosorbent Assay (ELISA) or Electro Chem-iluminescent Immunoassay techniques as their results can differ over time.

DETECTION OF VIRAL RNA BY RT-PCR

This is the most widely used examination carried out for the diagnosis of COVID-19 and is considered a successful one. Recently, it is accomplished using nasopharyngeal swabs or other specimens of the upper respiratory tract, like throat swab or saliva. A variety of RNA gene targets are used by different manufacturers. Most experiments target 1 or more of the genes Envelope (Env), Nucleocapsid (N), Spike (S), RNA polymerase based on RNA (RdRp) and ORF1. [3] Viral RNA can become positive in most symptomatic patients with COVID-19 within one week of symptoms and peaks as early as day 1. It becomes undetectable and then undetectable by week 3. In a few cases, rT-PCR detected viral RNA 6 weeks after the first positive test, while in some other cases, rT-PCR detected viral RNA positively after 2 consecutive negative tests 24 hours apart. [4] This can be entirely due to the error of research, reinfection or reactivation. For specimens other than nasopharyngeal swabs, the time-line of PCR positivity is distinct. It was noted that the PCR positivity in sputum decreased more slowly and was still positive after the nasopharyngeal swabs were negative. [5]

The rT-PCR positivity was highest in bronch-oalveolar lavage (93%), followed by sputum (72%), nasal swab (63%) and pharyngeal swab (32%), according to a review of 205 patients with reported COVID-19 infection. [6] False negative results were also seen due to incorrect sampling timing in relation to the onset of disease, its defective technique, especially nasopharyngeal swabs. As the primer architecture is unique to the genomic sequence of SARS-CoV-2, the specificity of most rT-PCR tests is 100%. Owing to technical errors or contamination of reagents, false positive findings can also occur.

DETECTION OF SARS-COV-2 ANTIBODIES

It is indirectly possible to diagnose COVID-19 infection by testing the immune response to infection with SARS-CoV-2. Serological diagnosis plays a very important role in patients with a mild to moderate degree of disease that progress late after 2 weeks of disease onset. With the criteria for rapid diagnosis, it has become a valuable tool to understand the community's extent of COVID-19 and to recognise resistant individuals or those who are potentially shielded from being infected. As early as the fourth day after the onset of symptoms, IgM and IgG antibodies have been shown to be positive; they are also at higher levels during the second and third weeks of illness. [7] In all of these patients, IgM and IgG seroconversion occurred between the third and fourth weeks of clinical disease onset, according to a report performed by Xiang et al in 85 patients. IgM starts to fall by week 5 and reaches a lower level, almost vanishing by week 7, but IgG levels continue to remain past 7 weeks. [8] (Figure 1). IgM and IgG antibody tests based on ELISA have greater than 95% accuracy for COVID-19 diagnosis. By testing paired serum samples with the initial PCR and then the second one 2 weeks later, the diagnostic accuracy can be further improved. Rapid point of care tests have been produced by different manufacturers for the detection of antibodies with variable consistency, sensitivity and specificity. It does not disclose the existence of the antigens used by them. These are strictly qualitative in nature and only suggest that SARS-CoV-2 antibodies are present or absent. [9] Few prominent companies such as Roche have introduced the detection of antibodies using the famous and very sensitive electrochemiluminescence immunoassay technique using the sandwich process. For the determination of antibodies against SARS-CoV-2, the anti-SARS-CoV-2 assay uses the recombinant protein representing the nucleocapsid (N) antigen. As stated in their literature, the overall specificity is 99.81% with a 95% lower confidence interval of 99.65%, while the sensitivity after 6-14 days of PCR confirmation ranges up to 65.5 -100%. [10]

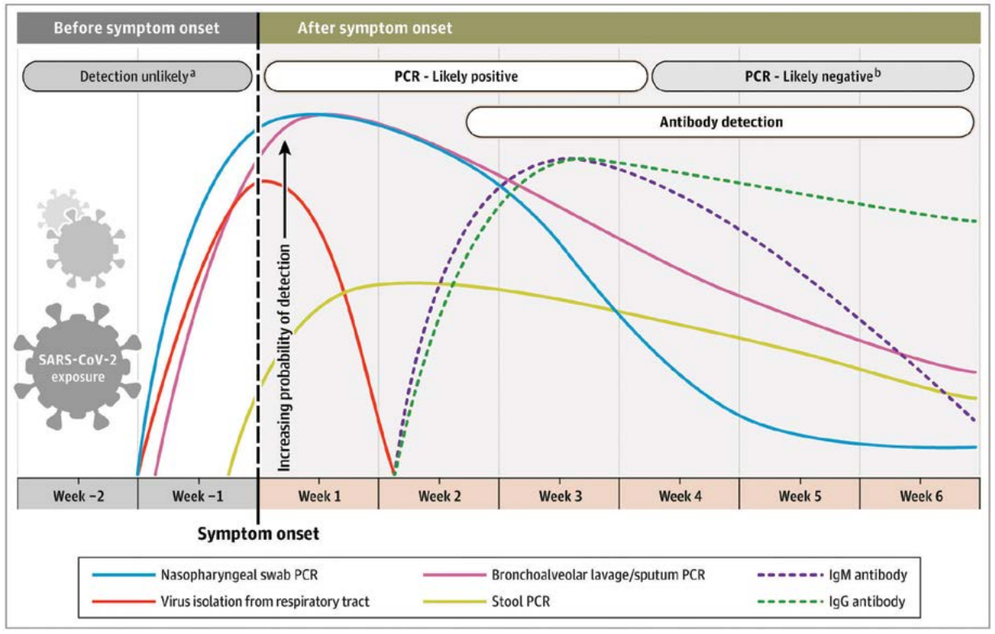

Figure 1: Adapted from: COVID-19: Screening a. COVID-19: Screening, testing, PUI, and returning to work – REBEL EM – Emergency Medicine Blog. 2020

CONCLUSION

For clinical correlation, a very useful timeline of diagnostic markers for COVID-19 detection has been devised. The time course for the PCR positivity and seroconversion seem to differ in children and in other age groups, which also involves a large population of asymptomatic individuals that are never diagnosed. There is still a major question that needs to be answered, i.e. how long the possible immunity lasts in asymptomatic as well as symptomatic people infected with the latest SARS-CoV-2.

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ORIGINAL ARTICLE

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FREQUENCY OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN DIABETIC ASIAN PATIENTS

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ABSTRACT

Objective: To see the frequency and bio-chemical changes in diabetes patients with NAFLD.

Methodology: It is a cross-sectional study, conducted at Indus Medical College Hospital, Tando Muhammad Khan. One hundred patients of either sex having type 2 diabetes mellitus attending diabetic out-patient were included in the study. A pre-designed study pro-forma was filled with relevant investigations and clinical assessments were carried out in all cases. All the patients underwent abdominal ultrasonography. Data were entered in SPSS-20 and analyzed.

Results: Out of 100 diabetic patients, 51% were males and 49 % were females. The mean age of patient was 46 years with ranges from 45 to 67 years of age. Out of 100 patients, 51 had fatty liver on ultrasound diagnosis, with 32 (67.1%) were males and 19 (32.2%) were females. Fatigue was present in 48 (52.1%), generalized weakness in 49 (53.26%), heaviness right upper abdomen in 20 (58.82%) and pain right upper abdomen in 19 (44.18%) of fatty liver patients. Corresponding figure in Non Fatty Liver Patients were 44 (47.74%), 43 (46.74%), 14 (41.18%) and 12 (35.30%), respectively. Itching was noted in 15 (60.00%) patients of

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fatty liver while it was 24(55.82%) in non-fatty liver patients. Serum triglyceride level was more than 160 mg/dL in 47 (92.15%) patients of fatty liver while serum cholesterol level more than 200mg/dL was seen in 24 (47.05%). Aspartate aminotransferase (AST) more than 35 U/L was noted in 7 (13.72%), alanine aminotransferase(ALT) more than 40 U/L was noted in 6 (11.76%) fatty liver patients while serum albumin and serum billirubin were within normal range in all fatty liver and non-fatty liver patients.

Conclusion: Non-alcoholic fatty liver disease (NAFLD) is more commonly seen in Type-2 diabetic patients. Serum triglyceride and serum cholesterol are significantly raised in NAFLD patients. Raised ALT and AST was not a common finding in our NAFLD study patients. Diabetic patients having heaviness or pain right upper abdomen with raised serum triglycerides and cholesterol should be more closely observed for NAFLD and liver complications.

Keywords: Non-alcoholic fatty acid liver disease, diabetes mellitus, frequency, Asian.

INTRODUCTION

NAFLD is associated with wide range of spectrum of disease, ranging from the fairly kind one-off hepatic steatosis (HS) to the other damaging tribulations of non-alcoholic steatohepatitis (NASH), hepatic fibrosis, and cirrhosis. [1-3] NAFLD is diagnosed when other liver diseases are excluded. For the diagnosis of NAFLD there are different modalities are available that includes labs testing, imaging or and definitive diagnosis by liver biopsy. [4-5]

The clinical and financially viable burden of NAFLD own grow to be evident and are likely to growth abruptly in the advent decades as a upshot of the amplified dominance and incidence of stoutness of two factors; obesity and diabetes. In general population the prevalence of NAFLD is about 25% and the prevalence of NASH is about 6.5%. Due to this high prevalence of NAFLD and NASH currently, the second most common indication of liver transplantation is NASH all round the world. NAFLD also associated with higher chances of cardiac morbidity and mortality worldwide. [3, 6-8]

NAFLD and type 2 diabetes mellitus are meticulously coupled phenomena. NAFLD may be painstaking as a hepatic manifestation of metabolic syndrome. In distinction to the acquaintance about NAFLD and class 2 diabetes, in attendance are imperfect and never the same facts on NAFLD commonness in patients with type 1 diabetes mellitus. Type 1 diabetes and type 2 diabetes mellitus prove foremost pathophysiological differences, but split dependable similarities as acceptably. Hyperinsulenemia and insulin resistance usually present in both type of diabetes.[9] Obesity, a well-known NAFLD hazard aspect openly correlated to type 2 diabetes and insulin resistance, is appropriate further prevalent in the type 1 diabetes populace. Taking these similarities and addition in the main extensive time exposure to in both types of diabetes mellitus, the spectrum of NAFLD and its long-term squeal might be clinically pertinent in patients with type 2 diabetes as well.

NAFLD usually occurs in all age group of patients but are more common in age group of between 40 to 60 years. 80% of NAFLD patients are asymptomatic, 20% of patients present with generalised weakness, GI symptoms, abnormal LFTs or rarely stigmata of chronic liver disease. [10]

The present study is designed to know the frequency and biochemical derangement in patients with Diabetes and NAFLD.

PATIENTS AND METHODS

This was a cross-sectional study done by using non-probable purposive sampling at Indus Medical College Hospital, Tando Muhammad Khan. 100 diabetic patients were selected who came in outpatient department. After taking informed consent, a pre-designed pro-forma was filled. Patient with chronic hepatitis C and alcoholic were excluded from the current study. Complete history taking about symptoms and clinical examination of patient were also done. All the patients were gone through the ultrasound imaging. Lipid profile and LFTs along with chronic liver disease testing were performed to rule out the cirrhosis. The data were analysed by using SPSS version 20. For descriptive analysis, mean and standard deviation were calculated and for and for categorical analysis frequency and percentage were calculated. Chi-square test was applied to know the significance of associated factors; p -value less than 0.05 was considered as significantly correlated.

RESULT

Out of 100 diabetic patients, 51 were males and 49 were females. The mean age of patient was 46 years with ranges from 45 to 67 years of age. Out of 100 patients, 51 had fatty liver on ultrasound diagnosis. 32 (67.1 %) were males and 19 (32.2 %) were females. Patients presented with different complains (Table 1) and abnormal LFTS (Table 2).

Table 1: Symptom in fatty and non – fatty liver patients (n=100)

Symptoms	Fatty liver patients	Non-fatty liver patients	P –value
Fatigue	48(52.1%)	44(47.74%)	0.77
Generalized weakness	49 (53.26%)	43 (46.74%)	0.78
Heaviness at RHC	20(58.82%)	14(41.18%)	0.01
Pain at RHC	19(44.18%)	12(35.30%)	0.23
Itching	15(60.00%)	24(55.82%)	0.21
Nausea	22(64.70%)	14(41.18%)	0.29
Anorexia	19(44.18%)	10(40.0%)	0.84

Table 2: Biochemical profile of fatty and non fatty liver diabetic patients

Investigation	Fatty liver patients (n=100)	Non-fatty liver patients (n=100)	P –value
Serum Triglycerides >150 mg/dl	47	39	0.65
Serum Cholesterol > 200mg/dl	24	18	0.18
Serum Alkaline Phosphate > 306 u/l	08	05	0.21
AST <35 U/L	07	04	0.23
ALT > 40 U/L	06	06	0.67

DISCUSSION

NAFLD is a common disease especially in Asian patients with diabetes and obesity. A recent study done in Japan in healthy individuals shows the prevalence rate of NAFLD is about 29%, in Italian study its around 20% and in general population of USA is also a 20%, but a study conducted by Luxmi et al [11] in Pakistan shows the prevalence of NAFLD in diabetic patients is 60.8% and in Saudia Arabia study by Akber et al. [13] The incidence of NAFLD in diabetic patients is 55%.[12-13]

In present study the prevalence of NAFLD in diabetic patients is 51%. In our current study we used the ultrasounsography method to detect the fatty liver, which has poor sensitivity of detection of fatty liver if patient has fatty content less than 33%. So frequency could be high if we used liver biopsy, a definitive diagnostic tool in our study. Many studies shows that NAFLD patients are usually asymptomatic, but in current study the most common presenting complains of the patients is fatigue and generalized weakness that is account for about 52.1% and 53.2% respectively, but in our study all the patients were diabetic which can also present with same complains of symptoms. A study conducted by Wingkin et al. described the fatigue and pain in right hypochondrium is the most common presenting complain. In our study right hypochondrium is account for about 44.8%. That is thought due to stretching of liver capsule that is also correlated with the amount of fat present in the liver.

It is established that diabetes mellitus through insulin resistance leads to increased free fatty acid load to the liver consequently high triglyceride synthesis and increased secretion of triglyceride rich very low density lipoprotein by the liver. Hypertriglyceridemia is strongly correlated with NAFLD and our study also supports this. Serum triglycerides were raised in 92.15% of fatty liver patients. Similarly serum cholesterol was raised in 47.05% of patients. The study by Luxmi et al [11] also reported raised serum triglyceride level in patients with fatty liver and same is the result from our study. [13-15] In our study level of serum alkaline phosphatase raised in 15% patients although few studies are suggestive that alkaline phosphatase only raised in old age women. ALT and AST are also higher in many studies but in our current study ALT were raised in 7 (13.6%) and AST in 6 patients (11.7%) respectively. Normal ALT level has also been reported in others studies, a study conducted by Mofrad [12] reported that histological spectrum is not significantly different in patients with raised or normal ALT.

CONCLUSION

Non-alcoholic fatty liver disease (NAFLD) is more commonly seen in Type-2 diabetic patients. Serum triglyceride and serum cholesterol are significantly raised in NAFLD patients. Raised ALT and AST is not a common finding in our NAFLD study patients. Diabetic patients having heaviness or pain right upper abdomen with raised serum triglycerides and cholesterol should be more closely observed for NAFLD and liver complications.

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ORIGINAL ARTICLE

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ASSOCIATION OF SERUM FERRITIN WITH C – REACTIVE PROTEIN IN PATIENTS WITH IRON DEFICIENCY ANAEMIA

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ABSTRACT

Objective: Main objective of this study was to see association of serum ferritin as acute phase reactant with C – reactive protein in patients with iron deficiency anaemia having underlying inflammatory process.

Patients and Methods:
This was a prospective and cross sectional study, conducted at Department of Pathology, Indus Medical College Hospital Tando Muhammad Khan for period of 6 months (November 2018 to April 2019). 68 patients with iron deficiency anaemia were included in this study. Blood parameters were assessed by Automated Haematology Analyzer Mindray BC-5000. Serum ferritin was assessed using Mindray CL1000i electrochemiluminesence assay. C – Reactive protein was analyzed by Automated Chemistry Analyzer Mindray BS-240, using immunoturbidimetric method. All patients were divided into three classes as per levels of serum ferritin. Group A (serum ferritin <10 µg/L), Group B (serum ferritin 11-150 µg/L) and Group C (serum ferritin >150 µg/L). The data was analyzed by SPSS version 21.0. Pearson's correlation tests were performed for statistical analysis.

Results: C – reactive protein (CRP) was most significantly raised in Group C (high ferritin) (34.52 ± 1.44, p-value <0.001) and was reduced in Group A (low ferritin) (5.92 ± 0.99, p-value <0.001). Haemoglobin was lowest in Group C (high feritin) (7.84 ± 1.09, p=0.003), and was highest in Group B (normal ferritin) (9.88 ± 097, p=0.003). There was strong positive relationship of ferritin with C-reactive protein (r=0.79, p <0.001) and strong negative relationship with haemoglobin (r=0.59, p<0.001).

Conclusion: Levels of serum ferritin was positively associated with C-reactive protein (CRP). In patients with underlying deficiency of iron, secondary inflammation may increase the level of ferritin in serum.

Keywords: Iron Deficiency Anaemia, Ferritin, C-Reactive Protein, Haemoglobin.

Article Citation:
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INTRODUCTION

Iron is one of the most copiously metals present globally; though iron deficiency anaemia is still emerging problem in health-related concerns globally. [1-5], and it is the most common type of deficiency of micronutrient which affect 1.62 billion individuals around the world. [6] Prevalence rate of iron deficiency anaemia in Pakistan is around 40 – 70%. [7] This condition is more prevalent in females and is taken as one of the most serious health problem to human life. [8]

Most common and essentially advised investigation for the assessment of total stores of iron in body is ferritin. [1] In state of low ferritin levels, iron deficiency anaemia is most common and obvious cause; though as an acute phase reactant, serum ferritin levels may be false normal or false high. Normal C-reactive protein (CRP) can be utilized for the exclusion of high ferritin levels caused by acute phase reaction.

Acute phase reaction is immunological mechanism which is caused in response to inflammation or infection, resulting in uphill or downhill of certain acute phase proteins, including ferritin. In inflammation, upregulation of ferritin by specific cytokines is not dependant on homeostatis of the iron. [8] Since 1970, it is known that level of ferritin in serum imitates the total iron in the body and acute phase reaction so there is difficulty in interpretation of serum ferrtin in the presence of inflammatory or infectious condition; therefore not a capable marker for status of iron and delay in diagnosis may lead to complications of iron deficiency anaemia. In these situations, the status of body iron can be measured by invasive techniques e.g. bone marrow or expensive techniques e.g. soluble transferrin (sTfR) or level of hepcidin. Haematocrit or mean corpuscular volume (MCV) is decreased in anaemia, but many factors affect their levels e.g. deficiency of vitamin B, thyroid disease, kidney disease or liver disease. It was obvious that certain investigations of acute phase reactions were needed for interpretation of concentration of ferritin to assess status of body iron, the joint Centres for Disease Control and Prevention (CDC) and World Health Organization (WHO) recommended the utility of one or two acute phase reactants e.g. C-reactive protein for correction of ferritin when inflammatory condition is evident. [9] Therefore this research was conducted to interpret the correlation between ferritin and C-reactive protein in patients with iron deficiency anaemia with normal or increased level of ferritin due to associated inflammatory status.

PATIENTS AND METHODS

This was cross-sectional, observational study, carried out at Department of Pathology, Indus Medical College Hospital Tando Muhammad Khan for the period of 6 months (November 2018 to April 2019). This study included patients of both genders i.e. males and females. Patients aged between 10 to 50 years having

hypochromic microcytic anaemia were included in this study. Patients already on iron replacement treatment and patients with iron overload syndromes were excluded from the study. Patients with co-morbid conditions e.g. alcoholism, pregnancy, bleeding disorders or haemoglobinopathies were also excluded from the study.

After informed consent, 5mL venous whole blood was obtained; 3mL was transported in gel-containing tubes for assessment of serum ferritin and C-Reactive protein and 2mL was transported to EDTA-containing tube to perform complete blood count. Blood parameters were assessed by Automated Haematology Analyzer Mindray BC-5000. Serum ferritin was assessed using Mindray CL1000i electrochemiluminesence assay. C – Reactive protein was analyzed by Automated Chemistry Analyzer Mindray BS-240, using immunoturbidimetric method. All patients were then divided into 3 groups: Group A containing patients with low level of ferritin (<10 µg/L), Group B containing patients with normal level of ferritin (11-150 µg/L) and Group C containing patients with high level of ferritin (>150 µg/L). All data was analyzed using SPSS 21.0. Pearson's correlation test was used for the establishment of association between iron deficiency anaemia with serum ferritin and C-reactive protein. P – value of <0.05 was considered ass statistically significant.

RESULTS

Among 68 patients, 29 (42.64%) were males and 39 (57.35%) were female (Figure 1). Low ferritin levels (36/52.94%) were found more common followed by normal ferritin levels (28/41.17%) and high ferritin (4/5.88%) (Figure 2). Mean age of patients in Group A, B and C were 29.21 ± 6.32, 28.87 ± 6.01 and 29.89 ± 5.89 years respectively with no statistical significant value (Table 1). Mean age, haemoglobin, red blood cell count, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, ferritin and C-reactive protein in all three groups are summarized in Table 1. C-reactive protein was highest in Group C (high ferritin level) with mean level of 34.52 ± 1.44 mg/L, followed by Group B (normal ferritin level) with mean level of 25.94 ± 2.33 mg/L and Group A (low ferritin level) with mean level of 5.92 ± 0.99 mg/L. P-value was statistically significant (<0.001) showing strong correlation between serum ferritin and CRP.

Pearson's correlation demonstrated statistically significant variation between three groups in relation to ferritin and CRP. In the end, a test for correlation was performed dependant variables and iron deficiency anaemia (Table 2). Ferritin revealed strong positive correlation with C-reactive protein, but negative correlation with haemoglobin (Table 2).

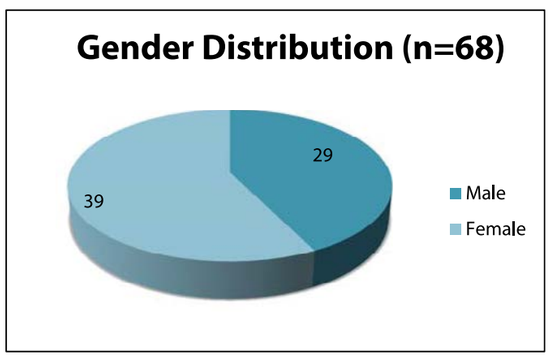

Figure 1: Gender Distribution (n=68)

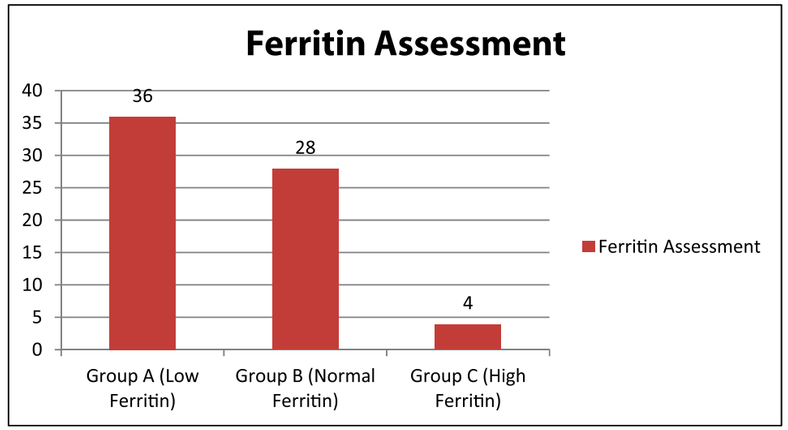

Figure 2; Pattern of Ferritin Level in Selected Population of the Study (n=68)

Table 1; Descriptive Analysis of Parameters (n=68)

Variable	Group A (Low Ferritin)		Group B (Normal Ferritin)		Group C (High Ferritin)		P-value
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	
Age (years)	29.21	6.32	28.87	6.01	29.89	5.89	0.11
Hemoglobin (g/dL)	9.42	1.02	9.88	0.97	7.84	1.09	0.003
Red Blood Cell Count (x10^{12}/L)	3.28	0.43	3.71	0.78	3.41	0.15	0.20
MCV (fL)	58.23	3.24	57.20	2.98	61.42	2.55	0.28
MCH (pg)	25.12	1.12	24.09	2.03	25.71	1.87	0.17
MCHC (g/dL)	26.87	1.79	26.03	2.21	25.87	2.19	0.29
Ferritin (µg/L)	6.31	1.80	84.22	6.42	161.42	7.88	<0.001
C-Reactive Protein (mg/L)	5.92	0.99	25.94	2.33	34.52	1.44	<0.001

Table 2: Pearson's Correlation of Iron Deficiency Anaemia with Test Variables (n=68)

Variable	Pearson's Value (r)
Hemoglobin	-0.59
Ferritin	0.79
C-Reactive Protein	0.92

DISCUSSION

Iron deficiency anaemia is major global problem of health concern. In various healthcare setups, serum ferritin is utilized as marker for iron status.[10] High or normal ferritin level is often associated with patients having underlying state of inflammation, chronic disorder or infection; hence diagnosis of iron deficiency anaemia is not accurate. This study showed high female predominance (57.35%) in comparison to males (42.64%). Similar findings were observed by Khan et al. [7] UNICEF and WHO recommends the use of additional inflammatory marker e.g. CRP for assessment of iron status in case of inflammatory condition. [2] In our results, group B and group C with normal and high ferritin levels respectively showed higher levels of CRP due to underlying inflammatory conditions and demonstrated positive correlation between CRP and ferritin. It also showed that from low to high ferritin levels, there was decline in haemoglobin levels as well as increase in levels of ferritin and CRP which was similar to findings of Khan et al. [7] Kalantar et al also showed high level of ferritin because of malnutrition inflammation complex syndrome (MICS) in patients with haemodialysis. [11] Allam et al utilized the hsCRP levels as the inflammatory marker and high level of ferritin in patients with diabetes mellitus type 2. [12] In study of nutritional health and examination survey by Gillum et al, it was observed that there was positive correlation of high ferritin levels with risk of obesity and metabolic syndrome. [13] Our results showed similar findings.

Eftekhari et al, in contrast, observed low level of ferritin in inflammatory conditions [14], while there was no influence of C-reactive protein in assessment of concentration of serum ferritin or prevalence of iron deficiency in population of Mexico by Cruzz et al. [15] In study conducted in Peshawar, high ferritin levels were observed in individuals with obesity and overweight due to presence of generalized inflammation. [15-18] Due to these observations, the use of ferritin as novel marker for diagnosis of iron deficiency anaemia is controversial in underlying inflammatory conditions. [17-18]

In our study, ferritin was not proved to be ideal marker for assessment of body iron in underlying inflammatory conditions. Though, positive correlation was found between ferritin and inflammatory status, addition of C-reactive protein was shown to be beneficial in diagnosis of status of iron in the body and help in making early diagnosis and interventions in iron deficient patients. However, studies on larger populations are recommended to assess various factors and to get strong correlation is necessary.

CONCLUSION

High level of ferritin in patients with underlying inflammatory conditions may mask the deficiency of iron in the body. Use of inflammatory marker such as C-reactive protein (CRP) with high or normal level of ferritin can be essential in diagnosis of iron deficiency. Ferritin was shown to be positively correlated with C-reactive protein.

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THE β-THALASSEMIA MAJOR PATIENTS: VARIOUS CLINICAL ASSESSMENTS

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ABSTRACT

The β-thalassemia major is identifiable with the estimation of hematological parameters like (Hemoglobin, Hemoglobin A1, Hemoglobin F, and Hemoglobin A2). In this study, all selected patients were affected with β-thalassemia major. Severely affected hematological values (HB, HCT, MCV, MCHC, WBC and PLT) were observed and affected immunochemistry values (ferritin, vitamin D, serum bilirubin total, serum bilirubin direct, serum bilirubin indirect, SGPT). The beta-thalassemia patients have conceded advancement and metabolic abnormalities that means the criticalness of remedial interventions. The closeness of these varieties from the standard may be a result of iron over-burden and poor nutritional diet. Liver enzyme (SGPT) values are high in beta-thalassemia because iron over-burden (Ferritin) is a primary driving reason for raised liver proteins and it causes liver sickness rheumatoid joint aggravation ailment and hepatic HCV. Bone maladies likewise happen in beta-thalassemia quiet because of deficiency of nutrient vitamin D. Pre-birth screening either thalassemia ailing or transporter and their sub-sequent offspring can be a most ideal approach to decrease the continuous recurrence of thalassemia; just by demoralizing the cousin marriages. Now days, stem cell transplant can cure it, but it is a complex procedure with many risks and won't benefit everyone with the condition. Doctors and scientists are working on developing gene therapies and other treatments to help people with beta thalassemia.

Keywords: β-thalassemia, blood CP, ferritin, ALT, vitamin D, blood transfusion.

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INTRODUCTION

Thalassemia is a single gene heredity blood disorder; it is transfered from parents to offspring due to premature destruction of red blood cells which leads to anaemia. [1] In thalassemia body cannot make normal forms of haemoglobin. [2] Due to this, body will not be able to take sufficient amount of oxygen and as results patients face many difficulties in long-term survival. It was the first disease which was studied by molecular genetics techniques. The term thalassemia is derived from the Greek word 'thalas' means sea and 'emia' means blood. Thalassemia was not recognised as clinical entity until 1925. [3]

Worldwide there are approximately 240 million people who are the carrier of beta thalassemia. Beta thalassemia is a genetic disorder. [4] It is an autosomal recessive disease. It is caused by reduced or absent of beta globin chain of haemoglobin. [5] Its high prevalence is present in Mediterranean, Middle-East, Central Asia, Indian subcontinent, and Far East. [5] Beta thalassemia occurs when there is a deficiency of beta globin chains; typically it is caused by direct down regulation in the synthesis of structurally normal beta chains. [6] The β-thalassemia is inherited as an autosomal recessive manner. At conception, each sibling of an affected individual has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier. [7] In beta thalassemia there is defect in beta globin gene, while beta globin is encoded by two genes. [8]. More than 200 mutations affecting the beta globin gene are now known to result in a phenotype of beta thalassemia. [6] Beta thalassemia can be classified into three categories: Thalassemia major, thalassemia intermediate, thalassemia minor. [9]

Patients of beta thalassemia minor have no symptoms and they spend a normal life and beta thalassemia intermediate patients have moderate anaemia, while patients of beta thalassemia major have severe anaemia and they require blood transfusion. [4] But the repeated transfusion can cause iron overload and because of this many disorders occurs like endocrine dysfunction, cardiomyopathy and liver disease afterward it leads patients to death. But if the blood transfusion does not take place then patient of beta thalassemia major will die on first five years of their life. [10] Natural pharmacological agents have been used to reduce iron over loaded in patients of beta thalassemia major. [4] In beta thalassemia, beta globin is not formed because of mutation. There are several types of mutations take place in beta globin gene which causes beta thalassemia. The mutation in beta globin gene is due to the single nucleotide.

The possible treatment of beta thalassemia contains bone marrow transplantation, which is very expensive and unaffordable for Pakistani patients. So the best way to prevent the future generation from this hazardous disease is to diagnose the both parents before they conceive a baby. If the parents are carriers of beta thalassemia then provide them a proper counselling for prenatal diagnosis in the 1st trimester of pregnancy to check either the fetus is affected or not. [11]

In this study, we observed clinical assessment of beta thalassemia major patients under trials of treatment.

MATERIALS AND METHODS

The study was conducted over four months in 2019. Blood samples collected from Fatmid Foundation Blood Center Hyderabad, Pakistan. The β-thalassemia major diagnosed patients were registered and they were following the regular schedule of blood transfusion. We selected 5 patients of β-thalassemia major. The samples were collected using ethylenediaminetetraacetic acid (EDTA) tubes. On these samples we performed hematological and biochemical test at LUMHS diagnostic laboratory Hyderabad Sindh.

Hematological and Immunochemistry test of β-thalassemia:

Blood samples were subjected for diagnosis of thalassemia. Hematological and immunochemistry parameters of blood including RBC count (million), hemoglobin (gm/dl), hematocrit (%), MCV (fL), MCH (g/dL), MCHC (g/dl)[12], hemoglobin A1 (%), hemoglobin F (%), hemoglobin A2 (%), WBC (U/L), neutrophils (%), lymphocytes (%), monocytes (%), eosinophils (%), basophils (%), platelet count (10^9/L), ESR (mm/hour), vitamin D total (ng/mL), serum iron (µg/dl), serum TIBC (µg/ml), ferritin (ng/ml), transferrin saturation (%), serum bilirubin total (mg/dl), serum bilirubin direct (mg/dl), serum bilirubin indirect (mg/dl), SGPT (ALT) (U/L), alkaline phosphatase (U/L), gamma GT (U/L), plasma glucose random (mg/dl), serum creatinine (mg/dl), T3 (ng/ml), T4 (µg/dl), TSH (µU/ml)and blood urea (mg/dl) estimated with an automatic analyzer.[13-15]

RESULTS AND DISCUSSION

As per the hematological and immunochemistry parameters of blood β-thalassemia major patients' uncovered noteworthy variety are surpassing over to the reference esteems. The thalassemia patients showed significantly lower values of hematological characteristics than healthy person values of hemoglobin (Hb), hematocrit (HCT), Red Blood Cells (RBCs), white blood cells (WBCs), while ESR and platelets (PLT) were higher (Table 1).

The thalassemia patient showed significantly same values of hematological characteristics than healthy person values of mean corpuscular hemoglobin (MCV) and mean corpuscular hemoglobin concentration (MCHC), Mean corpuscular hemoglobin (MCH). [12]

Table 1. Analysis of hematological parameters among β-thalassemia major patients

Characteristics	Healthy	Patient-I	Patient-II	Patient-III	Patient-IV	Patient-V
RBC (million)	4.415±	3.545±	3.485±	9.018±	3.248±	3.514±
4.3-5.9 (million)	0.036	0.027	0.017	0.041	0.257	0.018
Hemoglobin (g/dl)	11.08±	9.700±	9.600±	7.100±	10.00±	9.750±
12.0-16.0 (g/dl)	0.125	0.071	0.082	0.129	0.082	0.104
Hematocrit (%)	43.03±	29.75±	29.03±	21.13±	30.50±	29.90±
	0.085	0.065	0.149	0.048	0.204	0.187
M.C.V (FL)	79.10±	83.38±	83.50±	77.96±	87.05±	84.75±
76-96 (FL)	0.173	0.156	0.187	0.165	0.104	0.250
M.C.H (g/dl)	29.13±	27.22±	27.60±	26.50±	28.60±	27.63±
27-31	0.236	0.085	0.041	0.082	0.082	0.063

Characteristics	Healthy	Patient-I	Patient-II	Patient-III	Patient-IV	Patient-V
M.C.H.C (g/dl)	33.00±	32.73±	33.00±	34.08±	32.80±	32.40±
32-36 (g/dl)	0.082	0.085	0.071	0.111	0.041	0.071
Hemoglobin A1 (%)	96.03±	95.83±	90.75±	96.03±	96.43±	96.40±
95.0-99.0 (%)	0.085	0.048	0.065	0.085	0.085	0.071
Hemoglobin F (%)	1.600±	1.000±	6.200±	1.400±	0.600±	0.600±
< 2.0 (%)	0.041	0.041	0.041	0.082	0.041	0.041
Hemoglobin A2 (%)	3.200±	3.200±	3.100±	2.600±	3.000±	3.025±
< 3.7(%)	0.041	0.041	0.041	0.082	0.041	0.025
WBC (u/l)	7.800±	5.255±	7.925±	3.920±	2.490±	1.222±
4.0-10 (u/l)	0.041	0.016	0.031	0.012	0.022	0.010
Neutrophils (%)	59.93±	64.98±	55.48±	32.43±	26.75±	42.63±
40-75 (%)	0.214	0.085	0.085	0.063	0.065	0.125
Lymphocytes (%)	28.00±	25.33±	34.70±	57.40±	64.80±	42.28±
20-45 (%)	0.082	0.063	0.071	0.147	0.141	0.103
Monocytes (%)	4.188±	6.525±	6.725±	9.425±	3.975±	6.300±
2.0-10.0 (%)	0.010	0.048	0.063	0.085	0.048	0.082
Eosinophils (%)	2.500±	2.700±	2.700±	0.400±	4.025±	8.175±
1.0-6.0 (%)	0.041	0.041	0.041	0.041	0.063	0.063
Basophils (%)	0.225±	0.600±	0.500±	0.325±	0.425±	0.575±
< 1 (%)	0.025	0.041	0.041	0.025	0.025	0.025
Platelet count (10^9/l)	202.0±	183.5±	314.0±	180.5±	421.0±	399.0±
150-400 (10^9/l)	2.614	0.646	0.913	2.533	3.136	2.483
ESR (mm/1hr)	11.00±	76.50±	24.75±	22.00±	85.00±	16.25±
0-25 (mm/hr)	0.408	1.041	0.250	0.408	0.408	0.250

Some thalassemia understanding indicated high and some thalassemia tolerant demonstrated low estimations of hematological attributes than solid individual qualities like monocytes, eosinophils, basophils, lymphocytes, hemoglobin A1, hemoglobin F and hemoglobin A2. Level of ferritin was very high in all beta thalassemia patients than healthy ones. These levels reflect inadequate chelation and vulnerability to develop iron overload related complications. The serum ferritin level increases as the frequency of blood transfusion and the age of the patient increases. Liver enzyme (SGPT) values were high in beta-thalassemia understanding. Vitamin D level was very low in beta thalassemia patients, high prevalence of vitamin D deficiency was seen in beta thalassemic patients that may largely contribute to their bone diseases.

Table 2. Analysis immunochemistry parameters among β-thalassemia major patients

Characteristics	Healthy	Patient-I	Patient-II	Patient-III	Patient-IV	Patient-V
Vitamin D Total (ng/mL)	10.12±	3.455±	5.354±	4.224±	2.999±	6.652±
RF values (ng/mL)	0.287	0.125	0.126	0.129	0.125	0.085
Serum Iron (ug/dl)	120.4±	129.8±	191.3±	158.3±	252.6±	186.5±
33.0-193.0 (ug/dl)	29.53	1.631	1.350	0.558	1.459	0.898
Serum TIBC (ug/ml)	289.8±	202.8±	218.0±	146.0±	245.0±	211.5±
250-400 (ug/dl)	2.056	2.250	1.871	1.291	1.472	1.323
Ferritin (ng/ml)	180.3±	4469±	1971±	3561±	7475±	1520±
20-200 (ng/mL)	1.652	3.894	4.697	4.029	1.652	3.708
Transferrin Saturation (%)	58.28±	63.75±	88.25±	108.0±	101.8±	87.60±
RF values (%)	0.782	0.323	0.722	1.472	1.784	0.704
Serum Bilirubin total (mg/dl)	0.610±	0.770±	1.686±	1.405±	1.453±	0.478±
0.10-1.00 (mg/dl)	0.013	0.004	0.015	0.013	0.006	0.013
Serum bilirubin Direct (mg/dl)	0.268±	0.250±	0.370±	0.370±	0.490±	0.200±
≤ 0.3 (mg/dl)	0.017	0.004	0.008	0.008	0.004	0.008
Serum Bilirubin Indirect (mg/dl)	0.7	0.52	1.33	1.0125	0.96	0.2825
0.25-0.9 (mg/dl)	0.008165	0.01225	0.0082	0.02175	0.008165	0.00854
Plasma Glucose Random (mg/dl)	120	76.25	73.25	89.25	135.25	91.5
80-160 (mg/dl)	0.816497	0.85391	0.25	0.62915	1.108678	0.6455
Serum Creatinine (mg/dl)	0.455	0.4375	0.6675	0.25	0.37	0.4075
0.40-0.60 (mg/dl)	0.012583	0.00479	0.0085	0.00816	0.007071	0.00854
Blood Urea (mg/dl)	27.75	18.5	23.25	18	17.75	18.25
15-50 (mg/dl)	0.478714	0.6455	0.4787	0.40825	0.478714	0.25

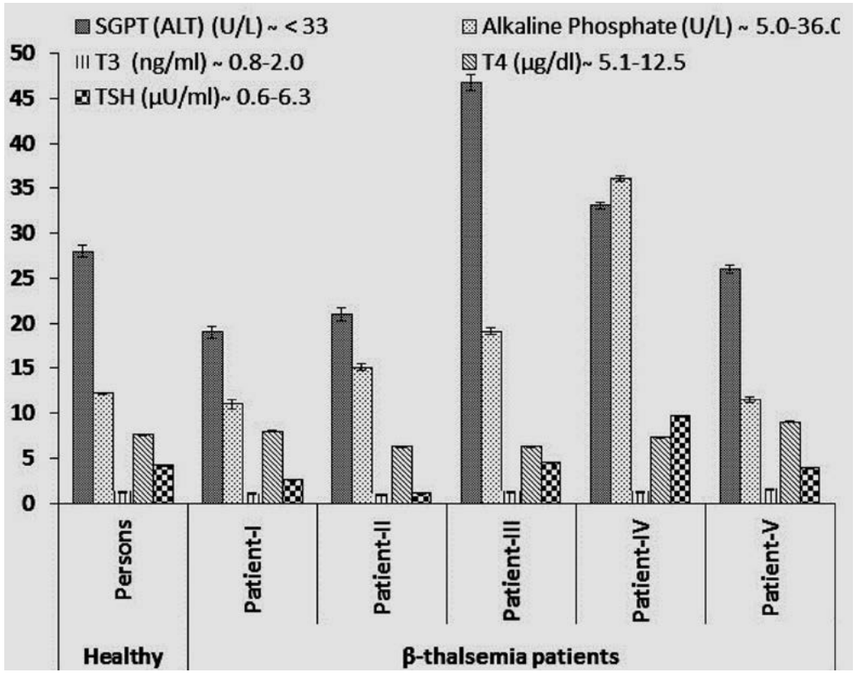

Figure 1. Analysis of thyroid profile and reno-hepatic enzymes activities assessment in the β-thalassemia major patients

The β-thalassemia major is identifiable with the estimation of hematological parameters (Hemoglobin, hemoglobin A1, hemoglobin and hemoglobin A2). In this study, all selected patients were affected with β-thalassemia major. Severely affected hematological values (Hemoglobin, HCT, MCV, MCHC, WBC and platelets) were observed; and also affected immunochemistry values (Ferritin, vitamin D, serum bilirubin total, serum bilirubin direct, serum bilirubin indirect, SGPT). Beta thalassemia major patients have conceded advancement and metabolic abnormalities that means the criticalness of remedial interventions. The closeness of these varieties from the standard may be a result of iron over-over-burden and poor nutritional diet. [16]

Liver enzyme (SGPT) values were high in beta thalassemia because Iron over-burden (Ferritin) is a primary driving reason for raised liver proteins and it causes liver sickness, rheumatoid joint aggravation, ailment and hepatic HCV. [17-18] Bone maladies likewise happen in beta thalassemia quiet because of deficiency of nutrient vitamin D. [19]

CONCLUSION

Pre-birth screening either thalassemia ailing or transporter and their sub-sequent offspring can be a most ideal approach to decrease the continuous recurrence of thalassemia, just by demoralizing the cousin marriages. Now days, stem cell transplant can cure it, but it is

a serious procedure with many risks and won't benefit everyone with the condition. Doctors and scientists are working on developing gene therapies and other treatments to help people with beta thalassemia.

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ORIGINAL ARTICLE

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PRELIMINARY LEVEL STUDIES ON DIABETIC RETINOPATHY AMONGST DIAGNOSED AND UNDIAGNOSED DIABETIC PATIENTS

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ABSTRACT

An attempt has made to investigate the disorder, diabetic retinopathy among the diabetic patients belonging to Hyderabad and its adjoining areas. In this context, the cases of diabetic retinopathy were investigated according to the questionnaire from the different hospitals of Hyderabad, Jamshoro and Tando Muhammad Khan. The investigations were made with the help of different tests like, Fundoscopy and Optical Coherence Tomography (O.C.T). It was concluded from the results achieved that majority of the diabetic retinopathy was due to heredity. Most of the patients had high blood pressure with hyperglycaemia and pain in bones, whereas, in some patients obesity with hyperglycaemia and high blood pressure was also prevailed. As far as the vision is concerned most of diabetic patients had blurry vision whereas, short and long sightedness was also found in many patients. Majority of the patients involved in this disorder having type 2 diabetic mellitus (INDDM).

Keywords: Diabetes mellitus, Diabetes retinopathy, Hyperglycemia, Insulin, Preliminary.

INTRODUCTION

Pancreas is an endocrine as well as exocrine gland. The endocrine secretions of pancreas are responsible for maintaining body's sugar levels. The most common disease resulting from impaired pancreatic hormone release is diabetes mellitus. [1] The 2 forms of diabetes, type 1 and type 2 are characterized by impaired insulin release. Type 1 diabetes is an autoimmune disorder also known as insulin – dependent diabetes (juvenile- onset diabetes) is the result of impairment of beta cells in younger people. Type 2 diabetes results in irregular secretion of insulin hormone and accounts for more than 90% of diabetes cases. It usually presents in obese adults. [2-3]

The diabetic retinopathy is a major public concern. It is a diabetic eye disease resulting from chronic high blood glucose levels causing damage to the retinal capillaries. It is the most common microvascular complication of diabetes mellitus. [5-7] Diabetic retinopathy is the leading cause of vision loss in working age adults. It is one of the most common causes of blindness in adults between 30 and 65 years of age in developed countries. It causes damage to the retina. The eyes are organs of sight enabling us to encounter shape, colour and movements of objects and persons around us. [8]

The inner most sensitive layer of eye is the retina. The cells in the retina namely Rods and Cones help in the formation of image on retina above the point of entry of optic nerve called blind spot. Diabetic retinopathy occurs when blood glucose level changes in retinal blood vessels. In some cases, these vessels will swell up and leak fluid into rear of the eye. [9-11] In other cases, abnormal blood vessels will grow on the surface of retina. The progression of significant diabetic retinopathy may occur without symptoms. There are two types of diabetic retinopathy: Non-proliferative and proliferative. In non-proliferative diabetic retinopathy, the initial visible lesions are micro aneurysms that form on the terminal capillaries of retina. Increased permeability of the capillaries is manifested by the leaking of proteinaceous fluid, causing hard exudates. Dot and blot haemorrhages occur from the red blood cells. These finding by themselves do not lead to visual loss and are categorized as non proliferative retinopathy. Proliferative retinopathy by contrast, develops when the retinal vessels are further damaged, causing retinal ischemia. The ischemia triggers new fragile vessels to develop a process termed neovascularisation. These vessels may grow into the vitreous cavity and may bleed into the pre retinal area or vitreous, causing significant vision loss. Loss of vision also may result from retinal detachment which often accompanies neovascularisation. [12-15]

The purpose of present study is to collect the information about retinopathy in diabetic patients belonging to Hyderabad city and its adjoining area. The emphasis of present study will also be on all the patients who are suffering from this disorder regardless of type hyperglycaemia or hyperglycaemia subjects. The present study shall hopefully give us an understanding about this disorder and the information sought will be use d in the society for getting preventive measures to get rid of the problem.

PATIENT AND METHODS

An attempt was made to collect the information about the diabetic retinopathy in the patients attending the hospitals of Hyderabad, Jamshoro and Tando Muhammad Khan. In this context 40 patients of diabetic retinopathy were interviewed according to a questionnaire prepared to collect the information about the diabetic disorder. In order to collect the information about eye different tests like, Fundoscopy and optical coherence tomography (O.C.T) was conducted by this we had the actual condition of the eye that is affected by the diabetic pathology. All the information with regard to the retinopathy was aggregated in the table form and then interpreted accordingly.

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RESULTS

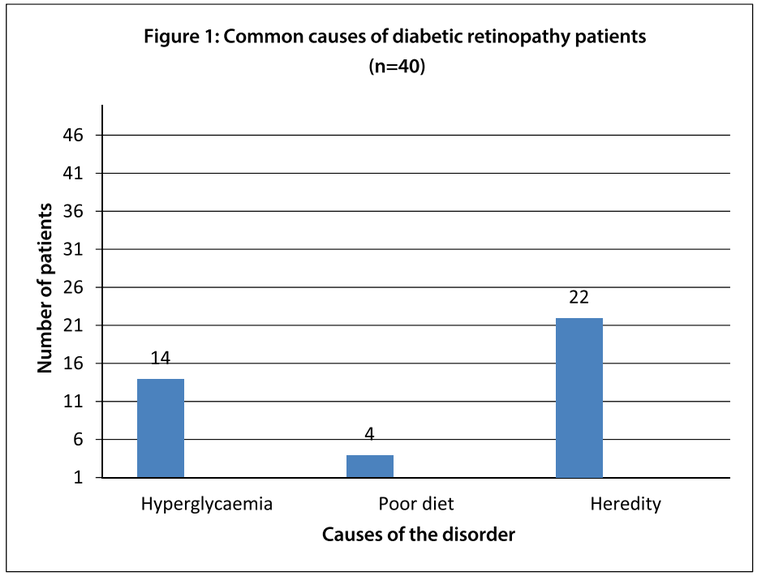

Figure 1 explains that as per data / information collected from different hospitals with respect to the diabetic retinopathy , the result indicates that from 40 patients examined 14 patients involved in diabetic retinopathy were hyperglycaemic whereas, in only 04 from all the patients examined, the disorder was developed due to poor diet. In rest of 22 patients as per their version and other diagnostic causes of the disorder retinopathy was heredity.

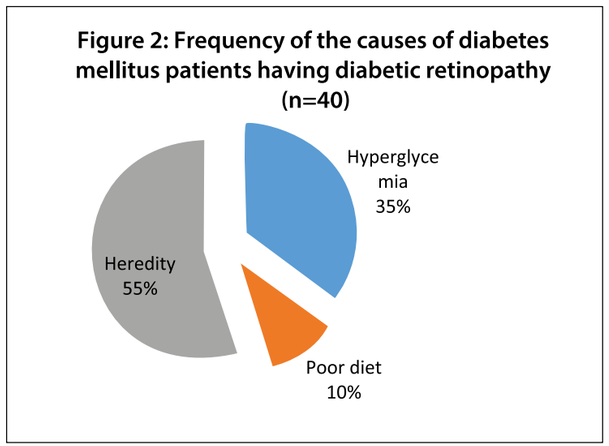

Figure 2 shows that the causes of diabetic retinopathy in percentage (%) are: 55% Heredity, 35% Hyperglycaemia and 10 % poor diet.

Table 1 showing duration of the disorder of the disorder of the patients investigated (n=40)

Number of Patients	Duration of Disease
2	5 Years
4	6 Years
2	9 Years
8	10 Years
2	11 Years
6	12 Years
2	13 Years
2	14 Years
6	15 Years
2	18 Years
2	20 Years
2	30 Years

Table 1 explains, as far as the age is concerned, the diabetic retinopathy was developed in the individual during different ages. From all the 40 patients, 8 patients having diabetes since 10 years, 06 patients having diabetes since 12 years, whereas 06 patients suffering from the same disorder since 15 years. However, rest of the patients examined were found involved with diabetes for 1-2 years.

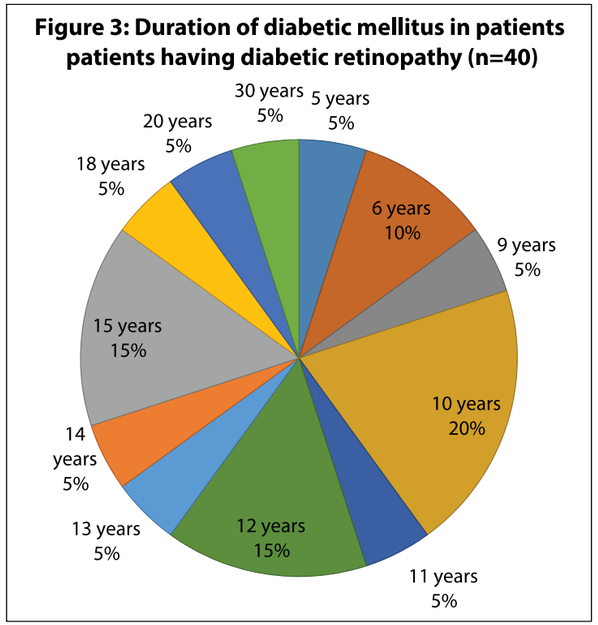

Figure 3 shows the % ratio of the duration which is minimum 5 years of duration 5% and the maximum 10 year duration 20%

Table 2: Clinical features in patients of diabetic retinopathy (n=40)

Number of Patients	Symptoms
12	Obesity, hyperglycaemia, high blood pressure.
4	Obesity, high blood pressure, swelling in hands and feet.
16	High blood pressure, hyperglycaemia, pain in bones.
4	Obesity, pain in joints, anaemic
4	Obesity, high blood pressure, nephropathy

Table 2 reveals that 16 patients out of 40 patients have suffering from high blood pressure, hyperglycaemia, and pain in bones; whereas, 12 patients were suffering from obesity, hyperglycaemia, and high blood pressure. Remaining 12 patients of DR patients had pain in joints, high blood pressure and nephropathy whereas obesity is common in all 06 patients. It was therefore concluded from this data about the prevalence of disorders in retinopathic subject that most common factor in diabetic retinopathy is the hyperglycaemia whereas; the obesity is also the cause of the diabetic retinopathy but at the secondary level.

Table 3: Patients of diabetic retinopathy having common visual problems (n=40)

Number of Patients	Visual problems
6	Blurry vision, long sightedness, short sightedness.
14	Blurry vision
12	Short sightedness, long sightedness
4	Blurry vision, dark spots
4	Vision loss

Table 3 reveals that 14 patients out of 40 patients of diabetic retinopathy had blurry vision, while 12 patients had long sightedness/ short sightedness. The 06 patients were suffering from blurry vision, long sightedness/ short sightedness; whereas, the other 04 patients had blurry vision with dark spots on retina of eyes. Remaining patients of diabetic retinopathy which are 04 in number had completely loss their vision. As per data is concluded the results of the vision difficulty in the shape of blurry vision were common problem whereas, the dark spots and complete vision loss was on low level.

Figure 4: Frequency of the type of diabetes mellitus patients having diabetic retinopathy (n=40)

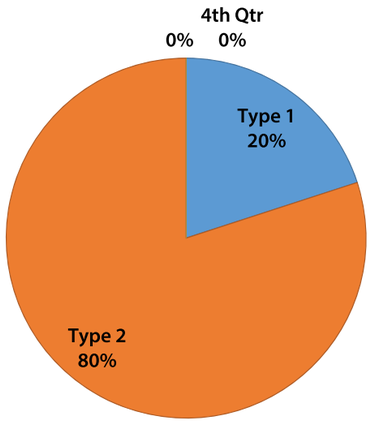

Figure 4 shows that 80% of patients of diabetic retinopathy have Type 2 NIDDM and only 20% of patients have Type 1 IDDM.

DISCUSSION

Our study has shown the different causes of diabetic retinopathy which includes hyperglycaemia, heredity and poor diet. It also includes the duration of the diabetes mellitus in the patients of the diabetic retinopathy which ranges from 5 years to 30 years. It includes the common disorders seen in the patients of the diabetic retinopathy which includes long sightedness, short sightedness, blurry vision and the vision loss. Our study has shown certain figures and results which are uncommon from other studies.

The incidence of diabetic retinopathy was estimated to be 15.7 % in one study. [9] The prevalence of diabetic retinopathy is as high as 55.3 % in a hospital-based study conducted in Karachi. [14] The explanation for this severe incidence variance is that many cases remain underdiagnosed. The prevalence of diabetic retinopathy was found to be 6.5 % of the studied population in a similar study conducted in China, whereas a higher frequency (32%) was seen in Indian patients. [15-16] As with the incidence in western countries, with 4.4 % of visually threatening illness, the US population reported 28.5 % of patients positive for diabetic retinopathy. [17] In a related study conducted in Spain, which showed a prevalence of 12.3 %, markedly distinct results were seen. [18]

In the future, broader spectrum studies are required to determine the frequency of diseases threatening this disastrous vision, and this must be done nationally. There is an immaculate need for extreme steps to spread awareness of this complication on a wider scale to patients suffering from diabetes, so that more people can be diagnosed earlier and can be tracked during the course of the disease.

Our research has a range of limitations. The data obtained in our research came from limited areas, which contributes to bias may effect sampling, since our study does not target all people in a group. In our research the

primary basis for the early or late development of the disease was not considered to be the disposition of jobs or educational status.

CONCLUSION

To sum up the present prevalence of diabetic retinopathy, a severe progressive vision threatening condition is described in this study. However through early diagnosis and timely treatment, this complication of diabetes can be prevented.

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ORIGINAL ARTICLE

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PREOPERATIVE SCREENING FOR BLOOD-BORNE INFECTIONS – ESSENTIAL TOOL FOR PATIENTS AND HEALTHCARE PROFESSIONALS

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ABSTRACT

INTRODUCTION: Universal preoperative blood-born HIV virus, HBV, HCV testing has been identified as a universal precautionary risk mitigation strategy. As a universal measure, safety kits are for the surgical team and post-exposure prophylaxis as further protection is mandatory. For patients prior to the onset of AIDS/liver cirrhosis/ hepatocellular carcinoma, early diagnosis of the disease and its treatment is often helpful. The purpose of this analysis was the measurement of HIV/HCV/ HBV seroprevalence for successful control programmes. The aim of this study was to examine the magnitude of viral infections as a global health problem, affecting millions around the world.

PATIENTS AND METHODS: In collaboration with the Department of Pathology of the Indus Medical College Hospital, the research was carried out in the Department of Surgery and Allied, Indus Medical College Hospital Tando Muhammad Khan. This analysis is a prospective study for the period from January 2019 to September 2019. Both patients admitted to elective/emergency surgery in the surgery department or those treated conservatively were included in the report. Visitors to The follow-up were excluded.

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RESULTS: A total of 305 patients admitted to the surgery department have been screened for HBV, HCB and HIV. Hepatitis C (HCV) was a common infection, followed by HBV, but there were also co-infections. The common age group affected was 21-50 years, with a male: female 3.28:1 ratio.

CONCLUSION: As part of routine pre-operative investigations, screening for HIV, HBV and HCV is mandatory in tertiary care centres in order to determine their prevalence and to prepare better preventive strategies.

KEYWORDS: Preoperative, hepatitis B, hepatitis C, human immunodeficiency virus, screening.

INTRODUCTION

Among those infections with Hepatitis B virus (HBV), Hepatitis C virus (HCV) and Human Immunodeficiency Virus (HIV), infections with different types of microorganisms such as bacteria, viruses, fungi, and parasites are normal in the Pakistan scenario. A leading cause of morbidity has emerged. Co-infection leads to the fact that the hepatitis virus and HIV share common routes of transmission. [1-3] Personnel in health care that have blood exposure are at risk of HCV infection. In co-infection, the presence of one virus affects the other virus's natural history. Serology-surveys are one of the key methods of determining the prevalence of HBV, HCV virus that can be used. Around 130-150 million individuals are chronically infected with liver cirrhosis and/or liver cancer and are at risk of developing it. More than 700,000 individuals suffer from liver diseases linked to hepatitis C. The high screening risk category is close to HBV. Hepatitis C does not always need treatment as the immune response will clear the infection in some individuals, and liver damage will not occur in some carriers of chronic infection. Hepatitis C treatment to date has been focused on 48 weeks of interferon and ribavirin injection therapy (expensive and risky). New DAA (direct antiviral agents) drugs have recently become much more effective, safer, shorter (12 weeks) and with a high cure rate. There is no HCV vaccine, but avoidance is compulsory. [4-5] AIDS, the acquired condition of immune deficiency, is a lethal disease caused by a retrovirus known as the human immunodeficiency virus (HIV) that makes the body of the person prone to life-long life-threatening opportunistic infections. In 2015, 2.1 million people were reported to be infected with HIV, with a reported 86,300 new HIV infections. The HIV prevalence was 0.26% (0.30% in men and 0.22% in women) in adults (15-49years). AIDS-related deaths have begun to show decreasing patterns with the country's rapid expansion of access to ART. Out of 2.1 million estimated cases in 2015, 1.4 million were diagnosed with HIV and 747,175 of these were treated with ART. [6] Post-exposure prophylaxis (PEP) for HIV consists of a comprehensive range of resources to prevent the development of infection in an exposed person, including: first aid care; therapy and risk evaluation; HIV testing and therapy; and the provision of antiretroviral medications, help and follow-up in the short term (28 days), depending on the risk assessment. [7] The purpose of this analysis was the measurement of HIV/ HCV/ HBV seroprevalence for successful control programmes.

PATIENTS AND METHODS

In the Department of Surgery, Indus Medical College Hospital Tando Muhammad Khan, this study was carried out. Both patients admitted for emergency and elective surgery and for conservative care are included in this report. This is a prospective form of research performed from January 2019 to September 2019 over a period of 9 months. As part of routine pre-operative investigations, screening for HIV, HBV and HCV is mandatory in tertiary care centres in order

to determine their prevalence and to prepare better preventive strategies:

- To avoid transmission to the surgical community.
- Universal precaution by the use of improved personal protective devices (PPE).
- Prophylaxis Post-Exposure (PEP).
- Medical therapy and further treatment of diseases.

The serum has been obtained and tested for serological tests using the normal prescribed protocol. HBsAg, Anti-HCV and HIV were measured using CLIA technology. Instead of vaccination/ interferons, ribavirin therapy, the, patients with sero-positivity for HBV and HCV are referred to physicians for therapy and further management. Using SPSS software for statistical analysis using descriptive statistics, results were obtained.

RESULTS

Tables 1 and 2 indicate that of 305 patients, 30 (9.83%) were seropositive for HBV, HCV and HIV in total. In 12 cases (3.93%) in which 09 were males and 03 were females, the hepatitis B surface antigen was tested positive. In 15 (4.91%) of which 11 were males and 04 were females, the Hepatitis C virus was positive. In 3 cases of co-infection were males. Majority of seropositive patients belonged to age group of >50 years. Hepatitis C (HCV) 15/30(50%) was the most prevalent infection, followed by HBV 12/30 (40%).

Table 1: Distribution of Infection in Pre-Operative Screening of Surgical Patients (n=305)

Infections	Males (n=156)	Females(n=49)	Total (n=105)	Percentage (%)
HBV	09	03	12	3.93
HCV	11	04	15	4.91
HIV	00	00	00	00
HBV + HCV	03	00	03	0.98
Total	23	07	30	0.83

Table 2: Pre-Operative Screening in Age Wise Groups (n=305)

Age Group (years)	HBV	HCV	HIV	HBV+HCV	Total	Percentage (%)	p-value
<20	02	02	00	00	04	13.33	<0.001
21-50	02	03	00	00	05	16.66	
>50	08	10	00	03	21	70	

DISCUSSION

Pakistan has a 1-3% comparable prevalence of Hepatitis B, according to the World Health Organization (WHO). Hepatitis C seroprevalence has variable distribution in various regions of Pakistan with approximate of 3%. [8] In our sample, HCV is 4.91% seroprevalent. In Pakistan, 12 million people are suffering from hepatitis infection. Analysis of our findings showed that the most important variables for HIV/HBV/HCV prevalence rates were age and sex (Tables 1 and 2). Male age groups of 21-5 years: female 2.3:1 ratio had higher prevalence due to higher sexual activity, exposure to the environment, and behavioural factors. [9]

Since admission to follow-up, universal HBV, HCV, and HIV screening with positive patients and the surgical team needs expected management strategies. In terms of illness, treatment, prevention, cost improvement and impaired result, patients and their families should be adequately advised. Patients should be adequately treated with ART (HIV), INTERFERON / DAA (HCV), and HBV vaccines if no emergency exists. The surgical team can use personal protective equipment (PPE) in emergency situations. If someone inadvertently gets exposure by needle stick injury or sharp object (NSI) hacking, exposure to blood/ body fluid (BBF), unfixed tissue and organs, recapping needles should not be overlooked and carefully handled as follows: Wash the wound with water immediately and do not use scrub or antiseptics, thoroughly wash after splash of blood / body fluid, and irrigate the eye with water or regular saline. Hepatitis B Immunoglobulins (HBIG) - HBIG should be administered as soon as possible (ideally within 6 hours and not longer than 48 hours) after an unintentional inoculation. At the same time, for HBsAg examination, the blood of the victim is drawn. If the test is negative, the vaccine should be started immediately and the full course (1 ml of adult formula 0, 1 month and 6 months) should be given. If the surface antibody test is positive, no further action is taken. Administer a booster dose of the hepatitis B vaccine to a previously vaccinated user. If there is exposure to HCV, there is no vaccine or PEP, so treatment must be administered on the basis of Interferon / Ribavirin / and DAA (direct antiviral agents) if the victim has a clinical disease. The rate of HIV seroconversion for percutaneous exposure after an AEB (accidental exposure to blood) is 0.3%. High-risk cases are screened for HIV according to the following schedule for seroconversion monitoring:

1. Base-line HIV test-at exposure period.
2. Repeat checking for HIV six weeks after exposure
   - At 12 weeks,
   - 6 months after exposure,

The patient's partner should also be tested for HIV, HBV and HCV. Positive cases should be forwarded for further management and ART to the NACO/ Helps therapy centre. [10-11]

CONCLUSION

HBV infections, followed by HCV, co-infections and HIV, were more prevalent. In both sexes, the most affected age group was >50years old. HBV is preventable by vaccination and should be implemented in compliance with the compulsory immunisation programme. The awareness campaign could be a preventive measure to vaccinate family members of seropositive patients. Both health care workers should be vaccinated against HBV. No vaccine is yet available for HCV and HIV, so only preventive measures are needed. Active government, educational, and media initiatives on safe sex, blood and blood products from a registered blood bank, the use of disposable consumables

in medical care, and proper management of bio-medical waste should be pursued for population awareness. For HIV, early diagnosis, ART therapy, counselling, spouse screening can be helpful in preventing the progression of the disease to AIDS, apart from preventive steps. For physicians, anaesthetists, interns, nursing personnel and other workers in the health care system, post-exposure prophylaxis as suggested would be preventive.

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MYOPIA AND ITS ASSOCIATED RISK FACTORS IN YOUNG ADULTS

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ABSTRACT

Objective: To determine the risk factors associated with myopia among young adults.

Methodology:
This cross-sectional comparative study was conducted by Physiology and Medicine Departments of Indus Medical College, TMK from October 2018 to March 2019 by non-probability purposive sampling. For this research, medical students of IMC TMK, already suffering from myopia enrolled after informed and written consent and all these students provided with self-structured proforma to determine the associated risk factors. This study was conducted on total 119 medical students (n=119), and divided in two groups according to presence of myopia, i.e., sixty-three (n=63) with myopia and fifty-six with no myopia (n=56) for comparison of associated risk factors. Students suffering from astigmatism, hypermetropia, hypertension, diabetes mellitus and refractive dysfunction other than myopia were excluded for this research study. Ethical approval was taken from the institutional ethics committee. All the data entered and analyzed by IBM SPSS version 20.0.

Results: Among total one hundred and nineteen study participants (n=119), 63 (52.9%) were the diagnosed cases of myopia and were using the glasses for myopia. To determine the association with risk factors fifty-six (47.1%) students with no myopia were selected for comparison to those with myopia (n=63). Out of sixty-three myopic participants, 37.0% were in the age group of 21-23 years. While 32.8% study participants who were in age group

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of 18-20 years, were not sufferers of myopia. Among sixty three cases of myopia (n=63), 43(36.1%) were females while 20 (16.8%) were males; while out of 56 non-myopic individuals (n=56), 38 were males and 18 were females. (p-value <0.01). Among sixty-three myopia patients, 57(47.9%) were reading >3 hours and out of 56 non myopic participants, 30 (25.2%) were reading/ writing for <3 hours. Reading or writing in hours compared between having myopia and having not myopia (p-value <0.01). Likewise, duration of watching television from near distance also compared between two groups, myopia (n=63) and no myopia (n=56) by Chi-square test. P-value was revealed (<0.01). Similarly, smart phone use time in hours compared between having myopia and having not myopia (p-value <0.01). Among sixty-three myopia patients, 56(47.1%) were using android/smart phone for >2 hours and out of 56 non myopic participants, 36 (30.3%) were using smart phone for <2 hours. When myopia related to family history there was close to significant association with positive family history.

Conclusion: This has been concluded that age, gender, reading/writing with near distance, android smart phone use for longer duration, watching television from short distance and longer duration as well as positive family history are the risk factors significantly associated with myopia.

Key words: Myopia, risk factors, young adults, near distance reading/writing, mobile use

INTRODUCTION

Myopia, also called as short sightedness is increasing globally and this may disrupt the psycho-social development as well as the way of life. The causes of upsurged prevalence are not still entirely clear, even though genetic as well as the environmental aspects are supposed to show a part.[1] Prevalence of myopia in a research study was appraised as 37 % among Pakistani populace.[2] One of the research studies has confirmed an advanced prevalence of myopia among younger age group as compared to the older individuals, and the risk factors that were found to be significantly linked were significant education and socioeconomic aspects.[3] Elder age individuals, advanced education, parental myopia, extra-close work, reduced outdoor, and the raised trend of urbanization are suspected to be self-determining predictors of myopia.[4-5] Investigating such risk factor associations might be helpful in guiding anticipatory community health programs and plans.[6] Myopia is one of the rising problems affecting large percentage of earlier age population and resultant sight deficit can only be corrected by spectacle.[7] Visual dysfunction is the recent global challenge to be controlled timely for the socioeconomic as well as the authorities dealing with public health of community/country. According to the recent Global Burden of Disease Study 2015, visual and hearing impairments are graded second afterward low backache and neck pain among the all-age causes for years lived with disability worldwide.[8] Good vision is vital for healthy life style whereas blurry indistinct vision might prime to grievances, difficulties in driving, injuries as well as way towards depression.[9] In the year 2016, Holden et al.[10] assessed about worldwide status of myopia that was 1.406 billion individuals i.e., 22.9% of the world populace found to be suffering from myopia with 163 million individuals of high myopia. It was further estimated for year 2050, there will be chances of 4.758 billion people with myopia (49.8% of the total world's population), and 938 million will be of high myopia. Understanding the various factors linked to myopia might help to clarify the mechanism of myopia formation and also to formulate reasonable preventive and control measures of myopia to protect people's quality of life due to vision. This study has been designed to determine the risk factors associated with myopia among young adults.

PATIENTS AND METHODS

This was a cross-sectional comparative study conducted by Physiology and Medicine Departments of Indus Medical College, TMK from October 2018 to March 2019 by non-probability purposive sampling. For this research, medical students of IMC, TMK, already suffering from myopia enrolled after informed and written consent and all these students provided with self-structured proforma to determine the associated risk factors. For comparison of risk factors, non-myopic students with good vision also included. Myopia is actually refractive disorder of the non-accommodated eye with a spherical equivalent of –0.5 dioptre (D) or lower.[11] This study conducted on total 119 medical students (n= 119), and divided in two groups according to presence of myopia, i.e., sixty-three (n=63) with myopia and fifty-six with no myopia (n=56) for comparison of associated risk factors. Students suffering from astigmatism, hypermetropia, hypertension, diabetes mellitus and refractive dysfunction other than myopia were excluded for this research study. Ethical approval was taken from the institutional ethics committee. All the data entered and analyzed by IBM SPSS version 20.0.

RESULTS

Among total one hundred and nineteen study participants (n=119), 63 (52.9%) were the diagnosed cases of myopia and were using the glasses for correction of refractive disorder. Fifty-six (47.1%) students with no other refractive disorder and no myopia (n=56) were selected for comparison to those with myopia (n=63). Out of 63 myopic participants, 37.0% were in the age group of 21-23 years. While 32.8% study participants who were in age group of 18-20 years, were not sufferers of myopia (Table 1). Among sixty three cases of myopia (n=63), 43 (36.1%) were females while 20 (16.8 %) were males; while out of 56 non-myopic individuals (n=56), 38 were males and 18 were females (p value <0.01) (Table 2). Among sixty-three myopia patients, 57(47.9%) were reading >3 hours and out of 56 non myopic participants, 30 (25.2%) were reading/ writing for <3 hours. Reading or writing in hours compared between having myopia and having not myopia (p-value <0.01) (Table 3). Similarly, smart phone use time in hours compared between having myopia and having not myopia (p-value <0.01). Among sixty-three myopia patients, 56(47.1%) were using smart phones for >2 hours and out of 56 non myopic participants, 36 (30.3%) were using smart phone for <2 hours (Table 4).

Likewise, duration of watching television from near distance also compared between two groups, myopia (n=63) and no myopia (n=56) by Chi-square test. P-value was revealed (<0.01) (Table 5). In assessing myopia related to family history, there was close to significant association with positive family history (p-value =0.05) (Table 6).

Table 1: Association of myopia with age groups (n=119)

			Age			Total
			18 -20 years	21-23 years	>23 years	
Myopia	Yes	Count	10	44	9	63
		% of Total	8.4%	37.0%	7.6%	52.9%
	No	Count	39	16	1	56
		% of Total	32.8%	13.4%	.8%	47.1%
Total		Count	49	60	10	119
		% of Total	41.2%	50.4%	8.4%	100.0%

Pearson chi square value=36.34 with df=2 p value <0.01

Table 2: Association of myopia with gender(n=119)

			Gender		Total
			Male	Female	
Myopia	Yes	Count	20	43	63
		% of Total	16.8%	36.1%	52.9%
	No	Count	38	18	56
		% of Total	31.9%	15.1%	47.1%
Total		Count	58	61	119
		% of Total	48.7%	51.3%	100.0%

Pearson chi square value: 15.47, df=1 and p value <0.01

Table 3: Association of myopia with near distance reading/writing time (n=119)

			Near distance readingorwriting			Total
			3 hours	<3 hours	>3 hours	
Myopia	Yes	Count	5	1	57	63
		% of Total	4.2%	.8%	47.9%	52.9%
	No	Count	4	30	22	56
		% of Total	3.4%	25.2%	18.5%	47.1%
Total		Count	9	31	79	119
		% of Total	7.6%	26.1%	66.4%	100.0%

Pearson chi square value: 16.19, df=2 and p value <0.01

Table No. 4: Association of myopia with duration of smart phone use (n=119)

			Smart phoneuse			Total
			2 hours	<2 hours	> 2 hours	
Myopia	Yes	Count	6	1	56	63
		% of Total	5.0%	.8%	47.1%	52.9%
	No	Count	6	36	14	56
		% of Total	5.0%	30.3%	11.8%	47.1%
Total		Count	12	37	70	119
		% of Total	10.1%	31.1%	58.8%	100.0%

Pearson chi square value=36.34 with df=2 p value <0.01

Table 5: Association of myopia with near distance watching television time (n=119)

			Near distance watchingtelevision			Total
			3 hours	<3 hours	>3 hours	
Myopia	Yes	Count	12	5	46	63
		% of Total	10.1%	4.2%	38.7%	52.9%
	No	Count	46	0	10	56
		% of Total	38.7%	.0%	8.4%	47.1%
Total		Count	58	5	56	119
		% of Total	48.7%	4.2%	47.1%	100.0%

Pearson chi square value =47.82, df=2 and p value <0.01

Table No. 6: Association of myopia with family history (n=119)

			Family History		Total
			Yes	No	
Myopia	Yes	Count	24	39	63
		% of Total	20.2%	32.8%	52.9%
	No	Count	31	25	56
		% of Total	26.1%	21.0%	47.1%
Total		Count	55	64	119
		% of Total	46.2%	53.8%	100.0%

Pearson chi square value 3.54, df=1 and p value=0.05

DISCUSSION

Myopia is demarcated as near sightedness instigated byinaptness between power of the optical parts of eye and the axial length. In this condition, image of the object projects in front of the retina, that's why corrective glasses or lenses are acquired for displacing the image somewhat backward on retina for clear retinal image. The causes of myopia are still unclear, instead some are suspected to be involved are genetical as well as modifiable life style/ environmental factors. [12] This has been fore told that, by year 2060, therewill be 26% chances of visual disability, which will have undesirable and damaging effects on their academic performance as well as psychosocial expansion. [13] In summary, myopia not only affects the physical and mental health of individuals but also puts a great burden on society. Myopic adolescents are more likely to be anxious than those without myopia. [14] This research project is designed to determine the risk factors linked to myopia among young medical students. This study revealed significant association of risk factors like age, gender, near distance reading/writing, duration of using mobile phone, watching television from near distance, and family history with myopia. Consistently revealed by Alvarez-Peregrina et al. [15] that there is impact of near distance doings i.e., reading, writing as well as viewing television, in the expansionto myopia. Life style bears linear impact on advance to myopia. One of the Saudi study revealed the prevalence of refractive dysfunctions as 45.8% and the maximum one was discovered as myopia i.e., 24.4%, next were hypermetropia (11.9%) as well as astigmatism (9.5%). [16] Sherwin et al. [17] similar to this study, established that those who were at work from a distance of < 30 cm bear almost twice chance of myopia when compared to those working from extensive distances. They also further discovered positive association of myopia with duration of reading. Some of the studies have also found linear association of myopia with higher levels of education. [18-19] In this research study, in assessing myopia related to family history, there was close to significant association with positive family history. This is similar to a Chinese study that revealed about seemingancestral accretion of myopia; might be made known by raised ratio of maternal as well as paternal myopia. This Chinese study found twice to thrice risk of developing myopia among those having positive family history for myopia.[21] Further more, similar to this study, duration of spending time on digital screen has also been quoted as the most likely modifiable ecological risk factor that can upsurge risk of myopia. [21] Myopia may disturb the quality of life and forth coming academic future of young adults. This further may progress to sight threatening complications like retinal detachment, cataract, open angle glaucoma and others. So, identifying these risk factors timely and then controlling these modifiable risk factors early may prevent from future burden of visual dysfunction and so this way next future of young adults towards bright future.

CONCLUSION

This has been concluded that age, gender, reading/writing with near distance, android smart phone use for longer duration, watching television from short distance and longer duration as well as positive family history are the risk factors significantly associated with myopia.

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REVIEW ARTICLE

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SEROLOGY AS PRECISE DIAGNOSTIC TOOL IN COVID-19

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ABSTRACT

Since its origin in Wuhan, China in the last week of December 2019, the coronavirus infectious disease-2019 (COVID-19), caused by the β-Coronavirus, dubbed SARS-CoV-2 has been a global pandemic affecting 212 countries and territories worldwide spanning all five continents. For its management and eradication, prompt and accurate diagnosis of the disease is central. For the diagnosis of SARS-CoV-2 in respiratory clinical specimens, real-time polymerase chain reaction (real-time PCR) using dual labelled TaqMan probe and targeting two genomic areas, typically RdRp and envelope (E) regions, of the virus is commonly used.

Since the stage of the infection cannot be determined during the collection of respiratory nucleic acid test specimens (NAT; RT-PCR), this can lead to false negatives (omission error) as the load of the virus in the respiratory exudates and the saliva progressively decreases with the increase in post-infection time. During clinical sickness that follows an incubation period of normally up to ~14 days, virus excretion will be maximum and clinical samples collected during this period are appropriate for PCR diagnosis than those collected after clinical sickness. In addition, there are other variables that can influence the accuracy of the test result, such as the quality of swabs and virus transport medium, PCR protocol and reagents, enzyme inhibitors, and man power competence engaged in executing diagnostic techniques. In COVID-19, viz., there are three clinical sickness classes: Asymptomatic, symptomatic, moderate and severely symptomatic. Available data indicate that, as was observed in the case of the COVID-19 infected Japan cruise ship 'Diamond Princess' with 3,711 people on board, about 50 percent of people exposed to SARS-CoV-2 infection may become asymptomatic. In the case of asymptomatic and moderate symptomatic cases, due to low virus load in the collected clinical specimens, an effective antibody assay must be used to cross-check the negative result in NAT / PCR. It is understood that with the remission of sickness, the virus

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load in the body and the amount of virus excreted in body fluids steadily decreases, whereas the quantum of particular antibody against the virus increases with time until the plateau. The anti-virus antibody stays in the host for a longer period of time and can be identified even after the infection has been eliminated from the body. NAT must also be accompanied by antibody testing to increase diagnostic efficiency and minimise omission errors. In addition, unlike NAT / PCR, the serology / antibody test is a valuable instrument for controlling the spread of viruses, estimating the actual number of cases and population epidemiological mapping of the disease. In addition, the availability of a precise antibody test system / assay will be useful for COVID-19 post-pandemic surveillance. The current review includes the results of the diagnosis of COVID -19 and antibody response kinetics published by various researchers / groups that support the rapid creation of a 'COVID-19 antibody assay' method for use in disease epidemiological studies.

Key words: COVID-19, Epidemiology, SARS-CoV-2, Polymerase Chain Reaction, Serology.

INTRODUCTION

In humans with a median incubation time of 3 days, SARS-CoV-2 triggers an acute viral infection. [1] Coronaviruses (CoVs) are RNA viruses of single stranded positive sense that occur in four genetic forms, namely, alpha-coronavirus, beta-coronavirus, δ-coronavirus, and gamma-coronavirus. Genetic research has shown that SARS-CoV-2 is a Beta-coronavirus (genus) and a genetic cluster of Sarbecovirus (lineage B), along with certain strains of bat virus with a genetic identity of > 96%. A total of seven CoVs causing mild to severe human disease have been identified; 04 with mild cold-causing seasonal circulation (HKU1, NL63, OC43 and 229E), and the remaining 03 are zoonotic ones, i.e., SARS-CoV (2003), MERS-CoV (2012) and SARS-CoV-2 (2019), originating in various bat species and transmitted to humans through an intermediate host; Civet in the case of SARS-CoV, Dromedary Camel in the case of MERS-CoV, and probably Pangolin [2] in the case of SARS-CoV-2, which has a genetic resemblance of approximately 79% to SARS-CoV and just 50% to MERS-CoV. Structural modelling has shown that SARS-CoV-2 binds to ACE2 with more than 10 times the affinity of SARS-CoV, which explains the faster transmissibility of SARS-CoV-2 in humans compared to SARS-CoV, as well as the higher number of confirmed cases of COVID-19 compared to SARS-CoV. [3] COVID-19 's basic reproduction number (Ro) varies from 2-3.3, which also explains its greater transmissibility compared to SARS and MERS. [4-5] As at 05:31 GMT on 24 May 2020, 28,15,429 COVID-19 cases were involved worldwide, affecting 213 countries and territories spanning all five continents (https:/www.worldometers.info/coronavirus/). As of that date and period, there were 1666828, 349113, 335882, 282370 and 73610 active cases in the USA, Brazil, Russia, Spain and India, respectively. Even after timely diagnosis using nucleic acid tests and introduction of social distancing and lockdowns, this shows active virus transmission. In order to map the population(s) exposed to the virus regardless of the outcome of the infection, it is important to examine the sero-epidemiology of the disease / infection at the earliest using effective antibody tests. In addition, in order to minimise the potential spread of the virus infection by such individuals, NAT negative individuals need to be checked by antibody assay(s). Antibody assays using various viral antigens such as RdRp, nucleoprotein, S1 protein, receptor binding domain (RBD) are used to classify and diagnose infected individuals on a small scale in different countries other than India. Reported results of antibody assays against RT-PCR in the diagnosis of SARS-CoV-2 infection are compiled in this study.

CELLULAR INFECTIVITY OF CORONAVIRUS

Coronaviruses (CoV) are a wide family of single stranded RNA viruses of positive sense that cause disease in human beings ranging from common cold to more serious diseases such as Extreme Acute Respiratory Syndrome (SARS-CoV of 2003), Middle East Respiratory Syndrome (MERS-CoV of 2012), and Coronavirus Infectious Disease - 2019 (COVID-19). While infections with SARS-CoV and MERS-CoV have a higher mortality rate than COVID-19, SARS-CoV-2 propagates much faster than the two previous diseases. CoVs of various strains have been known to infect and cause illness in poultry, bovine, porcine, canine and feline animals since 1930. SARS-CoV-2 is a novel coronavirus that has not been observed in humans before and has a higher rate of transmission than the two previous CoVs. There are only four structural proteins in the coronavirus: the spike (S), membrane (M), envelope (E) and nucleocapside (N) proteins. The CoV transmembrane glycoprotein (S protein) spikes are highly immunogenic and are an immune response goal. In the S protein, the receptor binding domain (RBD) is particularly targeted by neutralising antibodies. The receptor binding motif (RBM) with both SARS-CoV and SARS-CoV-2 in the RBD region plays a major role in virus neutralisation and only 59 percent is limited to the similarity of the amino acid residues between the RBM of both viruses; neutralising epitopes outside the RBM are also available. [6] On the viral surface, the S glycoprotein is trimeric and mediates the virus's entry into host cells. The S protein has two functional subunits that mediate the attachment of cells (the S1 subunit, consisting of four domains S1A through S1D) and the fusion of the endocytosis-required viral and cell membrane (the S2 subunit). The 1,273-residue SARS-CoV-2 (strain Wuhan-Hu-1) and 1,255-residue SARS-CoV (strain Urbani) spike proteins are 77.5 percent identical and structurally similar in amino acid sequence and bind to the cellular receptor via the S1B domain. Interaction with receptors induces permanent conformational changes in the spike proteins, resulting in endocytosis membrane fusion. [7] Host tropism and virus transmissibility are determined by the S protein. Both SARS-CoV-2 2019 and SARS-CoV 2003 RBD identify and bind to the susceptible cells of the angiotensin converting enzyme 2 (ACE2) receptor, while MERS-CoV binds to the DPP4 (dipeptidyl peptidase 4) receptor. [8-9] SARS-CoV-2 as a whole is genetically distinct from both the 2003 SARS-CoV and the 2012 MERS-CoV. [10]

TESTING FOR COVID-19

COVID-19 testing involves methods for detecting the existence of (i) the genome of the virus by reverse polymerase chain reaction (RT - PCR) or loop - mediated amplification of isothermal nucleic acid (LAMP) and (ii) antibodies produced in response to infection. Antibody detection can be used both for disease diagnosis and for population surveillance. Antibody tests indicate how many individuals are exposed to the infection and can recognise cases that are moderately symptomatic and asymptomatic. The precise estimate of the case fatality / mortality rate (CFR / CMR) of the disease and the population level of herd immunity can only be calculated from the serological survey results of antibody detection. However, since the disease only began in December 2019, the length of the immune response and immunity to COVID-19 is not yet known. For the diagnosis of COVID-19 using respiratory specimens, only

RT-PCR is now being used in the absence of an effective antibody assay system.

POLYMERASE CHAIN REACTION (PCR)

A process that amplifies a given segment of DNA to be detected is polymerase chain reaction (PCR). The SARS-CoV-2 is an RNA virus, reverse transcription polymerase chain reaction (RT-PCR) and its many modifications including Real Time RT-PCR (quantitative PCR) and its further modifications such as Syber green assay calculating amplicon temperature melting (Tm) and TaqMan assay using a dual-labeled probe in addition to 2 primers are used in nasopharmaceutical diagnosis. The probability of detecting the virus in the clinical specimen collected depends on how much time has passed since the individual was infected. In one sample, at week 1 (100 percent), a positive test outcome was highest, followed by 89.3 percent, 66.1 percent, 32.1 percent, 5.4 percent, and 0 percent at weeks 2, 3 , 4, 5, and 6, respectively (Symptom Based Strategy for Discontinuing Isolation for People with COVID-19 (Centers for Disease Control and Prevention, USA, 30 April 2020; SARS-CoV-2 RT-PCR Profile: a preliminary study). Infectious Clinical Diseases. The 19th of April 2020. Doi:10.1093 / cid / ciaa460/5822175).).) Compared to serology for antibody detection for the diagnosis of COVID-19, this genome detection kinetics is the disadvantage of RT-PCR and can lead to omission errors. In a cohort study consisting of 67 patients with COVID-19, the median period of SARS-CoV-2 RNA shedding in nasopharyngeal swabs, sputum, and stools was 12 (3-38), 19 (5-37), and 18 (7-26) days respectively. Just 13 urine (5.6%) and 12 plasma (5.7%) samples were positive for viruses. [11] Another study showed that viral RNA detection based on RT-PCR is sensitive and can confirm early SARS-CoV-2 infection effectively. [12-13] A cohort study [14] of 23 laboratory-confirmed COVID-19 patients (median age 62 years [range 37-75]) conducted at two hospitals in Hong Kong during January-February 2020 revealed a median viral load of 5•2 log10 copies per ml in the posterior oropharyngeal saliva or other respiratory specimens. The saliva virus load was the strongest within the first week after symptom onset and subsequently decreased with time. Viral RNA was observed 25 days after the start of symptoms in one patient. A higher viral load was associated with older age. The outcome of the PCR test is determined by the quantity of viral load in the specimen.

SEROCONVERSION AND ITS DETECTION

Reverse transcriptase polymerase chain reaction (RT-PCR) has regularly been used for its diagnosis since the beginning of COVID-19. Several authors have, however, pointed out the poor performance of this technique, particularly in terms of sensitivity; RT-PCR sensitivity may be as low as 38%. [10, 15-16] Serology was used as a supplementary assay to RT-PCR for the identification of anti-viral IgM / IgG. [17-18] RT-PCR detects only the genome of the virus, while antibody tests are helpful in testing the spread of the population as it shows exposure to the virus, and the antibody isotype (IgG / IgM) detected speaks about the time of infection with the virus. According to the WHO, seroconversion is the transition from seronegative status (no antibodies in the serum or present but below the detection limit) to seropositive status in which serum samples can detect antibodies. Isotype-switching, also called switching of the immunoglobulin class, is the transfer from one type to another of antibody development by B cells. The first antibodies to be produced against an antigen are IgM isotype antibodies, then the isotype changes to IgG antibodies, which are more

effective for immune defence. The isotype(s) of the antibody present in a serum / specimen patient may provide useful information on the timing of initial exposure to the virus, as well as information on disease progression and prognosis. IgM suggests new infection, and previous infection or convalescence is indicated by IgG. Detection of virus – specific antibodies is essential for [1] diagnosis of suspected cases with negative RT-PCR results, [2] identification of asymptomatic infection, and [3] monitoring of virus transmission and sero-surveillance in the target population to understand virus circulation. [12-13]

Serology was mainly an epidemiological method in the case of the SARS-CoV epidemic (2003-04), and could help assess the number of silent infections, disease development, patterns of virus spread, and the probable origin of the virus. [19] In order to better estimate the number of COVID-19 cases, including those that may be asymptomatic or have recovered (FDA, USA), antibody testing for SARS-CoV-2 is in increased demand. Serology tests will assess whether, by looking at their immune response, individuals have been exposed to a specific pathogen. RT-PCR tests currently used globally for the diagnosis of COVID-19, on the other hand, can only indicate the existence of the viral genome during infection and do not indicate whether a person has been infected and has subsequently recovered. By recognising individuals that have produced antibodies to the virus, antibody testing may provide greater information on the prevalence of a disease in a population. [20] Antibodies cannot be identified early in the infection and this restricts the efficacy of serological assays for COVID-19 diagnosis. [20] Serological examination, however, may play a critical role in recognising individuals who have previously conquered an infection and developed an immune response. No nation has accurate data on the prevalence of the virus in its population due to insufficient serological testing. Serological testing can be helpful for the diagnosis and detection of asymptomatic infections of suspected patients with negative RT-PCR results. Confirming reported cases of COVID-19 as early as possible using serological testing could reduce the risk of repeated sampling exposure and save valuable RT-PCR tests. [12-13] Seven cases with no symptoms and a negative RT-PCR result were positive for IgG and/or IgM antibodies in this report, which illustrates the significance of serological testing in achieving more reliable COVID19 pandemic scale estimates.

A human monoclonal antibody (MAb 47D11) that neutralises SARS-CoV-2 and SARS-CoV has been reported for the first time. [21] MAb 47D11 binds to an RBD (spike protein receptor binding domain) conserved epitope and neutralises both SARS-CoV and SARS-CoV-2 via a mechanism that is independent of the inhibition of ACE2 receptor binding. For the development of antigen detection tests and serological assays targeting SARS-CoV-2, this MAb will be useful.

ISOTYPES AND THEIR DIAGNOSTIC SIGNIFICANCE

- In early infection, IgM antibodies are developed
- In later infection, IgG antibodies are developed, and are also commonest antibody isotype in blood and other fluids of body. The IgG antibodies provide defence against infection and the immune system also has memory.

Local / mucosal immunity is associated with IgA antibodies and is located on the mucous membranes of the lungs, sinuses, stomach and

intestines. They are also present in blood, as well as in saliva and tears.

SEROLOGY ASSAY TYPES

- **Rapid Diagnostic Test: This is a qualitative lateral flow assay (positive or negative) used for the identification of antibodies (IgG and IgM) or viral antigens. IgM / IgG antibodies against nucleoprotein (N / NP) of SARS-CoV-2 are detected by available test systems.**
- **Enzyme - Linked Immunosorbent Assay (ELISA): This test can be qualitative or quantitative and can make use of patient samples of whole blood, plasma, or serum. It is possible to detect antibodies (IgM / IgG) against spikes (S) (either S1 or S2 as a whole or RBD), N and M.**
- **Neutralization Assay: This test detects serum / plasma antibodies that are successful against the virus in clearing up the infection. Several modifications to this test are accessible.**
- **Chemiluminescent-Immunoassay:This test is quantitative, and in whole blood, plasma, and serum, various forms of immunoglobulins like IgG, IgM, and IgA can be identified.**

VIRAL ANTIGEN DETECTION

ELISA can detect a particular viral antigen. The problem with the antigen detection system is that there may often be insufficient antigen present in the nasal swab to be detectable, particularly in asymptomatic individuals. There is no amplification procedure for viral proteins in an antigen test, unlike the RT-PCR test. The sensitivity of antigen detection tests for respiratory diseases such as flu ranges from 34 percent to 80 percent, according to the WHO, and half or more of COVID-19 infected patients could be missed by such tests, leading to omission errors. However, 91.7 percent (11/12) of patients were able to detect the virus in saliva in certain trials. [14]

ANTIBODY DETECTION KINETICS

SARS-CoV-2 IgG antibodies are normally detectable 10-14 days after infection, and typically peak about 28 days after infection. It is possible to detect IgM antibodies earlier. Since antibodies take time to develop, they are not the best indicators of acute infection, but they are ideal for detecting past infections / convalescence as they can remain in the bloodstream for several years. Anti-N / NP IgM could be observed on day 7 and day 28 in a cohort study consisting of 67 COVID-19 patients, while IgG was on day 10 and peaked on day 49 after disease onset. In extreme patients, IgM and IgG titers were significantly higher than in non-severe patients ($p < 0.05$). The length and essence of immunity against infection with SARS-CoV-2 is not yet understood. [11] The median antibody detection time for SARS-CoV-1 (12 days; IQR 8-15.2 days) and SARS-CoV-2 (11 days; IQR 7.25-14 days) was similar, but for MERS-CoV (16 days; IQR 13-19 days) was longer. [22] There was no detectable cross-neutralization against SARSCoV-2 by SARS patient serum. [23]

A analysis of acute SARS-CoV-2 antibody responses in 285 COVID-19 patients showed that 100% of patients tested positive for antiviral immunoglobulin G (IgG) within 19 days of symptom onset. [12-13] The severe group had higher IgG and IgM titers than those in the non-severe group. Serological testing can be helpful for the diagnosis and detection of asymptomatic infections of suspected patients with negative RT-PCR results. Seroconversion occurred concurrently or sequentially for IgG and IgM, and both titres of IgG and IgM were plateaued within 6 days of seroconversion (loc. cit.).

The seropositivity score was 94 percent for anti-NP IgG, 88 percent for anti-NP IgM, 100 percent for anti-RBD IgG, and 94 percent for anti-RBD IgM in serum samples available from 16 patients for 14 days or longer after symptom onset. [14, 24] Increases in IgG or IgM antibody levels against NP / RBD were observed in most patients 10 days or later after symptom onset. More patients experienced earlier anti-RBD seropositivity than anti-NP.

In female patients, the IgG antibody production was higher than in male patients at the early stage of the disease. [25] Although the underlying mechanisms are not understood, this difference in the level of IgG antibodies between male and female patients can contribute to negative clinical outcomes in male patients with COVID-19.

SEROLOGICAL ASSAYS

Serology was mainly used as an epidemiological method in the case of the SARS-CoV outbreak of 2003 that could help identify inapparent infections, disease progression mechanism, viral transmission pattern, and the probable origin of the virus. [19] Analysis found that patients with COVID-19 had IgM seroreactivity at day 4 after onset of symptoms, which peaked at day 9, while IgG increased dramatically 12 days after onset of symptoms, and all patients with viral nucleic acid were positive for IgG 30 days after onset of symptoms. [18] IgM antibodies were found in 87.5 percent and IgG in 70.8 percent of cases in patients suspected of COVID-19 and tested negative for the viral genome. They showed that COVID-19 diagnostic sensitivity was 77.3 percent for IgM with 100 percent precision, compared to 88.3 percent and 95 percent for IgG, respectively. In the case of COVID-19 diagnosis using the technique of virus genome detection, the test result can be affected by pre-analytical variables such as inconsistency in obtaining nasopharyngeal swabs, the different swabs and transport medium used, time and temperature of transport of specimens, and potential presence of nucleic acid / PCR inhibitors in the sample, etc. [26] Serological data analysis can be useful for evaluating exposure to the virus, but serology may be more difficult for patients with acute infection to be interpreted; cross-reactivity with other coronaviruses and pathogens may be an issue. [19, 26] The speed of diagnosis of COVID-19 infected patients can be improved by coupling the possible shortcomings and strengths of both viral genome detection and serological assays. [18] This research (loc. cit.) is a first step towards a deeper understanding of the antibody response to SARS-CoV-2 and offers valuable insight into the potential characteristics and usage of COVID-19 pandemic serological tests. A SARS-CoV-2 S1 serology ELISA kit was developed using the full length SARS-CoV-2 S1 protein expressed by CHO cell as the capturing antigen. The precision of this ELISA (means negative as negative) and sensitivity (means positive as positive) were 97.5% and 97.1%, respectively, with an overall accuracy rate of 97.3%. [27] On the first day after the initiation of the disease, the assay was able to detect SARS-CoV-2 anti-bodies and was able to detect particular antibodies in 28 out of 276 asymptomatic individuals and in one out of five PCR-negative near contacts of COVID-19 patients.

The presence of IgM would mean a recent infection, while a prior infection would indicate IgM negative and IgG positive. This monitoring technique will be most successful 1-2 weeks after the initial onset of symptoms, as well as helping to determine the immunity of herds and the possibility of new infections for those who

are returning from quarantine. The sensitivity of the antibody test ranged from 28.7 percent (symptom onset 1-7 days) to 73.3 percent (symptom onset 8-14 days) and 94.3 percent at symptom onset for more than 15 days. [28] During the first 7 days of symptom initiation (ranging between 67-72 percent), molecular tests have restricted sensitivity, which could be due to low viral load early in the course of the disease or variations in the selection technique. [28]

For large-scale sero-epidemiology studies, the use of RBD-IgG ELISA as a screening test for SARS-CoV-2 antibody, followed by confirmation using the plaque reduction neutralisation test, was adapted to evaluate population infection attack rates and identify disease severity and herd immunity. [29-30] A positive RBD ELISA outcome was predictive of a previous SARS-CoV-2 infection. Large-scale sero-epidemiologic studies will provide near real-time population infection attack rates. [31]

The potential role of IgM antibodies against SARS-CoV-2 as a diagnostic marker of recent in-fection has been assessed by recent studies. [32] Using an ELISA using SARS-CoV-2 recombinant NP antigen, it was shown that IgM antibodies were detectable in 85% of COVID-19 confirmed patients 1-7 days after symptom onset. [33] These authors suggested that while molecular testing remains preferred, with higher sensitivity, IgM targeting may be useful in suspected COVID-19 patients diagnosed as negative by molecular methods within the first 5.5 days after disease onset. Just about 28 percent of patients could detect IgM antibodies against RBD found in the S1 subunit of the virus spike glycoprotein by day 7 of post-symptom onset, while 73 percent were positive by day 14. [34] Recent studies have shown that IgA antibodies against the virus are detectable as early as one day after the onset of symptoms, close to IgM. [33] During the COVID-19 pandemic, identification of IgG antibodies against the virus may have a greater role to play in comparison to IgM and IgA isotypes. In addition, the long-lasting IgG response is close to that of IgA and is correlated with viral neutralising activity, which is important for disease recovery. [35-36] Serologic monitoring for the identification of IgG isotype antibodies against the virus will play an important role in determining the true prevalence of the virus. [32] Studies have also indicated a relatively high specificity of IgG-based serological assays for COVID-19 (> 95 percent). [12-13, 32, 37] Data indicated that IgG formed against various SARS-CoV-2 antigens was detectable in patients after at least 8 days after clinical disease, and more than 90% of patients were seropositive after day 14 of disease, while some individuals may take longer to become seropositive, depending on their immune status, or may never be seropositive if immunosuppressed significantly. [12-13, 34]

Neutralizing anti-bodies were detectable in 89% of patients up to 2 years after infection from previous immunity studies in recovered SARS-CoV patients, whereas IgG antibodies were undetectable at 6 years of age. [38-39] With respect to SARS-CoV-2, we have to wait until that time to have similar results. In different populations and exposure scenarios, the rate of asymptomatic COVID-19 infection has been estimated at 4 to 80 percent, and seroprevalence studies will therefore help to create a more reliable estimate of the number of infected individuals that will in turn help to determine the true case fatality rate (CFR) at regional, national and global levels. [40-42] Serological tests assess the proportion of people exposed to the virus. Early studies have indicated that detection of IgM and IgG usually occurs between 7-11 days after exposure in COVID-19 patients. The outcome of immunochromatography and chemiluminescent immunoassay for the detection of SARS-CoV-2 antibodies was not affected by heat inactivation of blood samples at 56°C for 30 min, but may raise the risk of infection for laboratory staff handling the tests. [43]

ASYMPTOMATIC CASES

A cruise ship, the 'Diamond Princess' housing 3,711 individuals, was quarantined for 2 weeks on 5 February 2020 after COVID-19 was diagnosed with a passenger going ashore. 634 people on board tested positive for SARS-CoV-2 before 20 February 2020, of which 306 were symptomatic and the remaining 328 were asymptomatic (50.5%). [3] There are two forms of asymptomatic cases of SARS-CoV-2 infection, i.e., 1) individuals with minor or moderate symptoms during the incubation period but with initiation of symptoms during the quarantine period, and 2) individuals with no symptoms all the time but positively screened for viral nucleic acid or antibodies. Asymptomatic infection is a problem, and super spreaders are considered asymptomatic individuals. Those with mild to no symptoms but positive for SARS-CoV-2 viral nucleic acid or positive for serum specific IgM antibodies are asymptomatic carriers. [3] There is evidence suggesting potential transmission from asym-ptomatic cases of SARS-CoV-2. The viral load detected in asymptomatic patients was close to that detected in symptomatic patients, indicating the potential for asymptomatic or minimally symptomatic patients to under-go transmission. [44] In faeces, but not in nasopharyngeal swabs, an asymptomatic case tested positive for the virus indicates a theoretical possibility of transmission through a faeco-oral path. [45] Suspected asymptomatic patients should be quarantined and tracked for 14 days, and their quarantine will end if two consecutive nucleic acid test samples obtained at intervals of more than 24 hours are negative. [46] In order to assess the number of individuals infected with little or no symptoms and estimate the actual number of reported cases, the application of antibody tests is appropriate for screening various age groups of people. With the presence of differences in the actual number of asymptomatic cases and their infectivity, it is important to elucidate broader observational and longitudinal studies utilising serological tests. [31] Strict quarantine of asymptomatic patients, however, is of great importance in managing the COVID-19 pandemic worldwide, and if several feasible transmission control steps are taken, then the epidemic may end rapidly and effectively. [3]

ASSAY FOR HOST IMMUNE RESPONSE

Myxovirus resistance protein A (MxA) has a low baseline (less than 15 ng / ml), long half-life (2.3 days) and rapid induction (1-2 hours) biomarker for viral infection. [47] MxA mRNA has been shown to be detectable in peripheral blood within 1-2 hours of interferon (IFN) alpha-stimulated white blood cells, and then MxA protein starts to accumulate. [48] In the case of MERS-CoV and SARS-CoV, these coronaviruses have been shown to increase the expression of MxA in the blood. [49] Many studies have shown that peripheral blood MxA protein expression is a responsive and precise marker of viral infection. MxA protein expression is regulated solely by type I IFNs. [47, 50] The MxA gene is expressed in mononuclear blood cells or locally in tissues, and other cytokines such as IL-1 or TNF-alpha apparently do not react to the MxA gene. [51]

RECOMBINANT VIRAL PROTEINS

Now that the SARS-CoV-2 genome sequence is known, it is possible to generate the viral

protein(s) of interest as a recombinant protein in E. Coli or Eukaryotic / Baculovirus systems for use in ELISA in large quantities. After the antigen is directly bound to the wells, a human serum test is added and a secondary antibody (usually labelled with the HRP enzyme) is added that responds to human antibodies (in the test serum) bound to the antigen, and a colorimetric or fluorometric output can be quantified by the presence of the mark (HRP etc.) in the secondary antibody.

CONCLUSION

In order to complement COVID-19 diagnosis by RT-PCR, the use of precise antibody assay systems is a must, as there are chances of false positives (in PCR tests) due to variability in virus load in the clinical materials collected for diagnosis. The stage of infection during the processing of clinical samples for nucleic acid tests is difficult to guarantee. During clinical illness, the virus load in respiratory exudates is likely to be maximal, and steadily decreases with sickness remission. Therefore, in nucleic acid studies, samples obtained late in the infection will turn out to be negative. However, antibodies elicited following infection with the virus can be detected for longer periods of time, and asymptomatic cases can also also be diagnosed by antibody testing. Serology, unlike NAT, is beneficial in understanding the spread of the virus and the disease's epidemiology.

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LETTER TO EDITOR

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THE RISK OF CORTICOSTEROIDS IN COMMUNITY-ACQUIRED PNEUMONIA

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A 71-year-old man with diabetes mellitus and osteoarthritis of the knee presented with a five-day history of epigastric pain and melena. Two weeks before his presentation, he completed a seven-day course of levofloxacin (Levaquin) and prednisone for the treatment of community-acquired pneumonia (CAP). On presentation, he was afebrile, hemodynamically stable, and breathing comfortably on ambient air. He had tenderness to palpation in the epigastric region and coarse rales on auscultation at the right lower base. Laboratory testing was notable only for a newly decreased hemoglobin level of 11 g per dL (110 g/L; range 13.5 to 17.5 g/dL [135 to 175 g/L]). An esophagogastroduodenoscopy was performed, which demonstrated a bleeding peptic ulcer that was treated with thermal coagulation.

The use of corticosteroids in clinical trials of CAP as adjunct to antibiotics dates back 60 years. It was hypothesized that corticosteroids could dampen the bacterial endotoxin-mediated cytokine storm, prevent progression to septic shock, and treat critical illness-related corticosteroid insufficiency. [(1)] Today, there is significant variability in the use of corticosteroids for the treatment of CAP in clinical practice. Our case illustrates an adverse patient event caused by inappropriate use.

It is essential to distinguish the management of severe CAP from non-severe CAP. The Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) 2019 guidelines define severe CAP as requiring support in a critical care environment. [(2)] The previous IDSA/ATS 2007 guidelines did not comment on the routine use of corticosteroids for severe CAP, but the guidelines were updated in 2019 to advocate for use only in patients with septic shock refractory to vasopressors and fluid resuscitation. [(3)]

Non-severe CAP occurs in patients treated in the outpatient or general inpatient setting. The 2007 and 2019 IDSA / ATS guidelines recommend against the routine use of corticosteroids in non-severe CAP. Previous studies have not demonstrated a mortality benefit and showed increased rates of hyperglycemia. [(4)] Furthermore, the harms associated with corticosteroid use are likely underreported. Studies evaluating the safety of corticosteroids often exclude patients at the highest risk of complications, such as those with a history of gastrointestinal bleeding, neuropsychiatric conditions, immunocompromised state, and concurrent use of nonsteroidal anti-inflam-matory drugs. Hyperglycemia, fluid retention, hypertension, delirium, psychosis, insomnia, osteonecrosis, and gastrointestinal bleeding may consequently be underestimated. The potential harmful adverse effects of corticosteroids for non-severe CAP outweigh the potential benefits. Our case illustrates the importance of avoiding the use of corticosteroids for the treatment of CAP.

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