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Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension. 2002;40(5): 679-86 No author given:

21st century heart solution may have a sting in the tail. BMJ. 2002;325(7357):184

Volume with supplement:

Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. Headache. 2002;42 Suppl 2:S93-9.

Issue with supplement:

Glauser TA. Integrating clinical trial data into clinical practice. Neurology. 2002;58(12 Suppl 7):S6-12.

Article published electronically ahead of the print version: Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells. Blood. 2002 Nov 15; 100(10):3828-31. Epub 2002 Jul 5.

2. Books and Other Monograph Personal author(s):

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Original Article

Vaccination and Pandemic Control in Bangladesh: Post Vaccination COVID-19 Positive Cases among Health Care Providers

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Abstract

Vaccination was started on a trial basis in Bangladesh from 27th January, 2021 and started mass vaccination from 7th February, 2021. Since starting of mass vaccination it was noticed that, the health care providers (HCPs) who received two doses of Astra-Zeneca were then reported of being infected. This cross-sectional study was conducted during the period of July to December 2021 and data were collected from July to August 2021. The main objective was to measure the proportion of post vaccinated Corona Virus Disease-19 (COVID-19) positive cases among healthcare providers working in different healthcare facilities in Bangladesh and aimed to collect available evidence to characterize these infections and correlations with different co-morbidities. This study was carried out among 450 vaccinated HCPs who received 2 doses of vaccine at various health care facilities (HCFs) from 32 districts of Bangladesh. Data were collected from HCPs (Doctors, Nurses, Lab technician) who willing to participate irrespective of age and sex. Among the HCPs nearly three-fourth (71.6%) was doctors, 21.3% nurses and 7.1% were lab technologists. Here, most of the (88.0%) respondents were in age group 21 to 40 years and other 22.0% was in age group 41 to 59 years. The number of Male-female respondents was equal and 77.8% of the respondents was Muslim followed by Hinduism (20.2%), Buddhist and Christian 2.0%. Study finds that 27.6% of the respondents was post vaccination COVID-19 positive (PVC-19+) (according to their rt-PCR test result). Less than one-fifth (18.7%) of the respondents had pre-existing co-morbidities among them 8.2% was suffering from hypertension (HTN), 6.0% asthma, 4% Diabetes Mellitus (DM), 2.0% Obesity, 1.1% ischemic heart disease (IHD) and 1.1% was others co-morbidities. Among the PVC-19+ cases most of them (84.6%) were in age group 21-40 years, male-female ratio was 1:0.9 and 81.5% was Muslim. More than three-fourth (77.4%) of positive cases were doctors, 17.7% nurses and 4.8% was lab technicians; among the PVC-19+ cases 87.9% was symptomatic. Three-fourth (75%) of the positive cases had fever, 51.6% had lost of smell and taste, 49.2% showed fatigue/ or malaise, 48.4% dry cough, 43.5% headache, 26.6% runny nose, 25.8% felt muscle pain, 19.4% sore throat, 18.5% shortness of breathing, 14.5% experienced joint pain, 9.7% had productive cough and 32.3% complained for other symptoms and signs. Majority of the PVC+19+ cases (57.26%) developed complications; among them 71.8% had tiredness/ fatigue, 31% difficulty in thinking/ concentrating, 21.1% headache, 19.7% cough, 15.5% dizziness, 14.1% loss of smell or taste, 12.7% joint or muscle pain, 12.7% fast-beating or pounding heart, 11.3% shortness of breathing, 8.5% chest pain and 29.9% developed other complications. Pre-existing co-morbidity was found in 66.94% of positive cases, among those 41.5% HTN, 36.6% asthma, 14.6% DM, 14.6% obesity, 4.9% IHD and 9.8% had others co-morbidity. Chi-square test for independence with $\alpha = 0.05$ was done to assess association, hypertension ($P = 0.009$) and asthma ($P = 0.001$) with PVC-19+ cases was statistically significant. Hypertensive and asthmatic HCPs are more likely to be COVID-19 positive even after complete vaccination. Healthcare providers are at high risk for contracting COVID-19 and might become infected at home or nosocomially while caring for patients or interacting with other staff members. COVID-19 vaccination together with incessant use of personal protective equipment (PPE) might be recommended for HCPs to combat its pandemicity.

Keywords: *Post vaccination, COVID-19, health care providers, SARS-CoV-2 .*

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   (All of the above co-authors were student of PHI course of Master of Public Health Program (MPH), Session 2020- 2021, NIPSOM).

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INTRODUCTION

COVID-19 pandemic was an alarming situation which affected the global community. In that crisis the frontline healthcare providers are playing the role of real-life heroes to combat this catastrophe. They are more prone to infection as they are in direct contact with COVID-19 patients during treatment procedures. The COVID-19 pandemic caused by Severe Acute Respiratory Syndrome-Corona Virus-2 (SARS-CoV-2) has challenged the health system of different countries all over the world.[13] COVID-19 has been declared as pandemic by World Health Organization (WHO) on 11th March, 2020 and Bangladesh detected its first COVID-19 case on 8th March 20209.[9] Vaccination was started on a trial basis in Bangladesh from 27th January, 2021 and started mass vaccination from 7th February, 2021 (Anon., December, 2021). Asthere are no clinically proven treatment options, the management of COVID-19 includes symptomatic management, infection prevention and control measures (e.g., social distancing andlockdown) which are effectively used to slow down the spread of the virus and flatten the epidemiccurve.[28] Second or third wave of COVID-19 infections were often noticed following premature relaxation of such control measures in many countries (Shunqing Xu, 2020). Vaccination was considered to be one of the most efficient prophylactic interventions and its development, also deployment is therefore, promising strategies to reduce disease transmission.[8,9] Healthcare providers (HCPs), being at the frontlines of the fight against the pandemic, had the highest risk of exposure to COVID-19 infection.[26] Thousands of healthcare workers have lost their lives being infected with COVID-19 during the pandemic.[13] According to the Bangladesh Medical Association (Association. 2021), 129 medical doctors and 3 dental surgeons have died from COVID-19 in Bangladesh. The total infected cases and mortality among HCPs in Bangladesh were unfortunately higher than those of neighboring countries, including India, Pakistan and Nepal.[26] Government and non- government agencies and organizations have recommended that HCPs should be prioritized and offered a vaccine due to their higher risk of exposure and active participation in facing the COVID-19 pandemic.[11, 18] Bangladesh Government had given priority to the healthcare providers for vaccination. They were at the frontline of the COVID-19 outbreak response and as such were exposed to hazards that put them at risk of infection even after full vaccination.[13] Since 7th February when the mass vaccination for COVID-19 had been started in Bangladesh, it was noticed that, the health care providers who received two doses of Astra-Zeneca were then reported of being infected after full vaccination.[9] This study was conducted to measure the proportion of post vaccinated COVID-19 positive cases among HCPs working in different healthcare facilities in Bangladesh and aimed to collect available evidence to characterize these infections and correlations with different co-morbidities.

There were many relevant studies regarding post vaccination positive cases, though affirmations could not be made due to insufficient epidemiological data on healthcare professionals. It was also evident that those studies had lack of information about the relationship between socio-demographic characteristics with positive cases, co morbidities, severity in positive cases and so on. Some studies demonstrated the effectiveness of vaccines[19] some studies provided data on postvaccinated skilled nurses.[1] Furthermore, similar studies had notbeen conducted in Bangladesh. This study provides information about socio-demographic characteristics; post vaccinated positive cases, clinical attributes, co-morbidities. This study reflects the disorder of health care workers after full dose of vaccination in Bangladesh and findings of this study would help the existing and future research work as well as would stand for a reference to compare the statuses of post vaccinated health care workers worldwide.

MATERIALS AND METHODS

This cross-sectional study was conducted during the period of July to December 2021 and data were collected from July to August 2021. The main objective was to measure the proportion of PVC-19+ cases among healthcare providers working in different healthcare facilities in Bangladesh. This study was carried out among 450 vaccinated HCPs who received 2 doses of vaccine at various HCFs from 32 districts of Bangladesh. Data were collected from HCPs (Doctors, Nurses, Lab technician) who willing to participate irrespective of age and sex, whereas HCPs of incomplete vaccination and severely ill HCPs were excluded from the study. Here 32 districts were randomly selected from 64 districts of Bangladesh then the name and telephone number of complete vaccinated HCPs were collected from Civil Surgeon Office and online interview and interview over telephone were done conveniently. Semi-structured pretested questionnaire and checklist were used for data collection. Collected data were checked and coded before analysis.

Data analysis: for descriptive statistics; frequency, percentage, mean, median, range and standard deviation (SD) was determined. Uni-variate, bi-variate analysis was done. For test of significance; chi-square test was done to assess the association and statistical significance. Data was analyzed by using statistical software (SPSS version 23) and calculations.

Operational definition:

- Cases: Cases refer to those healthcare providers, who were tested positive for COVID-19 by rt-PCR after complete vaccination.
- Breakthrough infection: A vaccine breakthrough infection is defined as the detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person ≥14 days after they have completed all recommended doses of an authorized COVID-19 vaccine.
- Duration of illness: The duration in between onset of symptoms and symptoms remission.

RESULTS

This cross-sectional study was carried out among vaccinated HCPs (Doctors, Nurses, Lab-technician) at different HCFs [Sadar Hospitals and Upazila (Subdistrict) Health Complexes] from 32 Districts of Bangladesh. Among the HCPs from different HCFs, a total of 450 healthcare providers were included conveniently in this study.

Table I shows the distribution of the respondents according to their socio-demographic status; here 44.7% of the respondents were in age group 31-40 and others 43.3%, 9.1%, 2.7%, 0.2% were in age group 21-30, 41-50, 51-60 and 61-70 respectively. Male-female ratio of the respondents was equal that is 50% and 77.8% of the respondents was Muslim 77.8% followed by Hinduism 20.2%, Buddhist 0.9% and Christian 1.1%.

Table- I: Distribution of the study population according to socio-demographic status (N=450)

Variables	Frequency	Percentage (%)
Age Group		
21-30	195	43.3
31-40	201	44.7
41-50	41	9.1
51-60	12	2.7
61-70	1	0.2
Sex		
Male	225	50
Female	225	50
Religion		
Islam	350	77.8
Hinduism	91	20.2
Buddhist	4	0.9
Christian	5	1.1

Table II shows the distribution of the respondents according to types of healthcare providers; where doctors were 71.6%, 21.3% nurses and 7.1% were lab technologists.

Table- II: Distribution of study population according to types of healthcare providers (N=450)

Types	Frequency	Percentage (%)
Doctor	322	71.6
Nurse	96	21.3
Lab technologist	32	7.1
Total	450	100

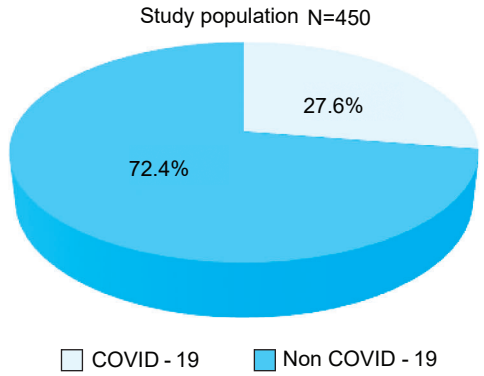

Figure- 1: Distribution of study population according to COVID-19 positive cases following vaccination

Figure 1 shows the distribution of respondents according to COVID-19 positive cases after vaccination; here 27.6% respondents were COVID-19 positives and others 72.4% were COVID-19 negatives (according to their rt-PCR test result)

Table III states the distribution of the respondents according to pre-existing co-morbidity; where 81.3% respondents not having co-morbidity, 18.7% having co-morbidity.

Table- III: Distribution of study population according to pre-existing co-morbidity (N=450)

Co-morbidity	Frequency	Percentage (%)
Yes	84	18.7
No	366	81.3
Total	450	100

Table IV shows the distribution of different co-morbidities among respondents; here 8.2% are suffering from HTN, 6% asthma, 4% DM, 9 2% obesity, 1.1% IHD and 1.1% are suffering from others co-morbidity.

Table- IV: Distribution of different co-morbidities among study population (Multiple response)

Co-morbidity	Frequency	Percentage (%)
HTN	37	8.2
Asthma	27	6
DM	18	4
Obesity	9	2
IHD	5	1.1
Others	5	1.1

Table V shows the distribution of the post vaccination positive cases according to their socio- demographic status. Among the COVID-19 positive cases 84.6% were found in age group of 21-40; others 12.1%, 3.2% were in age group 41-50 and 51-60 respectively. Mmale-female ratio was 1:0.9; 53.2% were Male and 46.8% female and most of the cases 81.5% were Muslim.

Table- V: Distribution of the PVC-19+ cases according to socio-demographic status (n=124)

Variables	Frequency	Percentage (%)
Age Group		
21-30	52	41.9
31-40	53	42.7
41-50	15	12.1
51-60	4	3.2
Sex		
Male	66	53.2
Female	58	46.8
Religion		
Islam	101	81.5
Hinduism	23	18.5

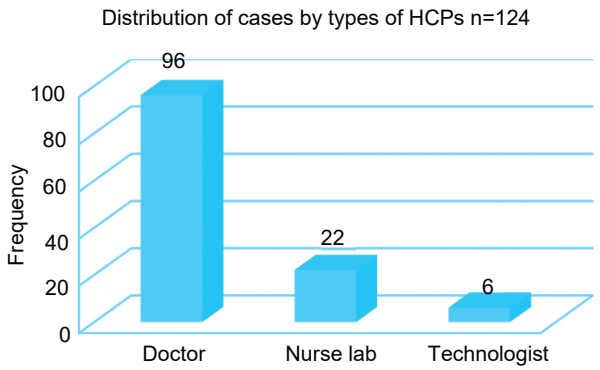

Figure- 2: *Distribution of the PVC19+ cases according by types of healthcare providers*

Figure 2 shows the distribution of the PVC-19+ cases according to types of healthcare providers; here 77.4% were doctors and others 17.7%, 4.8% were nurses and lab technologists

Table VI contains the distribution of the PVC-19+ cases according to their health condition after rt-PCR positive; where most of the cases had symptoms 87.9% and rest 12.1% were asymptomatic.

Table- VI: Distribution of the PVC-19+ cases according to their health condition after rt-PCR positive n=124

Health condition following vaccination	Frequency	Percentage (%)
Asymptomatic & tested rt-PCR positive	15	12.1
Symptomatic & tested rt-PCR positive	109	87.9
Total	124	100

Table VII shows the distribution of the PVC-19+ cases according to symptoms & signs of COVID-19; here 75% developed fever, 51.6% loss of sense of smell and taste, 49.2% fatigue/malaise, 48.4% dry cough, 43.5% headache, 26.6% runny nose, 25.8% muscle pain, 19.4% sore throat, 18.5% shortness of breathing, 14.5% joint pain, 9.7% productive cough an d 32.3 were complaining about other symptoms and signs.

Table- VII: Distribution of the PVC-19+ cases according to symptoms & signs of COVID-19 n =124 (Multiple response)

Symptoms & signs	Frequency	Percentage (%)
Fever	93	75
Loss of sense of smell & taste	64	51.6
Fatigue/Malaise	61	49.2
Dry cough	60	48.4
Headache	54	43.5
Runny nose	33	26.6
Muscle pain	32	25.8
Sore throat	24	19.4
Shortness of breathing	23	18.5
Joint pain	18	14.5
Productive cough	12	9.7
Others	40	32.3

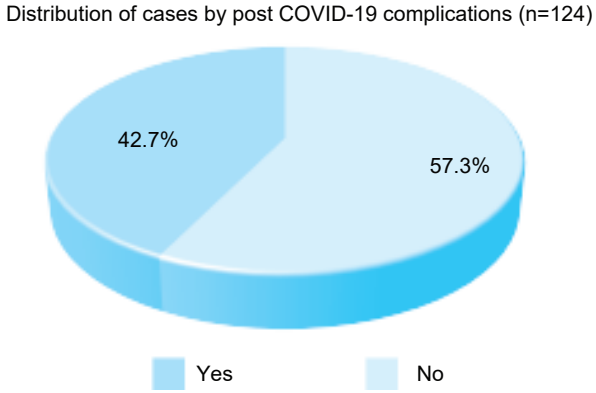

Figure- 3: *Distribution of the PVC-19+ cases according to post COVID-19 complications*

Figure 3 reflect the distribution of the PVC-19+ cases according to post COVID-19 complications; here 57.26% of cases developed post COVID-19 complications and rest 42.74% had no complications.

Table VIII presents the distribution of the PVC-19+ cases according to post COVID-19 complications; here 71.8% developed tiredness or fatigue, 31% difficulty in thinking or concentrating, 21.1% headache, 19.7% cough, 15.5% dizziness, 14.1% loss of sense of smell or taste, 12.7% joint or muscle pain, 12.7% fast-beating or pounding heart, 11.3% shortness of breathing, 8.5% chest pain and 29.9% had developed other complications.

Table- VIII: Distribution of the PVC-19+ cases according to post COVID-19 complications (n =71) (Multiple response)

Post COVID-19 complications	Frequency	Percentage (%)
Tiredness or Fatigue	51	71.8
Difficulty in thinking or concentrating	22	31
Headache	15	21.1
Cough	14	19.7
Dizziness	11	15.5
Loss of sense of smell or taste	10	14.1
Joint or muscle pain	9	12.7
Fast-beating or pounding heart	9	12.7
Shortness of breathing	8	11.3
Others	23	32.4

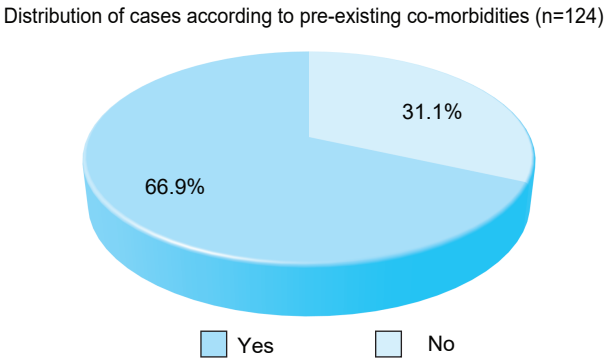

Figure- 4: *Distribution of the PVC-19+ cases according to pre-existing co-morbidity*

Figure 4 shows the distribution of the PVC-19+ cases according to pre-existing co-morbidity; here 66.94% of cases had no pre-existing co-morbidity and rest 33.06% had pre- existing of co-morbidity.

Table IX states the distribution of different co-morbidities among PVC-19+ cases; here 41.5% were suffering from HTN, 36.6% asthma, 6 (14.6%) DM, 14.6% obesity, 4.9% IHD and 9.8% were suffering from others co-morbidity.

Table- IX: Distribution of different co-morbidities among PVC-19+ cases (n =41) (Multiple response)

Co-morbidity	Frequency	Percentage (%)
HTN	17	41.5
Asthma	15	36.6
DM	6	14.6
Obesity	6	14.6
Others	6	14.6

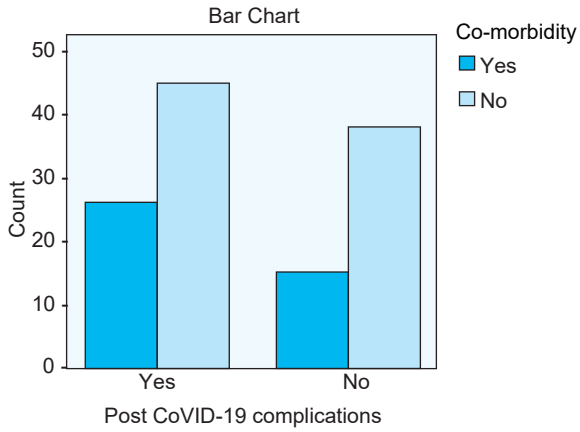

Figure- 5: *Co-morbidity as related to post-covid complications (non-significant)*

Association between post- COVID complications and co-morbidities:

Figure 5 shows chi-square test for independence with α = 0.05 was used to assess whether co-morbidity was related to post-COVID-19 complications. The chi-square test result was statistically non-significant, χ2 (1, N= 450) =0.02, P = 0.89, with Phi (φ) coefficient of 0.01. As seen in Figure 4, there is no association between post-covid complications and co-morbidities.

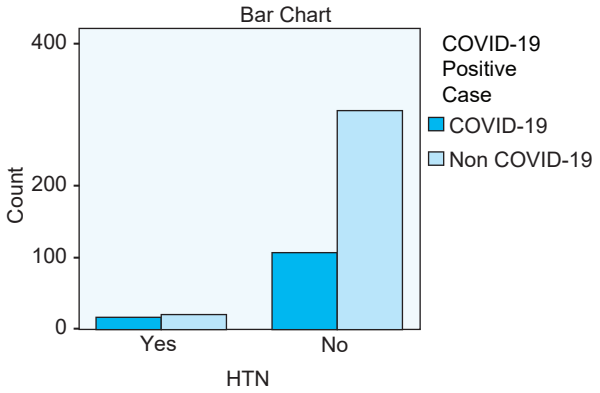

Figure- 6: *Hypertension as related to post vaccinated COVID-19 positive cases*

Association between cases and hypertension:

Figure 6 illustrates A chi-square test for independence with α = 0.05 was used to assess whether Hypertension was related to post vaccinated covid-19 positive cases. The chi-square test result was statistically significant, χ2 (1, N= 450) = 6.83, P = 0.009, with Phi (φ) coefficient of 0.12, indicating a small relationship. As seen in Figure 6, Hypertensive healthcare providers are more likely to be covid-19 positive even after complete vaccination.

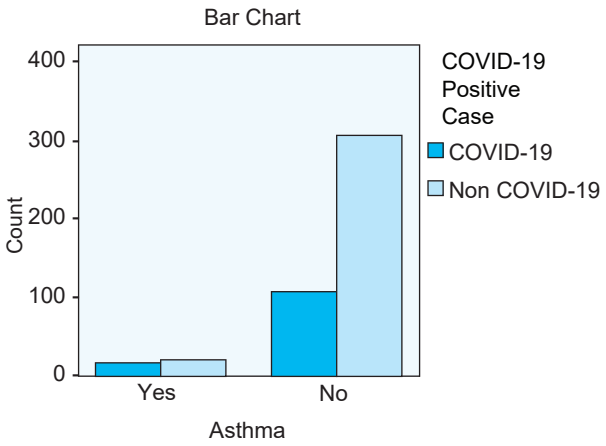

Figure- 7: *Asthma as related to post vaccinated COVID-19 positive cases*

Association between PVC-19+cases and asthma:

Figure 7 shows a chi-square test for independence with α = 0.05 was used to assess whether asthma was related to post vaccinated covid-19 positive cases. The chi-square test result was statistically significant, χ2 (1, N= 450) = 11.28, P = 0.001, with Phi (φ) coefficient of 0.16, indicating a small relationship. As seen in Figure 7, Asthmatic healthcare providers are more likely to be covid-19 positive even after complete vaccination.

DISCUSSION

A total of 450 vaccinated HCPs based on complete vaccination of COVID-19 after 14 days were includedin the study. Among them, 27.56% COVID-19 positive cases after vaccination were detected according to their rt-PCR test results and were mostly younger in age and the median age of the participants was 32 years (IQR: 28–36) and 84.7% were between 21–40 years age group. Our survey findings are consistent with another study conducted among HCPs in California, they found 20.6% COVID-19 positive cases and the median age was 38 years (IQR: 32–48) after complete vaccination.[15] Males represented 53.2% of the cases, with a male to female sex-ratio of 1.14, 81.5% cases were Muslim and 77.4% HCPs were doctors and others 17.7%, 4.8% were nurses and lab technologists respectively. According to Bangladesh Bureau of Statistics (BBS) 2018; male-female ratio in our country was 1.002:1, majority of the population was Muslim (88.4%) and according to Health Bulletin 2019; the ratio of Doctor, Nurse and Lab technologist is 11:5:1 which is very similar to this study population (10:3:1).[25]

Among the vaccinated HCPs who tested positive for COVID-19, 87.9% had symptoms and 12.1% were asymptomatic and had history of exposure to confirmed or suspected COVID-19 cases upon questioning. In the previously mentioned study conducted in California; 83.1% experienced COVID-19 symptoms and rest were asymptomatic which is this similar to this study.[15]

The COVID-19 vaccines are extremely effective at preventing serious illness, hospitalization, and death. No vaccine is 100 percent effective, and as such we have found some fully vaccinated people tested positive for COVID-19. Breakthrough cases typically report mild illness or no symptoms.[3,4] In this study, those who have recovered and suffering from COVID-19 (98.3%); tended to show a higher frequency of symptoms where 75% developed fever, 51.6% loss of sense of smell and taste, 49.2% fatigue/malaise, 48.4% dry cough, 43.5% headache, 26.6% runny nose, 25.8% muscle pain, 19.4%

sore throat, 18.5% shortness of breathing, 14.5% joint pain, 9.7% productive cough and 32.3% were complaining about other symptoms and signs and only 6.5% were hospitalized and rest, 93.5% took home isolation. Compared to this survey, a recent study at Washington State of COVID-19 breakthrough cases shows symptomatic COVID-19 and hospitalization rate were 78% and 10% respectively.[28] Most of the cases in our study presented with fever, anosmia, lethargy, dry cough, headache at initialpresentation of the disease which is very similar to a systematic review and meta-analysis of 148 studies from 9 countries.[17] The median (IQR) for the duration of illness was 10–16 days, which is consistent with a prospective cohort study conducted in a tertiary care center of Bangladesh.[22]

More than half of positive cases had developed post COVID-19 complications; where 71.8% developed tiredness or fatigue, 31% difficulty in thinking or concentrating, 21.1% headache, 19.7% cough, 15.5% dizziness, 14.1% loss of sense of smell or taste, 12.7% joint or muscle pain, 12.7% fast-beating or pounding heart, 11.3% shortness of breathing, 8.5% chest pain and 29.9% had developed other complications. Various post-COVID-19 symptoms have been reported in different studies. Post-COVID-19 symptoms can develop even in mild cases.[2] Most studies have reported fatigue, cough, respiratory distress, and headache as (the) dominant features.[7] In our study, tiredness or fatigue, difficulty in thinking or concentrating, headache, cough, dizziness was observed in 71.8%, 31%, 21.1%, 19.7%, 15.5% cases, respectively.

One-third of the cases had comorbidities existing prior to COVID-19 infection of which the most prevalent were HTN (41.5%) and asthma (36.6%). The relationship between co-morbidity with post COVID-19 complications were found non-significant. But the relationship between post-vaccinated positive cases with hypertension and asthma were found statistically significant.

Limitations:

Non-probable conveinent sampling was done. Data collection was done over telephone and online interview due to current COVID-19 situation. Study was done on people who received Astra-Zeneca vaccine only.

Ethical consideration:

Ethical permission from IRB of NIPSOM was taken before data collection. Verbal consent was taken from each and every participant over telephone. Privacy and confidentiality were maintained strictly. Participants had all rights to withdraw from the study anytime during tele-conversation. Information obtained were published for research and technical purpose without mentioning the name and address of the respondents.

CONCLUSIONS

Study finds that post vaccined healthcare providers at high risk for contracting symptomatic and asymptomatic COVID-19 and might become infected at home or nosocomially while caring for patients or interacting with other staff members. More than one-third of the post vaccinated COVID-19 HCPs were being infected again among them more than three-fourth were doctors. Most of the post vaccinated HCPs had symptoms, where fever lost of smell and taste, fatigue were predominent. Majority of the HCPs developed complication, among those tiredness/fatigue, difficulty in theinking/concentration, headach, cough, dizziness were common. One-third of the HCPs had comorbidities and signeficant association was found with asthma and HTN. Hypertensive and asthmatic HCPs are more likely to be COVID-19 positive even after complete vaccination. No death was traced among PVC-19+ HCPs.

Recommendations:

There should establish and follow an efficient triage system to assess patients with flu like symptoms at all healthcare facility levels in addition they need proper training based on appropriate IPC practices, lab safety protocols. Maintaining respiratory/ cough etiquette and hand hygiene practices should be continued even after vaccination. To administer booster dose is required for frontline healthcare providers to give more protection.

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Original Article

Assessment of Severity of Acute Pancreatitis in Children: Systemic Inflammatory Response Syndrome (SIRS) Score

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Abstract

Acute pancreatitis (AP) is a prompt inflammatory process of the pancreas and it may be ranged from mild to severe pancreatitis with variable involvement of regional tissues and remote organ systems. Though there are many scoring systems for adults but scarce of scoring system for assessing the severity of acute pancreatitis among paediatric cases increase their suffering. Systemic Inflammatory Response Syndrome (SIRS) can be useful for assessing the severity of acute pancreatitis in children. It is reported that SIRS has good sensitivity, specificity, positive predictive value and negative predictive value. The aim of this study was to assess the severity of acute pancreatitis in paediatric cases from the scores of SIRS. This cross-sectional study was coducted in the Department of Paediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh for a period of 1.5 years from May 2019 to October 2020. A total of 30 children with acute pancreatitis were selected purposively and SIRS was evaluated. The sensitivity, specificity, positive predictive value and negative predictive value of SIRS was calculated. Out of 30 acute pancreatitis children, 21 (mean age, 11.27±3.0 years) were diagnosed as mild AP and 9 (mean age, 10.53 ±5.0 years) as severe AP. Eighteen (60.0%) children were male and less than half 12 (40%) of children had pallor and most of them 24 (80%) had abdominal tenderness. There was no statistically significant difference between mild and severe AP in terms of serum lipase, amylase, BUN and CRP ($p > 0.05$). SIRS score was ≥2 in 9 (100%) severe AP patients and score was ≥2 in 7 (33.3%) mild AP patients and it was statistically significant ($p=0.001$). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of SIRS score in predicting severe acute pancreatitis was 100%, 77.8%, 63.6%, 100% and 84% respectively. This study finds that SIRS score can effectively assess the severity of acute pancreatitis in the paediatric age group. Systemic Inflammatory Response Syndrome (SIRS) score at admission can be used to assess the severity of acute pancreatitis.

Keywords: *Acute pancreatitis, systemic inflammatory response syndrome, sensitivity, specificity, positive predictive value and negative predictive value.*

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INTRODUCTION

Pancreatitis is a disease in which pancreas becomes inflamed and presence of histological inflammation within the parenchyma of pancreas.[1] Digestive zymogens inside the acinar cells responsible for the condition. Acute pancreatitis (AP) is a sudden inflammation that lasts for a short time and range from mild discomfort to a severe and life-threatening illness.[2] Chronic pancreatitis is a long-lasting inflammation and happens after an episode of acute pancreatitis. Nearly a quarter of children with acute pancreatitis have severe

clinical course and develops complications like organ dysfunction and local complications.

In the last two decades, the incidence of acute pancreatitis (AP) among the children has increased,[3] varying from 3.6 to 13.2 cases per 100,000 children.[4] Mortality rate is around 4 to 10% despite significant advances in the treatment of this disease.[5,6] The extent of the inflammatory response of the pancreas determines the severity of AP that can lead to complications such as pancreatic necrosis, effusions, shock, leads rapidly to multiple organ failure and even death. In infants and toddlers, symptoms may be subtle, vomiting, irritability and abdominal distension may suggest AP.[7] Initially, the duration of pain is quite variable, ranging from several hours to several days. As the disease progress, the attacks become more frequent and pain-free intervals shrink and vanish. Less common initial presentations include, sequel of exocrine or endocrine insufficiency: steatorrhea, weight loss and diabetes, biliary obstruction with recurrent episodes of mild jaundice, cholangitis, or vague attacks of indigestion.[8]

AP can be classified into mild, moderately severe, or severe and early identification of patients at higher risk of developing Severity of Acute Pancreatitis (SAP) may improve outcomes by providing more aggressive management.[5] The available scoring systems do not perform well in children, even PAPS and JPN score that is for pediatric population. No single parameter has been developed which is suitable for the early prediction of acute inflammation and necrosis.[9] The use of systemic inflammatory response syndrome (SIRS) as a simple screening tool at admission to identify children at risk for the development of Severity of Acute Pancreatitis. Systemic inflammatory response syndrome (SIRS) is an easy tool to identify children at risk for the development of severe acute pancreatitis. In patients with AP, the various inflammatory events cause intra-pancreatic injury and extra-pancreatic inflammation that has been termed the systemic inflammatory response syndrome (SIRS).[10] In adults, early ≥ 2 SIRS score, has been found to be associated with severe AP and persistent ≥ 2 SIRS score associate with multisystem organ failure and mortality. Criteria for SIRS in children include tachycardia (or bradycardia in infants <12months), tachypnea, elevated or suppressed body core temperatures, and leukocytosis or leukopenia. The presence of each of the 4 SIRS criteria can be easily assessed at the time of admission and as a "score" from 1 to 4 and represent an important means of identifying pediatric patients with AP at increased risk for severe disease.[11] In addition, SIRS can be calculated by very simple clinical and lab parameters. In absence of pediatric specific criteria for severe AP, SIRS score at admission may serve as an easy to calculate severity. The use of SIRS as a simple screening tool at admission to identify children at risk for the development of SAP. In this study, the aim was to determine the severity of acute pancreatitis by SIRS and utility of this in severity assessment of pediatric acute pancreatitis. The result of the study might be helpful for the physicians in early and meticulous diagnosis of severe acute pancreatitis who have more chance of development of complications.

MATERIALS AND METHODS

This was a cross-sectional study done from May 2019 to October 2020 in the Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. Children less than 18 years with abdominal pain admitted at the Department of Paediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, diagnosed as acute pancreatitis according to INSPIRE (International Study Group of Pediatric Pancreatitis: In Search for a Cure) criteria considered as study population. Patient with acute recurrent pancreatitis, chronic pancreatitis, pain in the abdomen due to other causes were excluded from the study.

Systemic Inflammatory Response Syndrome (SIRS) scoring system:
Pediatric SIRS Criteria: The presence of 2 or more of the following criteria defines SIRS.[12,13]

Age Group	Heart rate beats/min		Respiratory rate	Leukocyte Count	Temp °C
	Tachy cardia	Brady cardia	breaths/min	Leukocytes $10^3/mm^3$	
Newborn (0 d to 1 wk)	>180	<100	>50	>34	>38°C or <36°C
Neonate (>1 week to 1 mo)	>180	<100	>40	>19.5 or <5	>38°C or <36°C
Infant (>1 mo to 1 y)	>180	<90	>34	>17.5 or <5	>38.5°C or <36°C
Toddler and preschool (>1 to 5 y)	>140	NA	>22	>15.5 or <6	>38.5°C or <36°C
School age (>5 to 12 y)	>130	NA	>18	>13.5 or <4.5	>38.5°C or <36°C
Adolescent (>12 to <18 y)	>110	NA	>14	>11 or <4.5	>38.5°C or <36°C

NA= Not applicable.

Data collection:

After enrollment in the study at first history was obtained from the children/ parents/ caregivers and physical examination was done by researcher herself at the day of admission. History was taken in details and 5 ml venous blood was collected aseptically for laboratory investigation. Total count of WBC, S. creatinine, RBS, S. ALT and S. calcium were investigated and other laboratory investigations such as serum amylase, serum lipase, blood urea nitrogen, C-reactive protein were also assessed in Department of Biochemistry, BSMMU by autoanalyzer machine. After getting the reports of total count of WBC, patient's SIRS scoring was done and documented in questionnaire. A semi-structured questionnaire was used to collect data from the patients and recording the examination findings and investigation findings.

Statistical analysis:

Data were analyzed by SPSS software, version-25.0. Categorical variables were reported by frequency and percentage and compared by the Chi-square or Fisher exact test. All normally distributed continuous variables were presented by mean and standard deviation and compared by Independent sample t test. Continuous variables without normal distribution were reported by median and interquartile range and compared by Mann- Whitney test. Sensitivity, Specificity, positive predictive value, negative predictive value, diagnostic accuracy of SIRS was observed by comparing with NASPGHAN guideline definition of mild and severe AP. A *p*-value <0.05 was considered statistically significant for all tests.

Ethical consideration:

Institutional ethical committee approval was taken before commencement of the study. A consent form was constructed describing the title, objectives, procedure of the study, expected outcome, any potential risk to the subject etc. These statements were written in an easily understandable clear local language. Parents or caregiver decided themselves to be or not to be included in the study. This written informed consent was signed duly by the parents and principal investigator.

RESULTS

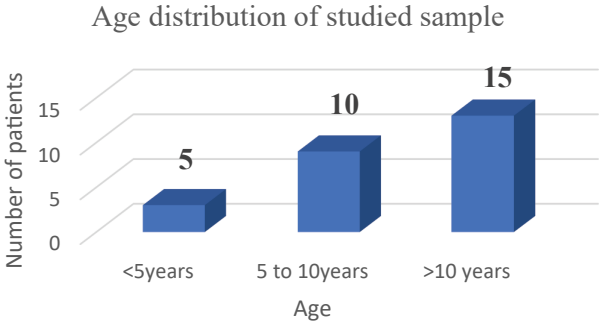

Figure- 1: *Age distribution of studied samples (n=30)*

Figure 1 states that among the studied sample, highest frequency of cases was seen in >10-year age group (15), followed by 5-10 year (10) age group and < 5 year (5) age group (Figure 1).

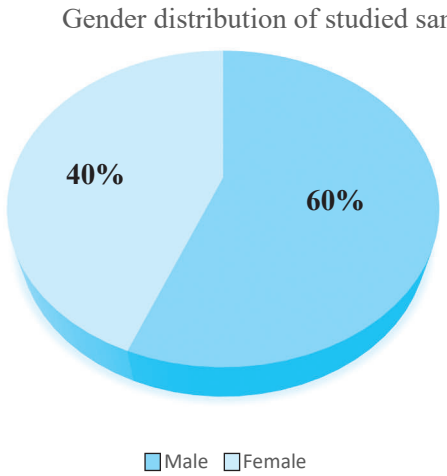

Figure- 2: *Gender distribution of studied sample (n=30)*

Figure 2 shows that among the studied samples, 18 (60%) were male and 12 (40%) female (Figure 2).

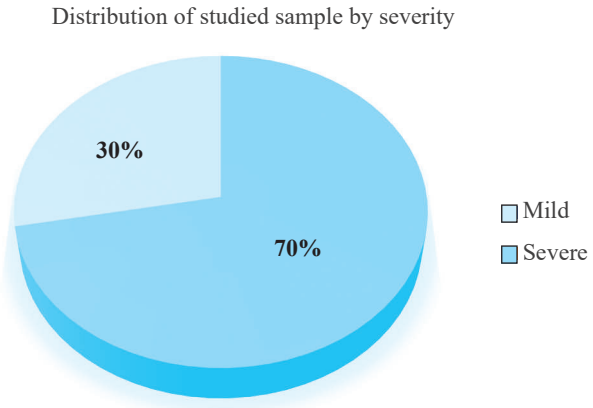

Figure- 3: *Distribution of studied sample by severity (n=30)*

Figure 3 shows that 21 (70%) cases were mild and 9 (30%) belongs to severe acute pancreatitis according to NASPGHAN classification (Figure 3).

Table I presents that out of 25 studied samples, 11 patients had pallor (44%) and shock was present in 4 (16%) of the patients. Most of patients had abdominal tenderness 23(92%), five (20%) patients had detectable ascites on clinical examination (Table I).

Table- I: Distribution of studied sample by physical findings (n=30)

	Findings	No	Percentage (%)
General findings	Pallor	12	40
	Jaundice	1	4
	Shock	6	20
	Dehydration	1	4
Abdominal findings	Abdominal tenderness	24	80
	Liver enlargement	4	16
	Ascites	6	20

Table II shows that there was no statistically significant difference of total count, S. creatinine, RBS and S. ALT between mild and severe AP ($p > 0.05$) but serum calcium level was significantly higher in mild AP than severe AP ($p = 0.001$).

Table- II: Comparison of haematological and biochemical parameters between mild AP and severe AP (n=30)

Variable	Total (n=30) Mean±SD	Mild AP (n=21) Mean±SD	Severe AP (n=9) Mean±SD	p value
Total count (K/mm3)	11.61±3.63	12.77±2.47	16.14±7.99	0.86
S. Creatinine (mg/dL)	0.69±0.66	0.63±0.12	0.88±0.91	0.07
RBS (mmol/l)	7.25±1.26	6.26±1.12	6.10±1.32	0.99
S. ALT (IU/L)	28.26±4.31	25.0±11.03	30.71±12.1	0.28
S. Calcium	9.22±0.86	9.8±0.67	10.4±0.51	0.001s

Independent sample t test was used to analyze data. s= significant

Table III states there was no statistically significant difference between mild and severe AP in terms of serum lipase, amylase, BUN and CRP ($p > 0.05$).

Table- III: Comparison of biochemical markers between mild AP and severe AP (n=30)

Variable	Mild AP (n=21)	Severe AP (n=9)	p value
	25th -75th percentile	25th -75th percentile	
Lipase (U/L)	710.0 (308.75-2578.5)	888.0 (558.0-2690.0)	0.67
Amylase (U/L)	478.0 (270.25-1050.0)	1481.0 (120.0-2090.0)	0.57
BUN (mg/dL)	10.13 (8.39-17.00)	11.0 (6.90-13.0)	0.27
CRP (mg/L)	18.36 (5.13- 36.36)	42.520 (12.82-58.17)	0.22

Mann-Whitney U test

Table IV shows that there was no significant (p=0.51) difference noted in weight among mild AP group (35.38±14.70 Kg) and severe AP (40.57±22.83 Kg) group. And non-significant difference was noted in height and BMI for age with p value 0.48 and 0.99 respectively.

Table- IV: Comparison of weight, height and BMI for age between mild AP and severe AP group (n=30).

Variable	Total (n=30) Mean±SD	Mild AP (n=21) Mean±SD	Severe AP (n=9) Mean±SD	p value
Weight (Kg)	36.84±17.00	35.38±14.70	40.57±22.83	0.51
Height (cm)	136.86±20.37	135.03±19.08	141.57±24.35	0.48
BMI (kg/m2) for age	18.53±5.43	18.54±5.08	18.51±6.71	0.99

Independent sample t test

Table V contains that there was no statistically significant difference of age and hospital stay between mild and severe AP ((p=0.86 and p=0.13, respectively). But there was statistically significant difference in terms of duration of pain and NPO days between the two groups (p=0.002 and p=0.02, respectively).

Table- V: Comparison of age, hospital stay, pain duration and NPO days between mild and severe AP (n=30).

Variable	Total (n=30) Mean±SD	Mild AP (n=21) Mean±SD	Severe AP (n=9) Mean±SD	p value
Age (yrs)	10.35±3.28	10.27±4.0	10.54±4.0	0.86
Hospital stay (days)	9.36±3.38	8.72±3.48	11.00±2.65	0.13
Duration of pain (days)	7.64±4.97	5.83±3.58	12.28±5.25	0.002s
NPO (days)	2.00±1.41	1.61±1.2	3.00±1.53	0.02

Independent sample t test, s-significant

Table VI presents that there was statistically significant difference in terms of systolic BP, diastolic BP, pulse and respiratory rate between mild and severe AP group (p=0.007, p=0.003, p=0.0001 and p=0.004, respectively). But there was no statistically significant difference of mean temperature between the two groups ((p=0.13) (Table VI).

Table- VI: Distribution of vital signs between mild AP and severe AP (n=30).

Variable	Total (n=30) Mean±SD	Mild AP (n=21) Mean±SD	Severe AP (n=9) Mean±SD	p value
Temperature (F)	98.58±1.48	98.3±0.83	99.31±2.44	0.13
Systolic BP (mmHg)	95.6±13.79	100.0±10.28	84.28±15.92	0.007 s
Diastolic BP (mmHg)	60.8±11.24	64.72±8.48	50.71±11.70	0.003 s
Pulse (bpm)	102.36±17.54	94.00±10.82	123.85±12.28	0.0001 s
Respiratory rate/min	22.48±3.38	21.33±2.37	25.42±3.95	0.004s

Independent sample t test, s- significant

Table VII comparing the severe and mild AP on the basis of SIRS score revealed, 9 (100%) patient of severe AP group (n=9) had SIRS score of ≥2 and 7 (33.3%) out of 21 patients in mild AP group had ≥2 score and it was statistically significant (p=0.001).

Table- VII: Comparison of SIRS score between mild AP and severe AP (n=30).

		Severity of acute pancreatitis based on NASPGHAN criteria			
		Severe	Mild	Total	p-value
Severity by	Severe (score≥2)	9	7	16	0.001s
SIRS score	Mild (score<2)	0	14	14	
	Total	9	21	30	

Fisher's exact test, s- significant

Diagnostic statistical analysis revealed sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of SIRS score in predicting severe acute pancreatitis was 100%, 77.8%, 63.6%, 100% and 84% respectively.

DISCUSSION

Acute pancreatitis is common in Pediatric Gastroenterology Department in Bangladesh. Predicting severity at the time of admission helps us for better evaluation and management. SIRS score may help us in distinguishing mild and severe acute pancreatitis patient.

In our study, more than half (50%) of the patients were >10 years' age followed by (33.33%) in the range of 5-10 years and 16.67% < 5 years. Similar results were found in a study done by Nydegger et al., [14] where 43.7% were in the range of 10–15-year, 31.9% within 5–10-year group and 24.4% were less than 5 years. The mean age of the children in the study was 10.35±3.28 years which was also similar with a study conducted by Musabbir et al., [15] a few years back.

More than half (60%) of the children in the study were male. Nearly similar findings were found in a study done by Vitale et al., [16] where 62 out of 118 children were male. Slight female preponderance was noted in a study done by Galai et al.,[17]. So, gender is no independent risk factor for the severity and outcome of acute pancreatitis.[18]

In the present study, among 30 cases 70% were in mild group and 30% in severe group. There was no significant difference in terms of age between mild and severe AP group (p=0.86). Our consistent findings were observed in a study done by Vitale et al.,[19] where there was no significant (p=0.96) difference in age group. But contradictory findings were found in a study done by Galai et al.,[17] where there was statistically significant (p=0.01) difference in mean age among mild AP (13.8 years) and severe AP (8.3 years).

In our study, there was no statistically significant difference in WBC, serum creatinine, RBS and S. ALT value between mild and severe pancreatitis groups (p > 0.05). Similar findings were found with the studies done by Galai et al,[17] Vitale et al, [16] and Farrel et al,[20].

S. calcium value was significantly (p=0.001) increased in mild AP (9.8±.67 mmol/l) than severe AP (10.4±.51 mmol/l) groups. Penag et al.,[21] observed that patients with POF had significantly lower value of serum calcium than patients without persistent organ failure (POF) on admission (1.55 ± 0.36 mmol/L vs 2.11 ± 0.46, p < 0.001). Decreased level of serum calcium was commonly seen in critical illness. Hypocalcemia may serve as a potential prognostic factor as it is more common in patients with severe form of acute pancreatitis.[21]

S. Lipase, S. amylase and BUN were not statistically significant (p=0.67, 0.57 and 0.27) in current study. Galai et al.,[17] also reported that S. Lipase was not significant (p=0.27) like our study. Vitale et al.,[16] also found no statistical significant difference in S. amylase level (p=0.35). But in their study, BUN was significantly different (p=0.0007) between mild AP and severe AP (10 mg/dl vs 20 mg/dl). Vitale et al.,[16] reported that CRP has discriminating value between mild and severe AP but we did not find it statistically different (p=0.220) like Izquiredo et al., [22].

In our study, statistically significant difference was noted in pulse and respiratory rate; p value 0.0001 and 0.004, respectively. These two parameters also the part with SIRS which was believed to have some discriminating value alone or as a part in differentiating mild and severe AP. There was also significant difference in systolic and diastolic BP between these two group and p value was 0.007 and 0.003, respectively. Zheng et al.,[23] found statistical significant difference in temp (p=0.001), heart rate (p=0.029) but no significant difference (p=0.688) in respiratory rate in between mild and severe AP group.

SIRS score is very easy to calculate, requires only 4 criteria and only one is lab parameter ie, leukocyte count. In this study, from severe AP group SIRS (score ≥2) identified all 9(100%) as severe case and from mild AP group SIRS identified 7(33.3%) as severe AP. This significant (p=0.001) findings from this study we can say it is better and easy to identify severe cases by very simple SIRS scoring. On the other hand, from severe AP group, no case identified as mild (<2 score) by SIRS but 14 (66.7%) case from mild AP group 21(70%1) identified as mild. In previous studies, SIRS was found to be a good discriminating factor between mild AP and severe AP. Presence of SIRS found to be associated with persistent organ failure, pancreatic necrosis, increased hospital stay and ICU admission.[13,24] SIRS (score ≥2) had sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) in predicting severe acute pancreatitis was 100%, 77.8%, 63.6%, 100%, respectively.

CONCLUSIONS

SIRS score showed the promising results in the study in case of assessing the severity of pancreatitis in paediatric age group. So, SIRS can easily identify severe cases at admission with simple three clinical and one laboratory parameter.

Limitations of the study: The small sample size was small. Data were during COVID-19 pandemic situation. Single center study scarcely represent the situation of the whole country.

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Original Article

Association of Serum Uric Acid and Liver Enzymes in Adults at Tertiary Level Hospital in Bangladesh

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Abstract

The level of serum uric acid (SUA) has been linked to metabolic syndrome, diabetes, and cardiovascular disease. The purpose of this study was to evaluate the relationship between SUA and serum liver enzymes in a Bangladeshi adult population. This cross-sectional study was conducted among apparently healthy adults aged >18 years, from March 2019 to February 2020 at the Department of Biochemistry, Sir Salimullah Medical College (SSMC), Dhaka. SUA, liver enzymes, lipid profile and other biochemical markers were measured in the collected samples by using standard methods. All statistical analyses were performed by using SPSS version 22.0 software and p<0.05 was considered statistically significant. A total of 140 subjects were selected and blood sample were collected for biochemical analysis. Among them 70 were male and 70 were female. Serum uric acid (SUA), Alanine transaminase (ALT), Aspartate aminotransferase (AST) and Gamma-glutamyl transferase (GGT) levels were significantly (p<0.001) higher in male than female group. Pearson's correlation analysis showed that there were significant positive correlation between SUA and serum ALT, AST, GGT (p<0.001). However, it also showed significant positive correlation between SUA and total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C), while negative correlation was found between SUA and high density lipoprotein cholesterol (HDL-C) (p<0.001). The role of SUA in the prediction of elevated liver enzymes showed area under the ROC Curve (AUC) 0.839 for ALT, 0.848 for AST and 0.809 for GGT respectively. SUA is positively related with ALT, AST, GGT in adults. More prospective studies are needed to clarify the complex relationship between SUA and liver enzymes in the general population.

Keywords: *Serum uric acid (SUA), ALT, AST, GGT, lipid profile.*

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INTRODUCTION

Alanine aminotransferase (ALT), aspartate amino-transferase (AST) and gamma glutamyl transferase (GGT) are the liver enzymes which comprise liver function tests. Among them ALT is the most specific marker of liver function, but AST and GGT are the less specific markers because they are present in other tissues.[1] Serum uric acid (SUA) is the major end product of the purine metabolism and the level of SUA is maintained by the balance between SUA production and excretion.[2] Intracellularly uric acid can act as a pro-oxidant inducing the release of inflammatory mediators and growth factors.[3,4] Uric acid has been shown to contribute to lipoprotein oxidation and inflammation which are thought to play vital roles in the development and progression of Non-alcoholic fatty liver disease (NAFLD).[5,6] Hyperuricemia has been linked to both MetS and cardiovascular disease.[7,8] The SUA was increased in most NAFLD patients which was an independent risk factor for NAFLD. Therefore, increased SUA may play the role of linking NAFLD with MetS.[9,10]

Serum biomarkers especially alanine aminotransferse (ALT) levels are sensitive in detection of hepatocyte injury in both obese and non-obese patients. ALT levels are related to Metabolic syndrome (MetS), diabetes mellitus, cardiovascular disease and nonalcoholic fatty liver disease (NAFLD). It was evident that in asymptomatic individuals

with mild elevations of ALT and AST, 98% had liver disease commonly fatty liver disease. High aminotransferase levels even within reference range are associated with the components of metabolic syndrome that was observed in a study. Furthermore, Serum uric acid (SUA) is significantly elevated in cardiovascular disease, diabetes mellitus, Metabolic syndrome (MetS) and is also considered as important risk factor for development of NAFLD. Evidence suggests that elevated SUA levels and increased activity of liver enzymes GGT and ALT (and to a lesser extent AST) are also associated with the development of Metabolic syndrome (MetS) and nonalcoholic fatty liver disease (NAFLD). This statement is supported by some studies conducted worldwide. It was reported that hyperuricemia and SUA even in the reference range are associated with elevated serum ALT in healthy Chinese adults. However, there is limited study on the association of SUA with serum AST and GGT among healthy adults in abroad.

ALT is a specific marker of liver inflammation and hepatocellular injury.[11] As, ALT is closely associated with fatty deposition in the hepatocytes, it is commonly considered as a surrogate marker for nonalcoholic fatty liver disease (NAFLD)[12,13]. Elevated ALT is related to a range of health outcomes such as metabolic disorders and cardiovascular diseases (CVD).[14] Recent studies showed that NAFLD is closely associated with obesity, hypertension, dyslipidemia, glucose intolerance, metabolic syndrome (MetS), as well as cardiovascular events[9]. Thus, NAFLD is considered to be a hepatic consequence of metabolic diseases[10]. Like ALT, AST levels were also elevated with MetS in several cross-sectional studies.[12,15] Thus, elevated AST also might be a risk factor for MetS. However, epidemiological studies suggest that elevated levels of GGT, another liver enzyme, predict subsequent development of several metabolic disorders such as hypertension, diabetes and MetS.[16,17] Some authors have speculated that visceral fat could play a role in the association of GGT with metabolic abnormalities and this enzyme could be considered as a reliable marker of visceral fat deposition.[18]

In our country, there is no report on the association of hyperuricemia and elevated liver enzymes in general adults. Consequently, this cross-sectional study was designed to investigate the relationship between SUA levels and liver enzymes (ALT, AST and GGT) in these adult subjects.

Furthermore, increasing evidence has suggested that not only hyperuricemia but also SUA within the reference range showed a positive correlation with the components of MetS.[19] A number of cross-sectional studies have shown that GGT is correlated positively with serum uric acid.[20,21] Therefore, the proposed study was designed to evaluate the association between serum uric acid and liver enzymes (ALT, AST and GGT) in the Bangladeshi adults.

MATERIALS AND METHODS

Study settings and Study population

This cross-sectional study was conducted from 1st March, 2019 to 29th February, 2020 at the Department of Biochemistry, SSMC, Dhaka, Bangladesh. The study was conducted on 140 subjects (70 males and 70 female). Apparently healthy people of 30 to 59 yrs were included in the study. These subjects were selected from the attendants accompanying the patients attending the outpatient department of SSMC and Mitford Hospital. Study population included both male and female categorized into four quartiles including hyperuricemia on the basis of SUA level. Inclusion criteria: (i) Healthy adults with age range of 30- 59 years (ii) Both genders. Exclusion criteria: (i) Subjects with DM and renal failure. (ii) Those taking anti-hypertensive, anti-diabetic, lipid-lowering and hypouricemic drugs. (iii) Chronic liver disease such as cirrhosis, liver cancer, viral hepatitis, autoimmune hepatitis and taking hepatotoxic drug (iv) Alcoholism.

Anthropometric data collection

Height was measured (without shoes) by measuring instrument and taken to the nearest centimeters. Body weight was measured in light clothing and without shoes. Weight was recorded in Kilogram. Body mass index (BMI) was calculated as weight in Kilogram divided by height in meter square.[10] Blood pressure was measured three times at 2 minutes' interval in a sitting position after at least 5 minutes of rest in a quiet room by using of manual sphygmomanometer with appropriate cuff. The mean of three BP measurements was calculated and used in all analyses. Before collecting specimen, each patient was interviewed and relevant information was recorded systematically in a pre-designed standard data sheet and then data was checked and edited.

Study Procedure

Apparently healthy subjects were selected from the attendants accompanying the patients attending the outpatient department of SSMC and Mitford Hospital, Dhaka. These subjects were recruited following history, physical examination and routine baseline biochemical

investigations. Ethical permission was taken from the Ethical Review Committee of SSMC. After proper counseling about aim, objectives, risk and procedure of the study were explained in details to all participants. Only voluntary candidates were recruited as research participants. They had the freedom to withdraw themselves from the study at any stage. Written informed consent was taken from all participants. Socio- demographic as well as other relevant data were taken and recorded in the data collection sheet with a prefixed questionnaire. A blood sample was collected for biochemical variables to be measured.

Blood Collection and Laboratory analysis

Each participant's overnight fasting blood sample, which included about 5 mL, was taken for biochemical evaluations. Serum uric acid (SUA), fasting blood glucose (FBG), triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), liver enzymes, and alanine aminotransferase were all measured in the blood biochemical studies. Alkaline phosphatase (ALP), gamma-lutamyl transferase (GGT), aspartate aminotransferase (AST), and ALT. Serum Kinetic techniques were used to determine the liver enzyme activity, and other biochemical parameters were examined by conventional colorimetric techniques. A biochemistry analyzer was used to measure the biochemical parameters. Biochemical tests were done in the Biochemistry laboratory of SSMC, Dhaka.

Operational definitions

- **Elevated liver enzymes** defined as ALT >45 U/L in male and >34 U/L in female; AST >35 U/L in male and >31 U/L in female; GGT >55 U/L in male and >38 U/L in female[22].
- **Hyperuricemia** was defined according to sex-specific SUA levels: SUA >7.0 mg/dL for male and >6.0 mg/dL for female[23].

Statistical analysis

Continuous variables were expressed as mean values and standard deviation (SD), whereas categorical variables were described as frequencies and percentages. Data with skewed distribution (SUA, ALT, AST and GGT) were log-transformed and then used for subsequent statistical analyses; the result was back-transformed to produce geometric means which were reported. SUA levels were divided into quartiles including hyperuricemia. Statistical methods followed were unpaired students' t-test, Analysis of variance (ANOVA) test where indicated. Bonferroni test was performed to show the difference in between different categories of SUA level. Pearson's correlation was performed to analyze the relation between SUA level and liver enzymes as well as between SUA and lipid profile. Multiple linear regression was performed to determine the relation between dependent and independent variables of interest after adjusting for other potentially confounding independent variables. We used the area under the receiver-operating characteristic curve (AUC) and 95% confidence intervals (CIs) to assess the predictive ability of serum uric acid levels to assess the risk for elevated liver enzymes. All statistical analyses were performed by using SPSS version22.0 software and $p<0.05$ was considered statistically significant.

RESULTS

In this study, a total of 140 subjects were selected. Among them 70 were male and 70 were female.

Table I showed the baseline characteristics of study subjects. The mean (±SD) age of male was 44.43±7.32 years and that in female was 42.80±6.92 years. It also showed that there was no statistically significant difference regarding age between two groups. In case of BMI, no significant difference was observed in between two groups. The mean (±SD) SBP in mmHg was significantly higher in male than female (130.83±12.08 vs 125.71±13.89, $p<0.05$). The mean (±SD) DBP in mmHg (87.50±9.66 vs 82.93±9.80, $p<0.01$) also showed significant difference between male and female.

Table- I: Baseline characteristics of study subjects (n=140)

Variables	All subjects (n=140)	Male (n=70)	Female (n=70)	*p*-value
Age (years)	43.62±7.15	44.43±7.32	42.80±6.92	0.175
BMI (kg/m^2)	24.11±2.86	24.51±2.87	23.71±2.81	0.099
SBP (mmHg)	128.27±13.22	130.83±12.08	125.71±13.89	<0.05
DBP (mmHg)	85.21±9.96	87.50±9.66	82.93±9.80	<0.01

Results were expressed as mean±SD. Unpaired student's t-test was performed to compare between group means.

Table II contains the mean±SD of the biochemical parameters. Serum uric acid (SUA), ALT, AST and GGT levels were significantly (p<0.001) higher in male than female group. Analysis of lipid profile showed that TC (p<0.05) and LDL-C (p<0.05) level were significantly higher in male than female subjects whereas HDL-C (p<0.01) was significantly lower in male than female group. However, in cases of TG and FPG no significant difference was observed in between groups.

Table- II: Biochemical parameters of study subjects (n=140)

Biochemical parameters	All subjects (n=140)	Male (n=70)	Female (n=70)	p-value
FPG (mmol/L)	5.34±1.11	5.45±1.16	5.22±1.04	0.228
*SUA (mg/dl)	4.94±1.35	5.46±1.33	4.49±1.32	<0.001
*ALT (U/L)	29.51±1.33	33.88±1.32	25.70±1.26	<0.001
*AST (U/L)	27.54±1.32	31.62±1.29	24.55±1.27	<0.001
*GGT (U/L)	35.48±1.46	43.65±1.42	29.51±1.34	<0.001
TC (mg/dl)	193.86±21.97	198.30±23.04	189.43±20.03	<0.05
TG (mg/dl)	157.01±26.09	160.14±21.15	153.89±30.06	0.157
HDL-C (mg/dl)	39.93±4.38	38.90±4.08	40.96±4.46	<0.01
LDL-C (mg/dl)	125.80±12.60	128.09±13.21	123.51±11.61	<0.05

Results were expressed as mean±SD and *geometric mean±SD.
Unpaired student's t-test was performed to compare between group means.

Table III (a) states the characteristics of study subjects categorized by serum uric acid (SUA) level. Participants in the higher quartiles of SUA and hyperuricemia showed an increasing pattern of age as well as BMI, SBP and DBP. Serum biochemical parameters such as ALT, AST, GGT, TC, TG, LDL-C and FPG all intended to increase from lowest to highest quartiles of SUA and hyperuricemic subgroup while HDL-C intended to decrease from lowest to highest quartiles of SUA and hyperuricemic subgroup (p<0.001).

Table- III (a): Characteristics of subjects categorized by SUA level in all subjects (n=140)

Variables	Quartiles of normal serum uric acid (SUA)				Hyperuricemia (n=18)	*p*-value
	Q1 (n=26)	Q2 (n=32)	Q3 (n=34)	Q4 (n=30)		
*SUA (mg/dl)	3.34±1.14	4.20±1.08	4.97±1.09	6.05±1.08	8.28±1.15	<0.001
Age (years)	37.54±5.85	39.75±5.61	44.06±5.60	48.50±5.53	50.33±4.70	<0.001
BMI (kg/m^2)	21.47±2.73	23.36±2.34	24.15±2.42	25.21±1.98	27.38±1.63	<0.001
SBP(mmHg)	118.65±12.37	122.19±10.77	127.50±12.51	135.93±7.45	141.67±9.39	<0.001
DBP(mmHg)	77.69±8.63	80.94±8.93	87.79±7.41	88.50±8.00	93.33±10.85	<0.001
FPG (mmol/L)	4.67±0.96	5.05±0.99	5.17±0.75	5.55±0.65	6.78±1.37	<0.001
*ALT (U/L)	23.44±1.34	26.91±1.29	29.51±1.26	33.88±1.20	39.81±1.16	<0.001
*AST (U/L)	21.88±1.38	25.70±1.25	27.54±1.27	32.36±1.16	37.15±1.16	<0.001
*GGT (U/L)	25.12±1.49	31.62±1.41	36.31±1.33	44.67±1.26	50.11±1.22	<0.001
TC (mg/dl)	178.42±21.50	183.47±14.89	190.18±12.88	205.60±14.75	222.06±22.10	<0.001
TG (mg/dl)	135.85±12.28	146.13±21.69	160.29±32.52	169.37±15.41	180.17±16.12	<0.001
HDL-C (mg/dl)	42.73±3.69	41.81±3.37	40.50±4.16	37.43±3.65	35.61±3.11	<0.001
LDL-C (mg/dl)	115.69±11.83	120.97±10.61	124.32±9.16	133.60±8.60	138.78±10.36	<0.001

Results were expressed as mean±SD and *geometric mean±SD.
ANOVA test was performed to compare all the variables between normal SUA and hyperuricemia.

Table III (b) presents the multiple comparison in between different categories of SUA level in all subjects. Significant difference was observed between the subgroups of Q1 vs Q3, Q1 vs Q4, Q1 vs hyperuricemia and Q2 vs Q4, Q2 vs hyperuricemia as well as Q3 vs hyperuricemia for all three liver enzymes (ALT, AST, GGT).

Table- III (b): Post-hoc analysis of serum ALT, AST and GGT for comparison in between different categories of SUA level in all subjects (n=140)

	Serum ALT (U/L) *p*-value	Serum AST(U/L) *p*-value	Serum GGT(U/L) *p*-value
Q1 vs Q2	1.000	0.566	0.521
Q1 vs Q3	<0.05	<0.05	<0.05
Q1 vs Q4	<0.001	<0.001	<0.001
Q1 vs Hyperuricemia	<0.001	<0.001	<0.001
Q2 vs Q3	0.996	1.000	1.000
Q2 vs Q4	<0.05	<0.05	<0.01
Q2 vs Hyperuricemia	<0.001	<0.001	<0.001
Q3 vs Q4	0.423	0.075	0.055
Q3 vs Hyperuricemia	<0.001	<0.001	<0.01
Q4 vs Hyperuricemia	0.116	0.090	1.000

Data were log transformed.
Bonferroni test was performed for multiple comparison in between different categories of SUA.

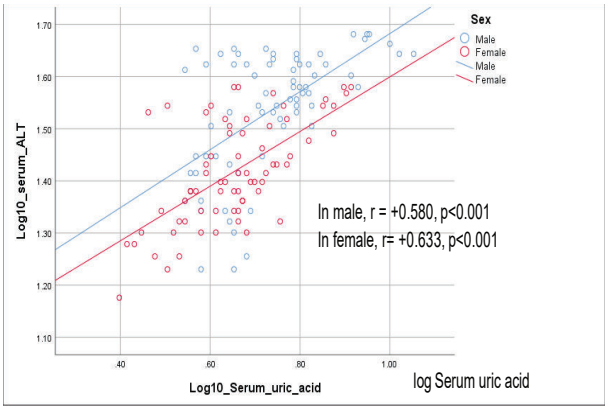

Figure- 1: *Scatter diagram showing correlation between log SUA and log serum ALT in male and female subjects*

Figure 1 illustrates the correlation between log SUA and log serum ALT in male and female subjects. It was evident that the two variables were positively and significantly (p<0.001) correlated in both genders.

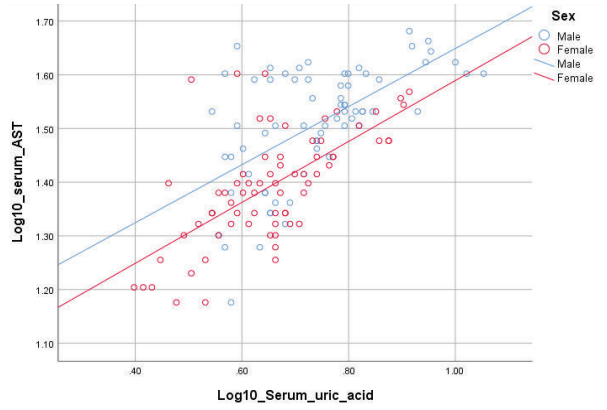

Figure- 2: *Scatter diagram showing correlation between log SUA and log serum AST in male and female subjects*

Figure 2 showing correlation between log SUA and log serum AST in male and female subjects. It was evident that the two variables were positively and significantly (p<0.001) correlated in both genders.

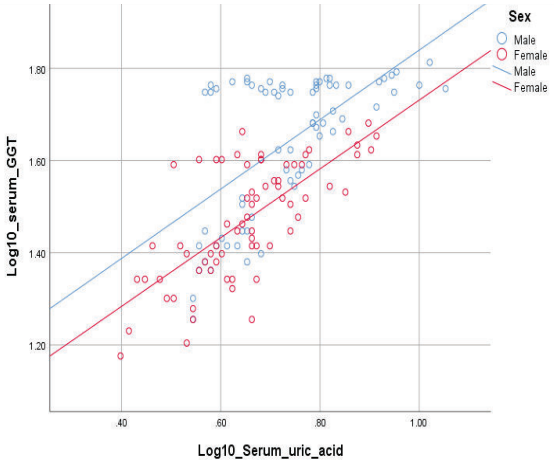

Figure- 3: *Scatter diagram showing correlation between log SUA and log serum GGT in male and female subjects*

Figure 3 showing correlation between log SUA and log serum GGT in male and female subjects. It was evident that the two variables were positively and significantly (p<0.001) correlated in both genders.

Table IV presents the role of SUA in the prediction of elevated liver enzymes in all subjects. AUC of SUA for ALT was found to be 0.839 (95% CI: 0.759-0.918) at cutoff point of 1.55 with a sensitivity of 77.8% and specificity of 73.8%. AUC of SUA for AST was found to be 0.848 (95% CI: 0.772-0.925) at cutoff point of 1.53 with a sensitivity of 77.8% and specificity 74.6%, while in case of GGT AUC of SUA was found to be 0.809 (95% CI: 0.723-0.894) at cutoff point of 1.62 with a sensitivity of 83.3% and specificity of 68.9%.

DISCUSSION

In this study it was observed that there was no significant age difference between male and female subjects. However, it was not consistent with the study done by Yang et al[23] who found a significant age difference between two groups. The study showed that BMI did not differ in between two groups. Similar results were observed by a Chinese study[24]. In this study, mean (±SD) SBP and DBP in mmHg of male differed to some extent from those of female (130.83±12.08 vs 125.71±13.89 and 87.50±9.66 vs 82.93±9.80, p<0.01). Similar observation was evident in other studies.[10,24] It was evident from the study that participants with hyperuricemia as well as those in the highest quartile (Q4) of SUA within reference range had elevated liver enzymes (ALT, AST and GGT). The data of this study also revealed that there is a stepwise increase in liver enzymes with increasing levels of SUA even within the reference range. Participants with increasing quartiles of SUA and hyperuricemia showed an increasing trend in levels of TC, TG, LDL-C, FPG as well as age, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP) except HDL-C which showed decreasing trend with increasing SUA level. Nearly similar pattern of observation was reported by two studies.[10,25] After stratification by the quartiles of SUA levels it was evident that the percentage of elevated liver enzymes (ALT, AST, GGT) were increased along with the increment of uric acid quartiles and also in hyperuricemic subgroup in subjects of both genders. However, male had a higher percentage of elevated ALT, AST and GGT than female in all of the SUA categories. Nearly similar findings were observed by some investigators.[10,24]

The present study showed that SUA was significantly and positively correlated with ALT, AST, GGT, TC, TG and

Table- IV: Diagnostic test indices and performance of SUA for predicting elevated liver enzymes in all subjects (n=140)

	AUC	Cut-off value of SUA	Sensitivity	Specificity	p-value	95% Confidence Interval	
						Lower Bound	Upper Bound
ALT	0.839	1.55	77.8%	73.8%	<0.01	0.759	0.918
AST	0.848	1.53	77.8%	74.6%	<0.01	0.772	0.925
GGT	0.809	1.62	83.3%	68.9%	<0.01	0.723	0.894

Results of ALT, AST and GGT were log transformed.
Then analyses for ROC curves were done.

LDL-C while inversely correlated with HDL-C in both genders which is consistent with other studies.[26,27] Furthermore, our data implied that increased SUA is independently associated with elevated liver enzymes (ALT, AST and GGT). A study carried out on Chinese adults by Chen et al[10] observed an association between uric acid and elevated ALT. After adjustment of multiple independent confounding variables along with SUA in multiple regression analysis where a significant independent association of SUA with liver enzymes was evident. Nearly similar observations were reported by.[10,28] Therefore, it is evident that increased SUA is associated with elevated liver enzymes. Zhang et al[29] reported that increased generation of uric acid mediated by high activity of xanthine oxidoreductase is able to accelerate the development of nonalcoholic fatty liver disease (NAFLD). Elevated uric acid induces the triglyceride accumulation by promoting the over-expression of pro-lipogenic enzymes sterol regulatory element binding proteins[30]. Evidence suggests that generation of uric acid catalyzed by xanthine oxidoreductase is accompanied by generation of reactive oxygen species. Thus, xanthine oxidoreductase induced oxidative stress lead to NAFLD development[31]. Elevated serum ALT levels are most closely related to liver fat accummulation and are commonly used as a surrogate marker for NAFLD in an epidemiological study[32]. Asymptomatic individuals with mild elevation of ALT, AST indicates the chances of liver disease, mainly NAFLD and hepatitis although AST is less specific liver enzyme[33]. A study on Framingham Offspring Heart Study demonstrated that both AST and ALT elevations up to 3 times the upper normal are associated with an increased risk for developing diabetes mellitus (DM). When restricted to normal values, only ALT was associated with incident DM. A recent cross-sectional study by Chen et al[10] found that positive relationship of elevated ALT with metabolic syndrome (MetS) was stronger than that of elevated AST. Furthermore, both NAFLD and MetS are associated with an increased risk of cardiovascular disease (CVD).[34]

GGT has been well established as a reliable marker of increased hepatic lipid content and hepatic insulin resistance by Thamer et al.[35] Both GGT and ALT have also been shown to predict the development of insulin resistance and DM stated by Vozarova et al[36]. Recent cross-sectional and longitudinal studies have found relatively independent associations between elevated serum GGT levels and hypertension or DM.[37,38] Cross-sectional studies of mostly middle-aged participants had shown linking ALT and GGT to components of the metabolic syndrome as well as T2DM and CVD.[39,40] However, it has been reported that SUA is significantly associated with hypertension, obesity, CVD, hypertriglyceridemia and hyperglycemia which may increase the risk of MetS.[41] Furthermore, SUA has been considered as an oxidative stress marker of MetS and CVD[9]. Thus, MetS has been considered to play an important role in the development or progression of NAFLD. Elevated serum uric acid levels have also been found to be associated with the development of NAFLD which can lead to cirrhosis and increased plasma activity of GGT and ALT[21]. Reason behind the pathogenesis of NAFLD appears to be insulin resistance which results lipolysis and excess deposition of fat on liver and together create inflammatory effects, oxidative stress and lead to elevate liver enzymes.[42,43] The predictive ability of SUA in the prediction of elevated liver enzymes (ALT, AST, GGT) were assessed by ROC curves. Area under the receiver operating characteristic curve (AUC) of SUA was used to identify subjects with elevated liver enzymes (ALT, AST, GGT). AUC of SUA for elevated ALT was found as 0.839 with the cut-off value of 1.55. Furthermore, AUC of SUA for elevated AST and GGT were 0.848 and 0.809 at cut-off values of 1.53 and 1.62 respectively. This observation is consistent with the finding of a study on Chinese adults conducted by Chen et al.[10] This indicates that SUA can be used as a predictor for elevated liver enzymes.

Thus, it can be concluded from the study that almost all the variables except HDL-C are increased with the increment of SUA level and hyperuricemia. Increased SUA is associated with elevated liver enzymes (ALT, AST and GGT) in adults and this association is independent of other confounding factors. This association suggests that SUA can be used as a screening test for NAFLD and other metabolic disorders.

CONCLUSIONS

Subjects in higher quartiles of SUA and hyperuricemia showed an increasing pattern of age with significantly higher BMI, SBP, DBP, FPG, ALT, AST, GGT, TC, TG, LDL-C and lower HDL-C. The variation of these parameters based on quartiles of SUA and hyperuricemia were almost similar in both genders. The percentage of adults with elevated liver enzymes increased with an increment in the SUA level in both genders while male had

a higher percentage of elevated liver enzymes than female in all SUA categories.

Pearson's correlation analysis showed positive correlation of SUA with ALT, AST, GGT, TC, TG, LDL-C and negative correlation with HDL-C among all subjects as well as in male and female subjects. In multiple regression analysis, it showed a significant independent linear association of SUA with liver enzymes (ALT, AST and GGT).

Disclosure of conflict of interest

No competing interests exist by the authors.

Statement of informed consent

"Informed consent was obtained from all participants."

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Original Article

Outcome of Early Active and Late Mobilization following Flexor Tendon Repair in Zone II of Hand

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Abstract

The functional outcome of flexor tendon injury after repair depends on multiple factors. Postoperative rehabilitation protocol plays an important role after a good repair for better functional outcomes. The aim of this study is to compare the outcome of early active mobilizations versus late mobilizations after flexor tendon repair in zone-II of hand. This Quasi-experimental (Nonrandomized control trial) was conducted from July 2018 to June 2021. Total 30 patients of flexor tendon injury in Zone-II of hand presented within 3 weeks were divided into two equal groups according to envelope technique, late mobilization (No intervention group) group- A and early active mobilization (Intervention group) group-B. All the flexor tendons were repaired with polypropylene 4/0 double strand score sutures and 6/0 epitendinous continuous sutures. In group-A mobilization started after 3 weeks and in group–B, intervention was given by active mobilization which was started at the day of operation. Buck Gramcko functional criteria and Louisville system were used for assessment of final result after 6 months of surgery. Male was predominant, M: F ratio was 3.3:1. Mean age of the respondent was 32.53±9.86 years. Dominant (Right) hand involvement was 70%. Student and service holder were the common involved group. Nearly three fourth (73%) of them had sharp cutting injury. More than half (53.10%) of the injuries were found in ring and little fingers followed by index (20.30%), middle (20.30%) and thumb (6.30%). Mean time interval between injury and operation was 11 days. Adhesion formation was the commonest complication that was 40% in group A and 20% in group B. More satisfactory outcome (87.50%) was found in group- B (Intervention group), that is patients who received early active mobilization; where the level of satisfactory outcome was less (62.50%) in group-A (Non-intervention group), that is patients who received late mobilization (p-value was significant <0.05). Early active mobilization following repair of flexor tendon in zone II of hand ensures better functional outcome with minimum complication compared to late mobilization.

Keywords: *Flexor tendon injury, zone II of hand, tendon repair, early active mobilization, late mobilization.*

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INTRODUCTION

The hand is one of the important medium of introduction to the outside world. Its unique repertoire of prehensile movements, grasp, pinch, hook-action and tactile acuity sets us apart from all other species. But intact and proper functioning flexor tendons are mandatory for any hand function.[1] Flexor tendon surgery at zone II is particularly difficult as fibro osseous sheath with pulley systems are there to prevent bow-stringing. The zone II is also important as two tendons Flexor digitorum superficialis (FDS) and Flexor digitorum profundus (FDP) pass through the fibro osseous sheath system. The two tendons maintain fairly constant relationship and that is important to prevent malfunctioning of tendons. For injured flexor tendon in the hand, the goal of treatment is recovery of functionally acceptable digital motion with intact tendon[2] Improving the results in zone II flexor tendon injuries remains a constant challenge to hand surgeons. It is now generally accepted that primary or delayed primary repair within four to six weeks should be done. Both flexor tendons should be repaired. An atraumatic technique is obligatory to minimize the formation of adhesions and scar tissues. Provided the repair has been done in a satisfactory manner, good results in zone II injuries depend on the post-operative management.[3] Optimizing the outcome

following flexor tendon repair requires a combination of factors, encompassing far more than suture bridging a severed tendon. Multiple injuries, smoking, and concomitant nerve injuries have shown to be factors leading to a less desirable outcome. Therapy with a certified hand therapist, however, results in higher patient satisfaction and range of motion scores.[4]Tendons treated with early passive digital mobilization are characterized by early epitenon proliferation and migration to the repair site. The formation of peritendinous adhesions is limited. Careful ultra-structural examination found that the gliding surface had been restored by a flattened layer of epitenon cells at 10 days after repair. In contrast, tendons treated with immobilization showed a repair response that was dominated by extrinsic mechanisms of repair. By 10 days after repair, the ingrowth of peripheral adhesions dominated the repair site. Precise tendon suture and early digital mobilization could alter the primary mechanism of tendon repair in favor of the desired mechanism.[5]The improved understanding of splinting techniques has promoted these mobilization protocols. It has been proven that postoperative immobilization leads to increased disability period, weak tensile strength, decreased final functional capacity, stiffness, and deformity. Further early postoperative mobilization leads to improved tendon healing, increased tensile strength, and decreased adhesion formation, early return of function, and less stiffness and deformity as compared to the immobilization protocol. However, as any other procedure it has its own demerits in the form of rupture of repaired tendons.[6,7,8] We conducted a study to evaluate the outcome of early active mobilization and compared with the late mobilization after repaired of flexor tendons in zones II of hand.

Surgical Anatomy and Biomechanics-The innervation of the FDS muscle is from the median nerve. The ulnar nerve innervates the muscle-tendon units of FDP of the ring and little fingers. The anterior interosseous branch of the median nerve innervates the FDP muscle-tendon units of the index and middle fingers and FPL of thumb. The vinculum brevis superficialis (VBS) and the vinculum brevis profundus (VBP) consist of small triangular mesenteries near the insertion of the FDS and FDP tendons. The vinculum longum to the superficialis tendon (VLS) arises from the floor of the digital sheath of the proximal phalanx. The vinculum longum to the profundus tendon (VLP) arises from the superficialis at the level of the PIP joint.[8]

Kleinert and Verdan (1983) classified the injuries of flexor tendons into five zones.

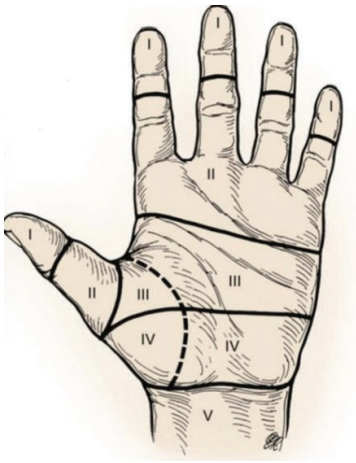
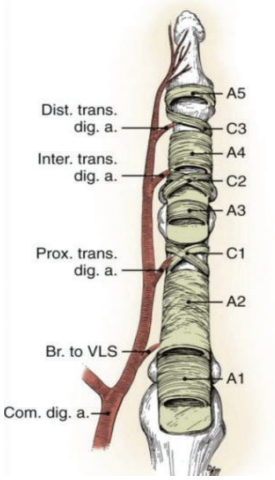


Figure- 1: *Flexor system has been divided into five zones. Zone 2, which lies within the fibro-osseous sheath, has been called "no man's land" because it was previously believed that primary repair should not be done in this zone.*[9]

Flexor zone II started from the distal palmar crease (proximal aspect of the A1 pulley) tothe insertion of the FDS tendon at the middle of the MPX, the "no man's land" because of surrounded by fibrous flexor sheathandzone I is distal to FDS insertion to up to FDP insertion. In each finger, the FDS tendon enters the A1 pulley and divides into two equal halves that rotate laterally and then dorsally (180 degrees) around the FDP tendon. The two slips rejoin deep to the FDP tendon over the distal aspect of the proximal phalanx and the palmar plate of the PIP joint at the Camper chiasm and then insert as two separate slips on the volar aspect of the middle phalanx.[3]



Figrue- 2: *Fibrous retinacular sheath, form the flexor pulleys, which can be identified as five heavier annular bands and three filmy cruciform ligaments. Distal transverse digital artery; intermediate transverse digital artery; proximal transverse digital artery; branch to vinculum longum; common digital artery.*[9]

Zones I and II of the FDS and FDP tendons are described by the fibro osseous digital sheath. Within this sheath, the flexor tendons are covered by a layer of flattened fibroblasts termed the epitenon. This specialized surface is the crucial gliding surface that must be restored for flexor tendon repair to be successful.[9]

Dynamics of flexor tendons- Excursion of a tendon can be affected adversely by extrinsic factors, such as contractures and adhesions, and enhanced by exercise and stretching. The total moment of the tendon on the joint is the product of tension and moment arm. As the moment arm increases, less tension is required to move the joint. With the moment arm kept constant, the independent variable is tension. Although tension may vary in response to muscle strength, the tension throughout the segments of the tendon cannot be changed. Tension seen by one part of the tendon is constant throughout the whole tendon. To change the force and torque seen by each joint crossed by a single tendon, therefore, the moment arm for the different joints must vary. The FDP has a different moment arm to each joint it crosses1.25cm at the wrist, 1.0 cm at the MCP joint, and 0.75 cm and 0.5 cm respectively, at the PIP and DIP joints. To move the joint through its full range of motion, the FDP must have an excursion of 1.57 cm.[10, 11]

MATERIALS AND METHOD

This Quasi-experimental (Non-randomized control trial) was conducted in BSMMU, Dhaka, Bangladesh from July 2018 to June 2021. A total of 30 patients were enrolled according to the inclusion criteria (FDS, FDP and FPL injury, presented within 3 weeks of surgery, stable fracture or no fracture with minimum contamination and sharp cutting or minor laceration, age of the patients were below 50 years with good digital circulation) and exclusion criteria (Lacerated injury, stiff joints of finger, comminuted or unstable fracture and medical problems, like paralytic hand, Raynaud's disease, arthritic hand) and informed written consent was obtained.

All the flexor tendons were repaired with polypropylene 4/0 double strand score sutures and 6/0 epitendinous continuous sutures.

The patients were divided into two equal groups by closed envelop technique during admission; the late mobilization (No intervention group) group- A and early active mobilization (Intervention group) group-B. In all cases, both the FDP and FDS or FPL in Zone-II were repaired with double strands modified Kessler core suture with locking epitendinous sutures with a knot inside the repair site, using polypropylene 4-0 and 6-0 sutures respectively. Postoperatively below elbow dorsal slab was applied, maintained the wrist in neutral or up to 10^0 palmer flexion in associated nerve repaired cases, MCP joint in 60^0-70^0 flexion, PIP and DIP joint in nearly full extension. In study group B, active flexion was started on the day of operation and follows the specific mobilization protocol (appendix-I) but in the control, group-A immobilization was continued up to 03 weeks after the operation then started finger mobilization study group. Post-operative findings were noted at 1st, 2nd POD and follow-up were given at 12-14 days, 3rd, 6th, 8th, 12th and 16th weeks. Complications were noted. Finally,the outcome was evaluated at 24th weeks according to Buck-Gramco functional criteria and the Louisville systemfor assessment of tendon function.

***Statistical analysis*:** Data was compiled and analyzed with the help of SPSS Version 26.0. P value <0.05 were labeled as statistically significant. The results were expressed with 95% Confidence Interval (CI) and adjusted for known confounders. The summarized data was interpreted accordingly and then presented in the form of tables and figures. Continuous variables were expressed as mean with standard deviation and categorical variables as count with percentage.

RESULTS

Total number of respondents was 30 and total fingers involvement was 60 and thumbs involvement was 4.

Table I contains that mean age of the study populations was 32.42±6.2 years, age distribution was almost similar in all group except in age group 10-20 years, where it was 6.7%; in other groups 27% to 40%.

Table- I: Age distribution of the respondents (n=30)

	Group A	Group B	Total
Age (Years)			
10-20	1(6.7%)	2(13.3%)	3(10.0%)
21-30	6(40.0%)	3(20.3)	9(30.0%)
31-40	4(26.7%)	7(46.7%)	11(36.7%)
41-50	4(26.7%)	3(20.0%)	7(23.3%)
Mean Age (Years)	32.10±5.6	32.54±6.8	32.42±6.2

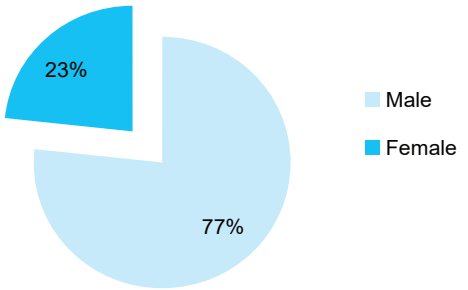


Figure- 3: *Sex distribution of the respondents (n= 30).*

Figure 3 shows the distribution of sex among the respondents, here 77% was male and male-female ratio was 7:2.

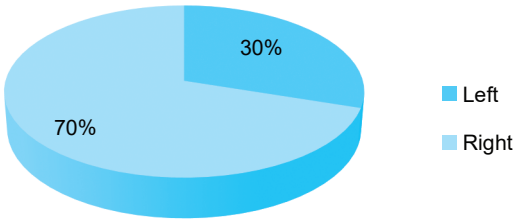


Figure- 4: *Hand involvement of the respondents (n= 30)*

Figure 4 states that right hand involvement was 70% and rest was left hand.

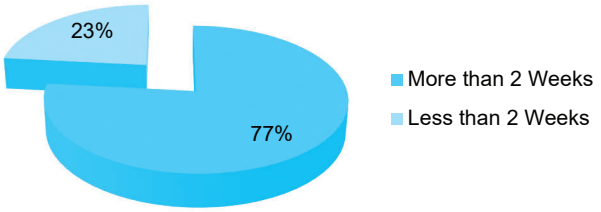


Figure- 5: *Distribution of time interval between injury and operation.*

Figure 5 illustrates that time interval between injury and operation was less than two weeks was 77% of patients where more than two weeks but within three weeks was 23%.

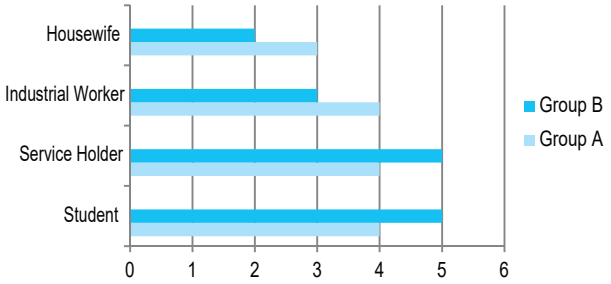


Figure- 6: *Distribution of the respondents according to occupation (n=30).*

Figure 6 shows taht distribution of occupation, among the patients of group-A (non- intervention) group A- industrial worker, service holder and students were almost the same member that was around 26% and remaining 20 was housewife in group B- service holder and students were 33% in each.

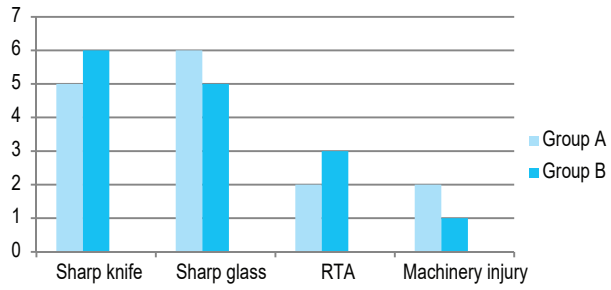


Figure- 7: *Distribution of the patients according to causation of injury (n=30)*

Figure 7 shows the distribution of the patients according to causation of injury, here 5,6,2 and 2 injuries were due to knife, sharp glass, RTA and machinery cause respectively. In group 6,5,3 and 1 were due knife, sharp glass RTA and machinery causes respectively.

Sharp weapon- glass cut or sharp knife (73%) was the most common form of injuries, that was significant ($p<0.05$) comparison with RTA and machinery injuries (27%).

Table II contains the distribution of injured fingers. Thumb index, middle, ring and little fingers injury was found in group A.3,7,6,10,6 and in group-B 1, 6,7,9 respectively

Table- II: Distribution of the patients according to the involvement of the fingers (n=64)

Involved Digit	Group A (n=32)	Group B (n=32)	Total n=64	p value
Thumb	3 (9.4%)	1 (3.1%)	4 (6.3%)	
Index	7 (21.9%)	6 (18.8%)	13 (20.3%)	
Middle	6 (18.8%)	7 (21.9%)	13 (20.3%)	
Ring	10 (31.3%)	9 (28.1%)	19 (29.7%)	0.20
Little	6 (18.8%)	9 (28.1%)	15 (23.4%)	

Table III presents the complications after repair, adhesion formation, superficial infection, contracture and rupture were found 6, 3, 4,2 in group A and 3, 1, 1, 2 in group B respectively.

Table- III: Distribution complications after repair (n=64)

Complications	Group A (Late Mobilization) (n=32)	Group B (EAM) (n=32)	P value
Adhesion formation	6(18.75%)	3 (9.38%)	0.045
Superficial infection	3(9.4%)	1(3.13%)	0.041
Contracture	4 (12.5%)	1(3.13%)	0.032
Rupture	2(6.25%)	2(6.25%)	-

Table IV shows that composite flexion, extension deficit, total active motion(TAM) and Buck Gramcko score were more in group study group B, compared to group control group-A. The p-value was <0.05 in every category, which is statistically significant. According to Louisville grading excellent and good result was found in 7 (21.9%) and 13 (40.6%) patients respectively in group A. Excellent and good result was found in 16 (50.0%) and 11 (34.38%) respectively in group B. Regarding complications- adhesion formation, superficial infection, contracture and rupture were more in late mobilization group.

Table- IV: L Specific digit-wise functional outcome according to Buck Gramcko Grade (n=64 fingers) at 24 weeks.

Involved Digit	Group -A					Group -B				
	Total	Excellent	Good	Fair	Poor	Total	Excellent	Good	Fair	Poor
Thumb	3	1(33%)	1(33%)	1(33%)	0	1	1(100%)	0	0	0
Index	7	2(28%)	3(42%)	2(28%)	0	6	3(50%)	2(34%)	1(17%)	0
Middle	6	1(17%)	2(34%)	2(34%)	1(17%)	7	4(42%)	2(28%)	1(14%)	0
Ring	10	4(40%)	5(50%)	1(10%)	0	9	5(55%)	4(44%)	0	0
Little	6	1(17%)	0	3(50%)	2(34%)	9	3(33%)	3(33%)	2(22%)	1(11%)
Total	32	9(28%)	11(34%)	9(28%)	3(9%)	32	18(56.25%)	10(31.25%)	2(6.67%)	2(6.67%)

Table V states that in group-A, out of 3 thumbs, the excellent, good and fair result was 33% in each. In the index finger out of 7 fingers, 28% had excellent, 42% had good and 28% fingers had fair results. In the middle finger, out of 6 digits, 34% had good and fair in each but excellent and poor results were 17% in each. In the ring finger, excellent result had 40%, good had 50% and fair result was 10% digit. In the little finger, excellent result had 17%, fair had 50% and poor had 34% digits. In group B, all the thumbs had excellent results, in the index finger, 50% had excellent, 34% had good and 17% fingers had fair results. In middle finger, 56% had excellent, 28% had good and 14% had fair results. In the ring finger, excellent result had 55%, good had 44% and no fair or poor results. In the little finger, excellent and good had 33% in each, fair had 22% and poor was 11% digit only.

Table- V: Comparison of final functional outcome according to Buck Gramcko and Louisville Grading (n=64).

	Group A (n=32)	Group B (n=32)	P value
Buck Gramcko Grade			
Satisfactory (Excellent+Good)	20 (62.5%)	28 (87.5%)	0.016
Unsatisfactory (Fair+Poor)	12 (37.5%)	4 (12.5%)	
Louisville Grade			
Satisfactory (Excellent +Good)	20(62.5%)	27(84.38%)	0.020
Unsatisfactory (Fair+Poor)	12(37.5%)	5(15.62%)	

Table VI presents that in late mobilization group satisfactory result was (62.5%) in both Buck Gramcko and Louisville grading criteria but in early active mobilization group satisfactory result was 87.5% according to Buck Gramcko grading and (84.38%) according to Louisville grading.

Table- VI: Rehabilitation protocol/Early Active mobilization (EAM) protocol. 12

Day 1 to 28	Splint	:	Dorsal splint with wrist 00-50 dorsiflexion MCP 700 flexion and IP full extension.
	Exercises	:	Shoulder, elbow, supination/pronation promoted.
	Hand	:	10times/session and 3session/day.
	Step 1	:	Try to active extension of all fingers, gaining extension at IP and MCP joints blocked only by a splint.
	Step 2	:	Active flexion of all fingers to possible flexion position without a forceful effort.
	Step 3	:	Passively flex the fingers at MCP and IP joints with the help of other hand, gradually increased the range of passive flexion

Table- VI (Cont'd): Rehabilitation protocol/Early Active mobilization (EAM) protocol

4-8 weeks	Splint : Intermittant, volar splint with wrist 100 _ 150 palmar flexion, MCP 700 flexion and IP extension, removed during exercise, scar mobilization done.
	Exercises : Shoulder, elbow and wrist exercises continued.
	Hand : 10 times/session and3 sessions/day. Block FDP of all fingers and isolated FDS function, and block FDS of all fingers and do isolated FDP contraction. Actively make fist, curling of all fingers into flexion, release and open actively extending to full extent.
8-12 weeks	Volar splint in 150-250 dorsiflexion, MCP 500-700 flexion, IP full extension (used only as night splint).
	Scar mobilization continued.
	Power grip allowed; ball exercises five times each session.
	Resume light work, food, drinking, button, knots, etc.
	Avoid heavy work.
12-14 weeks	No splintage.
	Stop scar mobilization.
	Power grip continue.
	Resume to daily household work but avoid heavy work.
	Exercise : Hand- continued same as above with an increased frequency of 50 times per session and 5 sessions per day.

Photograph:

Photo, A-B: Per-operative photo *C-E: Post operative at 24 weeks*

Photograph (A-E): Per-operative and post operativephotograph. Repair of FDS and FDP of Middle, Ring and little fingers and FDP of Index finger followed by EAM started at day of operation. Follow up at 24 weeks

Photo, F-H: Per-operative photo *I-J: Post operative at 24 weeks*

Photograph (F-J): Pre, per and 24 weeks postoperative photo of repair of FDS and FDP of Index, Middle, Ring and little fingers at zone-II followed by Late mobilization started at 21 days.

DISCUSSION

A flexor tendon injury in zone-II is a serious and complex injury, occurring commonly in young males of the working class and an excellent outcome depends on multiple factors. A delayed diagnosis, a poor suture technique, or an inappropriate rehabilitation regime can lead to deformity and disability. In most cases, the injury involves both tendons, which can cause significant morbidity to patients due to loss of grip and other functions if not repaired properly. The added benefits of a primary/delayed primary repair and early active mobilization are decreased rehabilitation time, adhesion formation, and rupture rate, and increased healing rate with adequate tensile strength.[12] The mean (± SD) age of the study population in group A was 32.50(± 11.34) years and in group B was 32.53(± 8.53) years. Most of the patients belong to 31-40 years age group. Flexor tendon injury in zone II is more common among the working age group, and common occupations were industrial worker, housewife, service holder and student. Male was the predominant (23/30, 6.7%) gender in this study, and dominant right-hand involvement was 70% 0f patients. Regarding etiology, 73.33% (22/30) of injury was accidental in nature by sharp weapons such as knives or broken glass. Machinery injury was 10% (3/10) and road traffic accident-related injury was only 16.67% (5/30), these result is correlated with otherstudy.[12,13,14] Ring and little finger involvement was more 53.1% (34/64) and thumb affected was less than only 6.4% (4/64), similar toother studies.[7,15] Results after a flexor tendon injury repair are inversely proportional to the delay in the repair of the tendons. The added benefits of a primary/delayed primary repair are decreased rehabilitation time, adhesion formation, and rupture rate, and increased healing rate with adequate tensile strength. 23(76.67%) of patients were operated on within 2 weeks of injury but the remaining 7(23.33%) of cases were operated on after 2 weeks. 14/64 (21.88%) digits had associated digital vessel injury and 21/64 (32.81%) digits had associated digital nerve injury that was also similar to the results.[12,14] Regarding complications, adhesion formation 9/32 (28.13%), superficial infection 4/32 contracture 4/32 (12.50%) and tendon rupture 3/32 (9.37%) were significantly more in the late mobilization group, compared with the early active mobilization group, 4(12.50%), 2(6.25%), 1(3.12%), 2(6.25%) respectively. Few of the adhesion digits improved with physiotherapy but 5 digits in the group A were treated with tenolysis after 6 months but no cases in the EAM group needed tenolysis and rupture cases were treated by tendon reconstruction and found satisfactory results. Our results were comparable with the study conducted by Strickland and the results of group B (study group) were similar to the result with Sainiet. al.; Trumble et.al.[12,16,17] In our study, we observed that the early rehabilitation group exhibited the lowest resurgery rate (6.25%), and also used fewer rehabilitation resources, on the other hand, resurgery ratein late rehabilitation groups was 21.88% (5-tenolysis and 2-tendon reconstruction) and took more time also for rehabilitation. Early controlled mobilization 1 week after surgery increased tendon tensile strength, avoided large callus formation, and reduced tendon adhesion.18 By contrast, continual immobilization during the fibroblastic phase resulted in disorganized cross-links among newly formed collagen fibres, leading to the contracture of ligaments, joint capsules, and volar plates.[19,20] A meta-analysis summarized the complication rates following flexor tendon repairs: the risk of tendon rupture was 3.6% for early passive motions and 5.3% for early active motions, compared with 16.0% for those receiving immobilization.[21] A study revealed that even 5 days of immobilization can cause substantial loss in skeletal muscle mass and strength, as well as with activation of the catabolic molecular signaling pathway. These disadvantages might not affect the resurgery rate directly but might compromise hand function and slow down the recovery, thus increasing healthcare resource usage.[12, 22] At 24 weeks follow upmean composite flexion was 189.68 ± 22.35 degree in late mobilization group and 201.25±21.66 degree in EAM group. Extension deficit was 36.87±16.15 degree in group A and 22. 38±12.43 degree in group B. Total active motion 163.13± 17.27 degree in group A and 192.19 ± 17.27 degree in group B. Buck Gramcko score was 9.66±3.51 in group A and 12.78±2.65 in group B. Excellent and good was graded as satisfactory and fair and poor was graded as unsatisfactory outcome. According to Louisville Grade, in the late mobilization group excellent, good, fair and poor results were found in 7(21.9 %), 13(40.6%), 9(28.1%) and 3(9.4%) digits respectively.12 In the early active mobilization group, excellent, good, fair and poor result were found in 16(50.0%), 11(34.38%), 4(12.50%) and 1(3.13%) digits respectively. There was a significant functional improvement in the early active mobilization group 84.38%, compared to the late mobilization group, 62.50%. According to Buck Gramckoscore, satisfactory results (excellent and good) were 62.5% (20/32) in late mobilization group, but 87.5% (28/32)in the EAM group, that is statistically significant. In finger-wise function, the little finger functional

outcome was less satisfactory comparison with other digits, that was 66,67% (6/9)in the EAM group, and only 17% (1/6) in late mobilization group. Chow et al. (1988), Saini et.al. (2010), and Hung et al. (2005) results were good to excellent in 77% of zone II flexor tendon repair with early mobilization protocol which is comparable to our study.[12,23,24,25]

CONCLUSIONS

Early active mobilization following primary repair of the flexor tendon in zone II of hand ensures better functional outcome with minimum complication compared to late mobilization.

LIMITATION

- Randomization was done by envelop technique of this RCT and 80% of follow up was strictltly maintain.
- All patients were collected in this study from a single tertiary level hospital which does not reflect the whole country.
- Respondents were included up to 3 weeks but if it would be within 5 days that reflect better results
- Rehabilitation could not strictly supervised.

Conflict of Interest

No conflict of interest, this study was conducted by self-funding at the department of Orthopaedics, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

Level of Evidence: Level II (Randomized Control Trail but follow up level was about 80% and Hand therapy was not supervised properly)

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Original Article

Health Seeking Behavior and Self-Medication Practice among Undergraduate Medical Students in a Selected Private Medical College in Bangladesh

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Abstract

There is a need to have a formal health program for the medical students, set guidelines for students to follow if they fall ill and provision of rational medication. Students need to be made aware of the dangers of self-treatment and investigation. This cross-sectional study was conducted among the undergraduate medical students of US Bangla Medical College (USBMC), Narayangonj from July to December 2022. The study aims to assess the health seeking behavior and self-medication among the students. Data were collected by interviewing students using a pre-designed questionnaire and twenty Likert items were prepared for data collection. Data were analyzed by using SPSS (Statistical Package for the Social Sciences) version 25. Total 293 students were interviewed, among them male - female ratio was 1.23:1 and the age range of the participants was 17 to 28 years. Most of the (70%) students were belonged to upper-middle class family; where 21% from upper class, 8% from lower middle class, and only 1% from the working class family. Regarding the father's educational status of the students more than two-third (69%) of their fathers completed university degree, 29% completed higher secondary or secondary level of education and few (2%) had informal education. Most of the students (81%) used to take medicine without prescription/ self medication. Among the students around one-fourth of them used to take both paracetamol (26%) and painkiller (24%) as self-medication; where 13% of the students used to take antibiotic. Regarding the opinion of the well established definition of 'Health' that is "Health includes physical, mental and social well-being and not just absence of disease/ infirmity" most of the students (90%) gave positive statement (agree 58% and strongly agree 32%); where 5% of them were neutral and rest 5% were disagreed. Nearly two-third (65%) of the students expressed their opinion positively (agree 49% and strongly agree 16%) on "seek help immediately when they develop some physical symptoms" that is they seek immediate help for their illness; where 14% of them were neutral and rest 21% were disagreed. More than one-third (35%) of the students stated the reason for self-medication related to their too busy schedule to visit physician and 21% stated that the illness was too minor for consultation; other reasons were knowledge about the drug and illness, follow old prescription, over the counter drugs etc. Almost one-third (30%) of the students opined positively that public health care facilities provide standard health care, but more than one-third (36%) did not comment and rest one-third (34%) differed on it. Remarkably used self- medicated drugs were paracetamol (26%), painkiller (24%), 13% and others NSAIDs/ Analgesics, Antacid/ PPI, Vitamins, antitussive, antihistamines. The statistical test revealed that there is a strong relationship of their opinion on attention to mental physical well-being for healthy lively-hood between coping ability, seek the best care from college hospital and seek help for sensitive matters other than own college hospital (at 5% level of significance). To ensure better health seeking behavior and good practice knowledge of medical students was not absolutely satisfactory. Awareness regarding demerits of self-medication like antibiotics resistance and side effect of drugs would be build among the students. This study would facilitate for increase of medical knowledge and promotion of higher health-seeking behavior.

Keywords: *Health seeking behavior, self-medication, undergraduate medical students*

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INTRODUCTION

Health seeking behavior is frequently described as any action made by people who are experiencing a health issue or illness with the intention of finding a suitable treatment.[1,2] It is preceded by a decision-making process that is also influenced by household and/or individual conduct, social norms and expectations, and provider-related features and behavior.[3] It is not homogeneous since sociocultural, economic, and socio-cognitive factors, as well as factors related to cognition or consciousness, all influence it.[2] During the COVID-19, the healthcare seeking was very challenging among general people including medical students.[3,5] The interaction of

these variables affects a person's decision-making significantly.[4] Self-medication and alternative medical treatment are also choices made by people who engage in health care seeking behavior.[6] The use of medications in this act makes it different from self-care because they have the potential to be beneficial or harmful.[6] Medical students are more likely to engage in this behavior since they are familiar with both medications and ailments. Different factors, such as individual and/or household behavior, societal norms, and expectations, influence one's health-seeking behavior and decision-making. The irrational use of pharmaceuticals is a topic of concern for both the general population and professionals.[6] The rates are high all throughout the world, reaching up to 68.0% in European nations significantly higher in underdeveloped nations 6and as high as 92.0% among Kuwaiti adolescents.[6, 8] The prevalence rates in the surrounding nations are 31.0% in India and 59.0% in Nepal.[6] There is limited research on self-medication in Pakistan, but those that have been done have found high rates of around 51.0%[10]. The fact that prevalence rates are increasing despite efforts to reduce this issue is especially concerning.[11]

MATERIALS AND METHODS

Study design, duration, and population

This cross-sectional study was done from July December 2022, among the undergraduate medical students to assess their health seeking behavior and attitude towards self-medication. The study took place at Community Medicine Department, US Bangla Medical College Hospital. Using a pre-tested questionnaire, this study finally collected 293 data from the medical students. A questionnaire was developed following an extensive review of the literature. It encompassed inquiries pertaining to the physical, social, and mental aspects of health. This questionnaire consisted of demographic queries and twenty Likert scale items, which were employed in this study to evaluate medical students' knowledge, attitudes, and practices regarding health-seeking behavior and self-medication. Each Likert item from the questionnaire was treated as an ordinal variable, and non-parametric tests were employed for analysis. Instead of grouping the Likert items to generate a single result, each item was examined individually. The data were analyzed using SPSS (Statistical Package for the Social Sciences) version 25. Frequencies were calculated for both independent and dependent variables. Given that the dependent variables were ordinal and the independent variables were categorical, either the Mann-Whitney U test or Kruskal-Wallis H test was selected as appropriate to determine if variations existed in the responses of participants based on different categories of independent variables. In the text, when expressing the percentage of participants who agreed with a particular question, the frequencies of "Strongly Agree" and "Agree" responses were combined. Similarly, the frequencies of participants who disagreed were combined by adding "Strongly Disagree" and "Disagree" responses. In tables, frequencies were presented using a five-point scale: "Strongly Disagree," "Disagree," "Neutral," "Agree," and "Strongly Agree."

Ethical Permission for data collection

The research has been performed following the Declaration of Department of Community Medicine, US Bangla Medical College Hospital, and the ethical approval was obtained from the Institutional Review Committee of the US Bangla Hospital, Rupgonj, Narayangonj, Bangladesh.

RESULTS

Table I shows the summary statistics of the medical students; total 300 students were address for this study among them 293 were selected as respondents, out of which 156 (53%) were male and 137 (47%) were female. The age of the participants ranged from 17 to 28 years with a mean age of 22.44 ± 1.49 years (Mean ± SD). Mean height and mean weight of the respondents were 164.06±12.33 and 63.23±10.24 (Mean ± SD). Mean ± SD family income was 88001.71±72811.52 taka.

Table- I: Summary statistics of the medical students (n=293)

Variables	Mean	Standard Deviation
Age in years	22.44	1.49
Height in cm	164.06	12.33
Weight in kg	63.23	10.24
Monthly Family Income	88001.71	72811.52

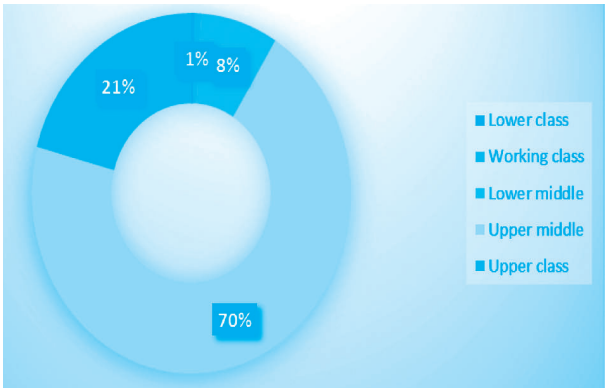

Figure- 1: *Distribution of Socio-economic condition of the respondents (n=293)*

Figure 1 shows the distribution of socio-economic condition of the respondents; among them 70% (206) students were belongs to upper middle class and 21% (61) were upper class and only few 1% belongs the working-class family.

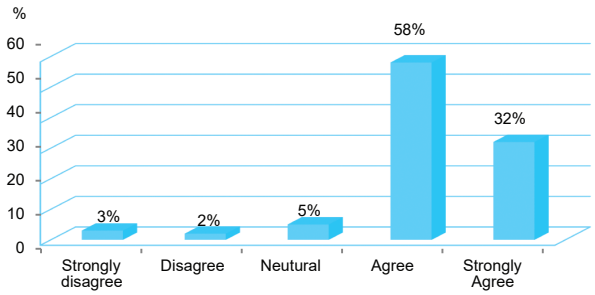

Figure- 2: *Statement regarding "I am well aware that health includes physical, mental and social well-being and not just absence of disease/ infirmity".*

Figure 2 shows the statement on *"I am well aware that health includes physical, mental and social well-being and not just absence of disease/ infirmity"*; here, 58% was agree, 32% was strongly agree, 2% was disagree and 3% was strongly disagree. That is 58% medical students were aware about their physical and mental health.

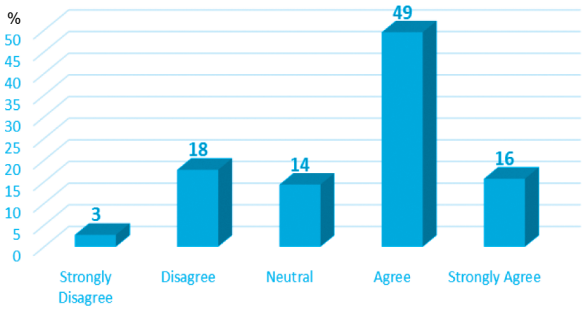

Figure- 3: *Statement regarding "I seek help immediately when I develop some physical symptoms".*

Figure 3 illustrates that 65% (49+16)% were agreed and strongly agreed upon the statement 'seek immediately when develop some physical symptoms', and 21% (18+3)% were disagreed and strongly disagreed.

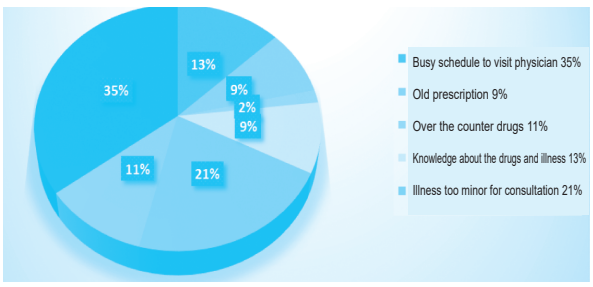

Figure- 4: *Pie-chart of reasons for self-medication*

Figure 4 shows the distribution of the main reason for self-medication; 35% stated self-medication as for busy schedule to visit physician, 21% told that illness was too minor for consultation and 9% students were self-medicated followed by old prescription.

Table II shows distribution of the students regarding the statement of "I don't think public health care facilities of Bangladesh provide standard care." Here, 36.2% of the students were neutral, 30% were agree + strongly agree with this statement and 34% (25+9) % were disagree and strongly disagree.

Table- II: I do not think public health care facilities of Bangladesh provide standard care

		Frequency	Percent	Valid	Cumulative Percent
Valid	Strongly Disagree	26	8.9	8.9	8.9
	Disagree	74	25.3	25.3	34.1
	Neutral	106	36.2	36.2	70.3
	Agree	79	27.0	27.0	97.3
	Strongly Agree	8	2.7	2.7	100.0
	Total	293	100.0	100.0	

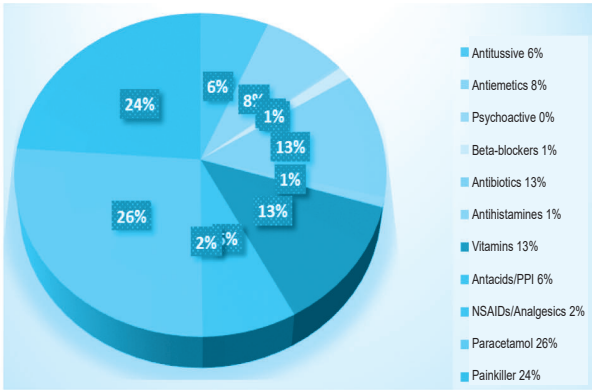

Figure- 5: *Name of the self-medicated drug*

Figure 5 states that the name of self-medicated drugs; among the students Paracetamol was taken by 26%, painkiller by 24%and 13% of students took antibiotic as self-medicated drug.

DISCUSSION

We fixated on the belief of issues in several aspects of health, temporal arrangement chosen by the patients to travel for a check-up, mode of consultation, seeking the assistance of other medication, and self-medication among the medical students in Bangladesh. This study is totally different from alternative studies as this has explored health-seeking behavior by taking the context of mental and social factors additionally to the physical facet of health, as health is simply not regarding physical well-being or simply mental well-being, not like alternative studies that have targeted on a particular disease/condition. [12, 11]

This study conducted among medical students of a teaching hospital in Bangladesh incontestable that ninetieth (19%) of the responders were standard regarding the physical, mental, and social aspects of health. Still, fifty-one (51%) wanted to facilitate only if their physical symptoms got worse, twenty first (21%) of the responders did not think about issues of thoughts, feelings, and header ability with ups and downs of life as issues of health, and twenty seventh (27%) of them didn't understand issues in making/maintaining a purposeful positive relationship with people as issues of health. Despite having an equivalent tutorial background, still, twenty eighth (28%) of responders believed that solely weak and unproductive folks suffer from problems with mental and social well-being. it's to be noted that respondents of this study square measure presently being trained to be health professionals beneath an equivalent info. the sole distinction prevailing among the responders is that the socio-economic variables. And this has brought this inequality among respondents as social, economic, and legal variables have an effect on the approach health and sickness square measure perceived by a private.[14]

Talking regarding the sick state of social health of the scholars, this could be connected to the character of their study and therefore the time demanded by their course that restricts their social life. Since medical education may be a long and demanding course, medical students square measure liable to get distressed which might cause bated psychological feature functioning and depression.[15] Medical students square measure prone to of these compared to others of an equivalent age bracket.[16] Our study known that twenty seventh of the scholars felt that they neglect their social well-being, while 16.8% of the respondents were unaware that the issues in making/maintaining a purposeful positive relationship with people square measure issues of health. About 42.8% of the respondents World Health Organization wanted to facilitate for sensitive matters and taboo associated diseases selected alternative hospitals/clinics than their own college's hospital. this means their concern towards confidentiality and stigma. A previous study distinguished that the scholars square measure involved that seeking psychological state care would raise queries among colleagues and schools concerning their stability and appropriateness that's demanded by the medical fraternity.[17]

Besides this, medical students face totally different barriers whereas seeking attention. The worry of stigma, problems with confidentiality, confusion on seeking facilitate, worry of unwanted intervention whereas seeking mental health care, and barriers like financial problems, lack of your time, and worry of facet effects whereas seeking physical health care square measure such known barriers.[18] Renee et al. have additionally mentioned in their study that medical centers outside the university supply students' decent distance for them to feel assured of their confidentiality.[19]

All these findings simply show an equivalent issue, despite what this tutorial qualifications, training, and level of awareness square measure, there will be socio-cultural determinants that have an effect on the state of health. folks tend to mix within the ideas of health, disease, and healthcare-seeking behavior in keeping with their lifestyles and their several demographic circumstances, such that, data of medication alone cannot guarantee higher healthcare-seeking behavior.[20]

The findings of our study square measure in line with this. Health-seeking behavior may be a terribly complicated matter as what is outlined as health or health facility varies with cultures, life experiences, socio-economic variables, and legal variables.[14,21] health care seeking behavior differs from person to person because it may be a terribly personal matter[22] and health care involves interaction with alternative people.[23]

CONCLUSIONS

Health-seeking behavior may be an advanced and extremely personal matter of a private that is generally determined by their demographic circumstances. The information of bioscience has not satisfactorily ensured higher health-seeking behavior and sensible practices. The high prevalence of observe of self-medication adds another burden. There is a requirement for timely and evidence-based teaching-learning techniques; thought of

individual and/or unit behavior, community norms, and expectations for holistic approach; and capital punishment legislation to scale back the barriers and upgrade the health seeking behavior of medical students.

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Case Report

Diagnosis of Caroli's Disease: a Rare Case Report

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Abstract

Caroli's disease is a rare disease caused by Ductal Plate malformation. Patients may present with history of intermittent abdominal pain, pruritus and/ or symptoms of cholangitis. Cholangitis, liver cirrhosis, and cholangiocarcinoma are potential complications. It is rarely diagnosed in childhood. A six (06) years old was presented with intermittent abdominal pain, fever, pruritus, and hepatomegaly at the Department of Paediatric Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. After evaluating history, signs/ symptoms, physical examination, biochemical, ultrasonographic and endoscopic findings; this case was provisionally diagnosed as a compensated chronic liver disease with portal hypertension due to cause of cholestasis. Finally magnetic resonance cholangiopancreatography (MRCP) was done for further evaluation and the diagnostic findings of MRCP was suggestive of Caroli's disease. After consultation the MRCP report with Pediatric Surgery Department of BSMMU the patient was advised for liver transplantation due to multifocal involvement of liver. Lastly patient was discharged with supportive management.

Keyword: *Caroli's disease; cholangitis, MRCP*

INTRODUCTION

Caroli's disease is a rare cystic malformation of the liver caused by Ductal plate malformation (DPM).[1] It is transmitted by autosomal recessive inheritance but autosomal dominant inheritance is also reported. Usually, it is present in childhood and early adulthood. But neonatal presentation also occurs. Intermittent abdominal pain due to cholangitis and hepatomegaly are common clinical presentations.

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CASE DESCRIPTION

An 8-year-old immunized boy 2nd issue of consanguineous parents, presented with jaundice off and on since birth. He also developed pruritus since 6 months of age and gradual abdominal distension since 3 years of age. He had no history of fever, recurrent abdominal pain, vomiting out of blood, the passage of black tarry stool, any other bleeding manifestation or blood transfusion. He had a history of passage of dark urine and clay-colored stool. His family history is significant. He had a history of sib death who also suffered from jaundice since birth and died at 7 months of age. On physical examination, he was pale, deeply icteric, non-edematous, clubbing, leukonychia, and thenar and hypothenar muscle wasting were present, weight, and height were below 3rd centile. The abdomen was distended and the flanks were not full. Hepato-splenomegaly was present and ascites were absent. Other systemic examinations revealed normal findings. We provisionally diagnosed this case as a compensated chronic liver disease with portal hypertension due to cholestasis cause.

CASE MANAGEMENT

On admission, the patient was managed symptomatically. Investigation report revealed low hemoglobin % (Hb% 7.3 gm/dl), raised ALT (102 U/L), raised AST (197 U/L), raised gamma-GT (100U/L), raised ALP (495 U/L), direct hyperbilirubinemia (Total S. bilirubin 7.5 mg/dl and direct bilirubin 6.23 mg/dl) with normal S. albumin (35 gm/L) and prothrombin time (14.10 sec). Ultrasonography of the whole abdomen revealed coarse hepatic parenchyma and splenomegaly. Endoscopy of upper GI revealed Grade II esophageal varices.

After evaluating history, physical examination, and biochemical findings, the decision was made to do MRCP. MRCP report (Figure 1) revealed multiple hyperintense almost rounded areas of multifocal cystic dilatation of segmental intrahepatic bile ducts having continuity with the central biliary tree. Finding suggestive of Caroli's disease. Finally, the patient was diagnosed as Caroli's disease.

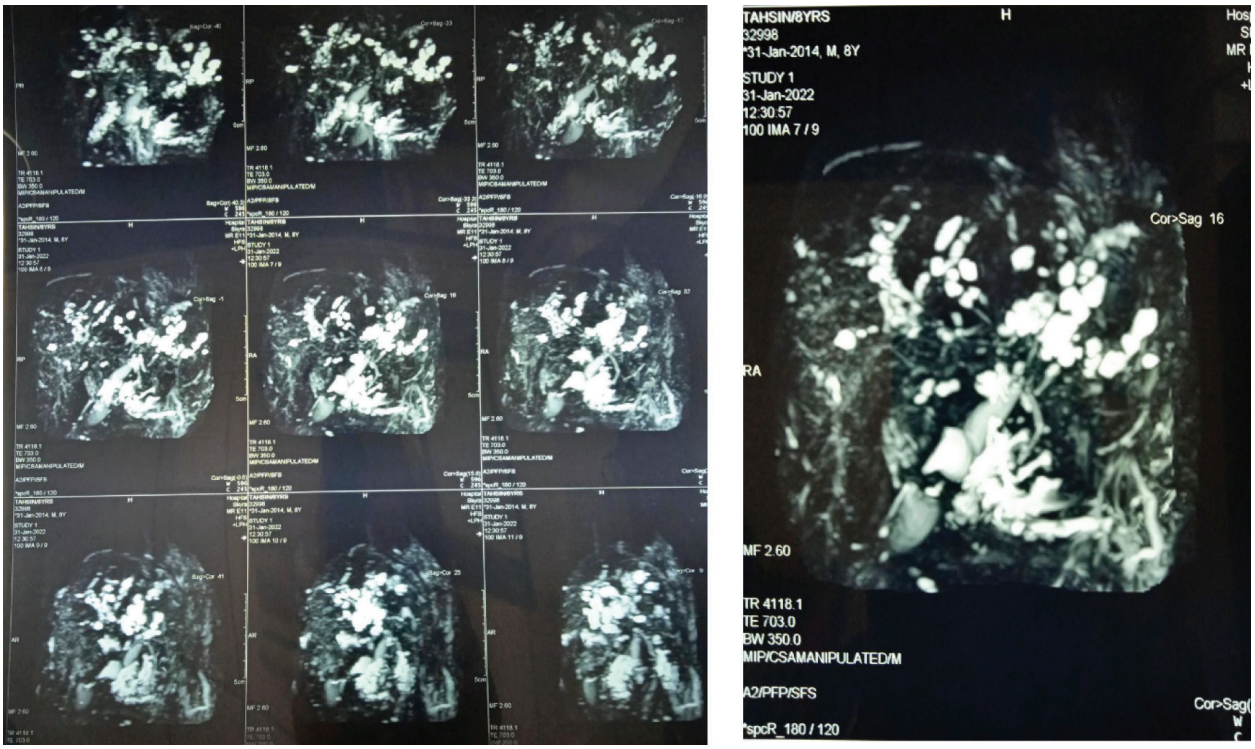

Figure- 1: *MRCP film shows Multiple hyperintense almost rounded areas of multifocal cystic dilatation of segmental intrahepatic bile ducts having continuity with the central biliary tree.*

After getting the MRCP report, we counseled with pediatric surgery department. However, due to multifocal involvement, the patient was advised for Liver transplantation. We discharged this patient with supportive management.

DISCUSSIONS

Caroli's disease is a rare congenital disease of the liver characterized by non-obstructed multiple segmental or saccular dilatations of the intrahepatic bile duct.[2] It was first described by French physician Jaques Caroli in 1958. When it is associated with hepatic fibrosis it is termed Caroli's syndrome (CS), which is more complex and is linked with portal hypertension.[3] Caroli's disease is also classified as a type V choledochal cyst. Usually, it affects both lobes of the liver in a diffuse manner. When Mono lobar involvement occurs, the left lobe is more commonly involved.[4] The main embryonic basis is Ductal plate malformation (DPM). The anatomic manifestation of cystic disease of the liver is determined by the level of involvement of the biliary tract.[5] Caroli's disease is characterized by DPM of the larger intrahepatic bile ducts, whereas malformations at the level of the interlobular bile ducts lead to congenital hepatic fibrosis.[1]

The most common presentation is intermittent abdominal pain and hepatomegaly. The patient may present with pruritus and jaundice.[6] The patient may also present with the features of complications like Cholangitis, cholelithiasis, portal hypertension, biliary abscess, septicemia, liver cirrhosis, and cholangiocarcinoma. On physical examination, hepatomegaly is usually present; splenomegaly can be present if portal hypertension develops. Palpable kidney indicates renal involvement.[7]

Duct ectasia and irregular, cystic dilation of the large proximal intrahepatic bile ducts with a normal common bile duct are the imaging findings of Caroli's disease.[8] These findings can be visualized with ultrasonography, endoscopic retrograde cholangiopancreatography, and magnetic resonance cholangiography. Direct visualization of the biliary tract with endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography (PTC) is the gold standard diagnostic modality for Caroli's disease. The emerging diagnostic modality of choice for Caroli's disease is magnetic resonance cholangiopancreatography (MRCP). The "string of beads" pattern of the ectatic intrahepatic bile ducts is the characteristic MRI appearance of Caroli's disease.[9] The characteristic CT imaging and

ultrasonographic findings of caroli's disease is a central "dot-sign" appearance.[10] Nuclear scintigraphy is another diagnostic modality in which the characteristic beaded appearance of the intrahepatic bile ducts can be visualized.

The treatment option for Caroli's disease depends on its clinical features and the location of the biliary abnormalities. Ursodeoxycholic acid (UDCA) is the litholytic therapy for primary hepatolithiasis. Cholangitis can be treated with appropriate antibiotics and UDCA to prevent further episodes. Surgical resection (partial hepatectomy; lobectomy) remains a good option for segmental or unilobar involvement. For diffuse involvement in the liver, Orthotropic liver transplantation (OLT) is the only modality of treatment.[11] There is no definite indication or timing of OLT for patients with Caroli's disease. The primary indications of OLT which have been reported in different studies are signs of hepatic decompensation, defined as ascites, encephalopathy, coagulopathy, portal hypertension, jaundice, prolonged prothrombin time, or decreased albumin and recurrent cholangitis.[12]

CONCLUSIONS

Caroli's disease is a rare congenital malformation of the intrahepatic bile duct. Though it is rare, clinicians should it keep in mind as a differential diagnosis of recurrent abdominal pain and cholangitis. Radiological investigation such as MRCP is helpful in diagnosing this condition. Usually, the patient is managed symptomatically. However, surgical treatment may be required in specific circumstances.

Author's contribution:

Conception and design: Lubana Akram

Manuscript drafting and revising it critically: Lubana Akram, Rubaiyat Alam, Md.Rukunuzzaman

Approval of the final version of manuscript: Lubana Akram, Rubaiyat Alam, Md.Rukunuzzaman

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Data availability statement: Share upon request

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Case Report

IgA Vasculitis in an Adult Man- a Case Report

***Mahin T[1], Faria L[2], Mottaleb AKMA[3], Shumy F[4], Qader MA[5]**

Abstract:

IgA vasculitis is rare in adult. A significant portion of adult cases may present with renal involvement. Although most of these cases can be managed symptomatically, some cases may require immunosuppressive treatment. Unless diagnosis and appropriate treatment is initiated early IgA nephropathy in adult may result in chronic kidney disease. Immunoglobulin A vasculitis (IgAV) is an acute disorder causing generalized vasculitis principally involving skin, gastrointestinal (GI) tract, kidneys and joints. Here, a 28 year old man was presented with purpuric rash with leg ulcer, inflammatory arthritis involving multiple joints, abdominal pain and vomiting. He had mild pedal edema and normal blood pressure. Investigations showed raised inflammatory markers, haematuria, and nephrotic range proteinuria with normal liver and renal function. Biochemical and immunological evaluation of lupus nephritis, ANCA associated vasculitis and other causes of glomerulonephritis were negative. Renal biopsy with direct immunofluorescence showed features of IgA nephropathy. Patient was treated with steroid and mycophenolate mofetil with a good response.

Keywords: *IgA vasculitis, leg ulcer, prednisolone, mycophenolate mofetil.*

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INTRODUCTION

IgA vasculitis is the most common vasculitis in childhood with incidence decreasing with age.[1] The occurrence of IgAV in adults is approximately 3.4- 14.3 cases per million.[2,3] It commonly involves skin, gastrointestinal tract, kidneys, joints and rarely lungs and central nervous system (CNS).[1,4] There is slightly male predominance with a male to female ratio of 1.5-2:1, but some studies have found equal distribution in both sexes.[5,6] It is typically an acute self-limiting illness usually managed with supportive treatments. However approximately 7% of all cases IgAV may present with nephritis or nephrotic syndrome which may progress to chronic kidney disease.[7] What makes this case unique is here we present a case of IgA vasculitis with nephropathy in an adult who needed management with immunosuppressive therapy and had a good response.

CASE HISTORY:

A 28-year-old non-diabetic normotensive gentleman presented with multiple purpuric rash along with leg ulcer for 20 days which was initially reddish painful nodules in the lower limb and subsequently became ulcerative. He also had pain and swelling of right knee, both ankle and small joints of right hand for same duration. He also complained of abdominal pain and vomiting for 2-3 days. He denied any history of fever, bloody diarrhea, and flu like symptoms or urinary symptoms in last 3 months. He had no history of taking any antibiotics or any nephrotoxic drugs prior to this illness. On examination, he had mild ankle edema and his blood pressure was normal. Along with ulcerative lesion in both lower limbs he had petechial rash behind legs, buttock and upper limbs (Figure 1). His initial lab reports revealed mild normocytic normochromic anemia with raised inflammatory markers, renal functions and liver functions were normal. Urine microscopy showed plenty of RBC and a 24 hour urinary total protein was 7.39gm/day (Table 1).

Table- I: Initial lab results of the patient

Characteristics	Results
CBC	Haemoglobin-11.9 g/dl, Leukocyte-14,200/mm^3,Platelet-389,000/mm^3
ESR	37 mm in 1st hour
C- reactive protein	45.6 mg/L
Serum creatinine	0.9 mg/dl
ALT	49U/L
PT and APTT	normal
Urine R/E	P.C-30-35/HPF, RBC-Plenty/HPF, protein- 3+
24 hour urinary total protein	7.39 gram/24 hours
USG of abdomen	Fatty liver (grade-2)

Figure- 1: *Purpuric rash in the lower limb including ulceration*

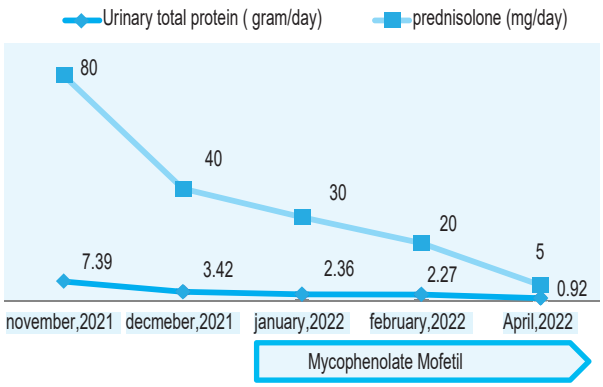

Figure-2: *Line chart showing response of proteinuria to treatment*

His serum complements including C3, C4 level were within normal limit, antinuclear antibody, RA factor, Anti-CCP antibody, C-ANCA, P-ANCA, hepatitis B and C serology were negative. Patient was diagnosed as a case of IgA vasculitis with Nephritis and a renal biopsy was done which revealed mild to moderate global mesangial cell hyperplasia and deposition of IgA, C3 and C1q in immunoflurescence microscopy. He was started on oral prednisolone with gradual tapering along with oral Losartan potassium. Mycophenolate mofetil was added for persisting proteinuria after 2 months. Within 5 months his skin ulcers disappeared and proteinuria reduced to 0.92 gm/24 hours (Figure 2).

DISCUSSION

IgA vasculitis is usually more severe in adults with tetrad of non-thrombocytopenic palpable purpura, arthritis/ arthralgia, gastrointestinal and renal involvement. Cutaneous manifestation may also include urticarial and macular lesion, rarely, hemorrhagic bullae and ulcerative lesion[8]. In our case patient had palpable purpura and skin ulcer. Arthritis and arthralgia may involve 74% of the patients, joints may be swollen, tender and painful but usually no erythema or effusion. Knees and ankles are most

commonly affected; rarely fingers and wrist may be involved[9]. Our patient had involvement of knee joint, ankle joint and small joints of right hand. IgA nephropathy in adult is frequent, affecting from 45%t to 85% of patients.[10] The risk of progression to renal insufficiency is 5-30%.[8,11] Both hematuria and nephrotic range proteinuria as in our case may be present in 29% cases.[12]

Renal Biopsy may reveal mesangial proliferation, leucocyte migration, crescent formation along with deposition of IgA and C3.[13] In our patient, the pathological change in the light microscope was similar and there was IgA and C3 deposition on immunoflurescence.

IgAV is self-limiting in nature in up to 89% adults which can be managed with symptomatic treatment [14]. Oral steroid is recommended in patients with severe rash, renal involvement, severe colicky abdominal pain or scrotal /testicular involvement[8]. In a few studies steroids was found to induce complete remission of nephritis.[15] Floege and feehally adapting KDIGO guideline suggest 6 months therapy of steroid if proteinuria >1 gram/day persist despite renin-angiotensin receptor blockage and blood pressure control.[16] Bernardio et al, reported a case of IgAV in an adult patient with SLE mild proteinuria who was treated with colchicines, steroid and azathioprine with good outcome.[17]

Hocevar et al did an analysis of baseline clinical features and co-morbidities of adult IgAV cohort over 9 year period. It showed hypertension, diabetes and obesity were more prevalent in patients with IgAV then age matched controls. In the study population kidney, GI and articular involvement due to IgAV was 45%, 30.2% and 38.5% respectively. 10% patient was diagnosed with acute kidney injury and arterial hypertension concurrently with IgAV.[18]

According to Yaseen et al. clinical course of IgA vasculitis in adult is different from paediatric population due to its high risk of evolving to end stage renal disease. There is still controversy regarding immunosuppressive therapy in severe IgAV. Recent studies are providing data regarding potential benefits of targeting mucosal immune system, toll- like receptors, complements and tyrosine kinase inhibitors in management of IgA nephropathy. Still there is paucity of high quality evidence based guidelines in management of severe IgAV.[19] .

CONCLUSIONS

IgA vasculitis is rare in adult. Around 5-30% patient with IgA vasculitis with renal involvement may progress to chronic kidney disease. Early diagnosis and treatment is of prime importance in this case.

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Obituary news September-2022

BMA would like to express deep condolence on deaths of the following notable physicians in recent past:

Sl. No.	Name	Date of Death
1	Dr. Khokan Chandra Saha	05/06/2022
2	Dr. Shamsun Nahar Swapna	06/06/2022
3	Dr. Farhad Jamal	07/06/2022
4	Dr. Jannatul Ferdous Bonna	14/06/2022
5	Dr. Farhana Yeasmin Pinon	15/06/2022
6	Dr. Jahid Hasan	15/06/2022
7	Dr. Shamsur Rahman Moyna	20/06/2022
8	Dr. Hasina Mamataj	20/06/2022
9	Dr. Aditi Sarkar	29/06/2022

May Allah bless the departed souls.
Our heartiest commiseration to the deceased's family, our prayers are with them during this difficult moment of their life.

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