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Editorial

- COVID-19: Are We at the End of the Pandemic ? 1
  U K Das

- Tribute 5
- Journal Club 6

Medicine Digest

- New Application Prospect of Angiotensin Receptor Naprilysin Inhibitor 8
  P K Dutta

Review Article

- Role of ARNI in the Treatment of Heart Failure 13
  M K Uddin

Original Articles

- Evaluation of Aspartate Aminotransferase to Alanine Aminotransferase Ratio in Non Alcoholic Fatty Liver Disease Patients 18
  F Hussain P Karmakar

- Perceived Stress and Associated Factors among the Doctors of Bangladesh Study 23
  J Das S Chowdhury S D Sharma D Deb

- Diagnostic Utility of Fine Needle Aspiration Cytology and Cell Block in Evaluation of Palpable Thyroid Swellings 28
  T Khastagir R Anjum S Khanum M Barua R Mahmud M Z Rahman

- Complications Following Thyroid Surgery 33
  S Das M S Hossain T Sen

- Prevalence of Anemia in Children Aged Six Months to Sixty Months : A Hospital-Based Study 37
  M S Uddin B R Muhuri L Akther B A Siddiqa N Alam

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Editorial

Marine City Medical College Journal

COVID-19: Are We at the End of the Pandemic ?

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A novel beta coronavirus that causes severe pneumonia was first described in December 2019, in Wuhan, the capital city of Hubei province, in China[1]. Subsequently, it was given the name Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) and the disease Coronavirus Disease 2019 (COVID-19) rapidly progressed to a global pandemic.[2] World has witnessed its devastating effects resulting in huge loss of life, jeopardised health care delivery system and economies. As of today, 6 Feb 2022, more than 5.7 million people died and many more are still suffering from post-COVID complications.[3] It posed a huge burden to the health care particularly for ICU bed, oxygen, and ventilator initially. The whole world is waiting eagerly to see the the end of the COVID-19 pandemic. Scientists, researchers, and world leaders working accordingly to curtail the pandemic by implementing the measures to prevent the transmission of the SARS-CoV-2 virus, using effective therapies for the disease, and vaccination to prevent infection. Health measures like universal masking, hand washing with soap water, and physical distancing are useful in prevention of transmission of the virus. Effective vaccines are developed in a very short period of time and the global vaccination program is going on successfully. Devices to improve oxygen concentration and delivery have been used according to the patient's needs like oxygen concentrator, non-rebreather mask, high flow nasal cannula, and ventilator (Table I).[4]

Table I Devices Used in Supplemental Oxygen Therapy.*

Device	Flow (Liters/min)	F_1o_2	Indications	Advantages	Disadvantages
Nasal cannula	1-6	0.24-0.401	Nonsevere respiratory distress	Is comfortable for patient	Has limited flow
			Need for supplemental oxygen at home	Has low cost	is associated with mucosal drying and epistaxis
			Low oxygen requirement	Does not interfere with oral intake	Unreliable F_1o_2
					is esaily dislodged
Simple face mask	5-10	0.35-0.60	Moderate oxygen requirements	Has low cost	Interferes with oral intake
			Need for sedation for procedure	Profides higher F102 than nasal cannula	May cause patient discomfor
			Mouth breathing	is associated with less entrainment of ambiont air	is associated with carbon dioxide relention
			Need for acrosolized medications	is capable of delivering humidified oxygen	is dependent on tight fiting mask for oxygen delivery
Face tent	5-15	0.35-0.5	Moderate oxygen requirement	Is comfortable for patient	Does not provide reliable control of F_1o_2
			Discomfort with tight-fiting mask	Has higher F_1o_2 delivery	
				is capable of delivering humidified oxygen	
Venturi mask	2-15	0.24-0.5	High oxygen requirement	Provides precision the oxygen concentration	May cause patient discomfor
				delivered	Prevents patient from eating or drinking
				Is capable of delivering humidified oxygen	May require experienced personnel when seting
				Has high gas flow (Oxygen plus entrained air)	up high flow system
Nonrebreather	10-15	06-0.9	High supplemental oxygen requirement	Has high F_1o_2 (Up to 0.9)	Causes patient discomfort
			(e.g. in patients with carbon monoxide	Can be used in emergency situations	Prevents patient from eating or drinking
			poisoning, smoke inhalation,		Requires close monitoring
			acute tramua with severe desatura.		
			tion, or acute decompensation and in		
			those who need preoxygenation before		
			intubation)		
High flow nasal cannula	15-60	0.3-1.0	Hypoxemic respiratory failure	Allows patient to eat, drink and speak	May cause patient discomfort
			(eg. pneumonia, interstitial lung disease,	Provides improved control of F_1o_2	(Owing to high flows)
			pulmonary edema, acute respiratory	Provides high flows that meet the patients	May cause mucosal dryness and injury
			distress syndrome, care after extubation	minute ventilation	Requires experienced personnel
			etc) also ueful in critically	Provides modest PEEP (Prevents atelectasis	is more costly than other forms of oxygen delivery
			hypoxemic p0atients who should not be	and improves functional residual capacity)	
			intubated	Provides washout of CO_2 in dead space	

CO_2 denotes carbon dioxide, F_1o_2 the fraction of impired oxygen, FRC functional residual capacity and PEEP the positive end-expiratory pressure.

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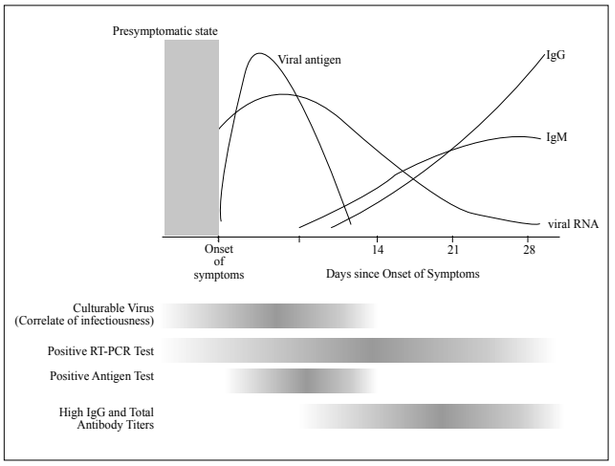

Figure 1 Pathophysiology and timeline of viremia, antigenemia and immune responsed during acute SARS-CoV2 infection[5]

According to data from China, 81% of people with Covid-19 had mild or moderate disease (Including people without pneumonia and people with mild pneumonia), 14% had severe disease, and 5% had critical illness.[6-8] Symptoms range from asymptomatic and presymptomatic, mild to moderate illness, severe illness with hypoxia leading to hospitalisation, and may progress to critical condition requiring assisted ventilation. The symptoms and signs ranges from mild symptoms to critical condition. Typical symptoms are fever, rhinorrhoea, cough, loss of taste or smell, nausea and vomiting. Less common symptoms include sore throat, myalgia, arthralgia, diarrhoea, rash, red eyes. Clinical features of severe COVID-19 includes difficulty in breathing, dyspnea, chest pain, confusion, loss of speech or mobility and cyanosis. Identifying risk factors for hospitalisation and death are older age groups, obesity, cardiovascular disease, chronic lung disease and diabetes.[5-9]

Diagnosis depends upon the understanding of the pathophysiology, viremia, antigenemia and immune response during acute SARS-CoV-2 virus infection (Fig 1). Laboratory investigations may reveal lymphopenia and elevated levels of d-dimer, lactate dehydrogenase, C-reactive protein, and ferritin; the procalcitonin level is typically normal. Raising white-cell count with lymphopenia, prolonged prothrombin time, and elevated levels of liver enzymes, lactate dehydrogenase, d-dimer, interleukin-6, C-reactive protein, and procalcitonin is associated with poor outcome. Typical imaging findings are ground-glass opacifications or consolidation.[1]

Table II Symptoms of COVID-19 and Signs of Symptoms of Severe COVID-19

Symptoms of Signs
Typical symptoms of COVID-19
Fever or chills
Congestion, rhinorrhea
Cough
Fatigue
Loss of taste or smell
Nausea, vomiting
Less common symptoms of COVID-19
Sore throat
Headache
Myalgias, arthralgias
Diarrhea
Rash
Red or irritated eyes
Signs or symptoms of severe COVID-19
Difficulty breathing
Shortness of breath (Dyspnea)
Persistent chest pain or pressure
Confusion
Loss of speech or mobility
Cyanosis

Adapted from the Centers for Disease Control and Prevention (CDC)[13] and the World Health Organiztion (WHO).[14] This list does not include all possible signs or symptoms of coronavirus disease 2019 (COVID-

Coronaviruses are RNA virus that are divided into four genera; of this alpha coronaviruses and beta coronaviruses are known to infect humans.[10] Both typically cause common cold symptoms, but two beta coronaviruses-Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV)-can cause pneumonia, respiratory failure, and death.[10]

Four coronavirus outbreaks occurred in last twenty years: SARS in 2002 and 2003, MERS in 2012, and COVID-19 since 2019. All these beta corona viruses infecting humans by binding Angiotensin Converting Enzyme 2 (ACE-2) receptors.[10,11] SARS-CoV-2 is a RNA virus has RNA-dependent RNA polymerase and proteases, which are targets of drugs under investigation.

Scientific evidence suggests the need for 'universal' corona virus vaccine which will protect against all corona virus diseases. As there is predictions that new coronavirus will emerge and infect humans in future and might become pandemic.[12]

Several vaccines that are highly effective in reducing the incidence of hospitalization and death have been authorized, however, vaccine coverage remains insufficient. Clinical trials have shown that receipt of a third dose (booster) that does not match the primary vaccination (Heterologous booster) may result in a higher neutralizing-antibody response than the receipt of a matching (Homologous) booster, particularly after primary vaccination with an adenoviral-vector vaccine. Analysis provides further evidence that the infection rate is lower in persons who are boosted with a heterologous mRNA vaccine.[13] It appears that in an ideal world, widespread access to and acceptance of vaccines to prevent SARS-CoV-2 infection could end the current pandemic, however, given imperfect vaccine uptake and ongoing emergence of variants, it is likely that SARS-CoV-2 will become endemic. Thus, there is a continued need for therapies to reduce the risk of disease progression, prevent transmission, and be widely available to meet the global demand.[14] Neutralising monoclonal antibodies against SARS-CoV-2 spike protein, immune modulators, and antivirals are the currently available classes of effective therapies (Table III). Of these, antivirals are likely to curtail pandemic as this group of drugs active against all variants given the absence of variation in their viral target.[15] Whereas, ongoing transmissibility resulting in rapid emergence of variants with adaptive mutations in the spike protein can result in escape from vaccines and monoclonal antibodies. Vaccines are needed to prevent infection and disease progression and antivirals are required to keep vulnerable patients out of hospital.[14,15]

Table III Current and pending therapeutics for COVID-19 in the United States

Vaccines	Neutralizing Monoclonal Antibodies		Immune Modulators
Ad26.COV2.5: (Johnson & Johnson-Janssen)	Bamlanivimab-etesevimab	Bamlanivlmab-etessvimab	Baricitinib
mRNA-1273: messenger RNA vaccine (Moderna)	Casirivimab-imdevimab	Casirivimab-imdevimab	Dexamethasone
BNT162b2: messenger RNA vaccine (Pizer-BioNTech)		Sotrovimab	Tocilizumab
		Antivirals	
		Molnupiravir	Remdesivir
		Nirmatrelvir-ritonavir (Paxlovid)	
		Remdesivir	
Outpatient			**Inpatient**
		Mild-to-moderate	Severe-to-critical
		COVID-19	COVID-19
Uninfected	**Exposed, Uninfected**	**Infected with SARS-CoV-2**	

Ongoing viral transmission and mutations resulted in the emergence of four variants of concerns: alpha, beta, delta, and omicron. Delta variant is the more transmissible and most invasive. It caused higher death toll in many countries like India, Brazil, and South Africa, and still prevails in many countries though the daily total number of deaths declining.[16] In November 2021, a new variant of concern 'Omicron' first identified in South Africa spreading rapidly worldwide. Though the variant is most transmissible but it is less invasive than delta.[17] A surge in the hospital admission rate and death is observed in many countries due to its increased transmission rate. Hopefully, a new study shows significant neutralisation activity against omicron variant after the booster (Third) dose.[13] In addition, both homologous and heterologous boosters have been shown to be immunogenic and safe. The data we currently have available show us that COVID-19 vaccines are still very effective at preventing serious illness and death against all of the current variants of concern.[13] Many experts say it will end up with the pandemic or remains endemic like common cold.

Three antiviral drugs (i.e Remdesi- vir, molnupiravir, and PF-07304814) were tested to see the efficacy against omicron. All the three individual drugs have shown their activity against omicron and can be used in patients infected with the new variant.[17,18]

Natural infection with SARS-CoV-2 elicits strong protection against reinfection with the B.1.1.7 (Alpha) 1,2 B.1.351 (Beta) 1 and B.1.617.2 (Delta). In a national database study in Qatar, the authors report that the effectiveness of previous infection in preventing reinfection with the alpha, beta, and delta variants of SARS-CoV-2 was robust (At approximately 90%). Such protection against reinfection with the omicron variant was lower (approximately 60%) but still considerable.[19] In addition, the protection of previous infection against hospitalization or death caused by reinfection appeared to be robust, regardless of variant.[19]

Throughout the world vaccine inequity is the barrier to progress against Covid to end the pandemic.[20] At least, there is chance to end the public health emergencies like hospitalisation and death by addressing the inequities of access to vaccines and health care.[20,21] Third dose of vaccine (Booster dose) has been effective in preventing the omicron.

Several vaccines that are highly effective in reducing the incidence of hospitalization and death have been authorized, however, vaccine coverage remains insufficient.[14]

Antiviral therapies that reduce the risk of COVID-19 progression are needed. A novel antiviral compound molnupiravir has been shown to reduce hospitalisation or death in at risk unvaccinated adults with COVID-19.[15] Convalescent plasma, monoclonal antibodies, re-purposed antivirals, and novel antiviral compounds effective against SARS-CoV-2 virus have been used in hospitalised patients and successful outcomes observed in many countries.[22,18]

As the COVID-19 pandemic is ongoing we need to follow public health and social measures to prevent the SARS-CoV-2 transmission and the disease COVID-19. Several effective vaccines are available to prevent infection, disease progression and deaths. Globally, vaccine inequity, insufficient vaccine coverage, and access to health care including effective novel antiviral drugs are great challenges. If the inequities can properly be addressed we will be able to end the COVID-19 pandemic.

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Tribute

Professor (Dr) Md Mahtab Uddin Hassan
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(25.12.1958 - 12.11.2018)

The Editorial Board of Marine City Medical College Journal would like to express their heartfelt condolences to the family of Professor Dr. Mahtab Uddin Hassan who passed away on Monday 12 November 2018 at the age of 60 years. Professor Hassan served as a Principal of Marine City Medical College from 1st April 2017 to 12 November 2018. Professor Hassan had a long and productive career in Internal Medicine and made significant contributions to the doctors community. He authored over 50 articles and chapters covering a wide range of topics, including electrolyte disorders, acute kidney injury, rhabdomyolysis and heat stroke. He spent much of his academic career in Chittagong Medical College, where he held several leadership positions, including President of Teachers Association and Head of the Department of Medicine. Editorial Board would like to thank Professor Dr. Mahtab Uddin Hassan for all of his varied contributions.

Myocarditis or Pericarditis Following mRNA COVID-19 Vaccination

Eric S. Weintraub, Matthew E. Oster, Nicola P. Klein. JAMA Netw Open. 2022;5(6):e2218512.

Data from population-based cohort studies in Ontario, Canadaand showed higher rates of myocarditis or pericarditis following receipt of mRNA-1273 (Moderna Spikevax) compared with BNT162b2 (Pfizer-BioNTech Comirnaty) and that for both vaccines, the rate was higher when the interdose interval (The timing between dose 1 and dose 2) was 30 days or less. The reported rates for myocarditis and pericarditis among male individuals were higher than those among female individuals for all but 1 age group (25 to 39 years). The highest reported rate was observed for male individuals aged 18 to 24 years following dose 2 of mRNA-1273; the rate in this age group was more than 6 times higher than the rate following dose 2 of BNT162b2. So alonger time interval (56 days or more) between two doses of primary mRNA COVID-19 vaccination series may be associated with a lower risk of myocarditis or pericarditis. So they suggested an 8-week interval may be optimal for some people aged 12 years or older, especially for male individuals aged 12 to 39 years.

Another new contribution of this study is the finding that a heterologous second dose with mRNA-1273 after first BNT162b2 was associated with higher reported rates of myocarditis or pericarditis than both doses with mRNA-1273 (ie, mRNA-1273 for both dose 1 and dose 2). As COVID-19 vaccination programs have expanded to include younger age groups and additional booster doses, vigilance in monitoring for myocarditis or pericarditis and other adverse events will be essential for regulatory authorities to protect the public and mitigate the pandemic.

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COVID-19 in 2022 : The Beginning of the End or the End of the Beginning ?

Carlos del Rio, Preeti N. Malani. JAMA. 2022;327(24):2389-2390.

This year is the third year of the coronavirus pandemic Even after the surge of Omicron variant the number of daily cases had been declining to their lowest levels in more than 6 months. But it seemed that SARS-CoV-2 was moving towardendemicity as US infections and infections in other countries are again rising in May 2022. The reported number of cases is likely a gross underestimate of actual infections because many infections are unreported. Several factors help explain the current trends: The emergence of the BA.2 subvariant of Omicron and the more recently identified subvariant called BA.2.12.1, the limited durability of protection from infection both from vaccination and prior infection, and lifting of mandates (Such as mask use) and other restrictions across the country.The clinical manifestations of omecron infection are mild upper respiratory symptoms (Such as sore throat and pharyngitis). Many patients report gastrointestinal symptoms (eg, diarrhea, nausea, and vomiting) along with nonspecific symptoms (eg, muscle aches,

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Volume 01 | Issue 01 | April 2022 | 6-7

headache, nasal congestion, and fatigue). There is little cross immunity between different subvarients of omicron, so an infected person with one variant may also have infection with other subvarient.As of May 25, 2022, when daily reported COVID-19 cases are increasing and approaching 100 000, about 9.2% of counties are in the high Community Level.

A fourth dose of mRNA vaccine in high-risk individuals (Older adults and those who are highly immunocompromised) has been proposed as a preventive strategy. But Data from Israel suggest that a fourth dose is associated with marginal benefit.However, it is increasingly clear that with Omicron and its many subvariants, protection from severe disease requires 3 doses of an mRNA vaccine, something the CDC has termed “up-to-date.”

With the increased availability of effective antiviral agents and monoclonal antibodies within 5 days of symptom onset, will be effective if planning these are easily available to those individuals who are not connected to the health care system. However Response rate ofnirmatrelvir/ritonavirmolnupiravir treatment is only available for unvaccinated individuals not for vaccinated individuals, Yet until the data become available, it is reasonable to prescribe these medications to people who are infected and at high risk of severe COVID-19.

The authors concluded that While many questions remain about the future of the pandemic, it is clear that SARS-CoV-2 will not be fully eradicated. If COVID-19 moves toward endemicity, then it should not disrupt everyday life. However, with ongoing transmission and with an estimated 10% to 30% of individuals experiencing long COVID symptoms after infection, this issue will require careful attention to further define the syndrome and possible intervention Data suggest that vaccination can decrease the risk of long COVID and thus continuing to focus on improving vaccination rates must remain the cornerstone of COVID-19 prevention and mitigation not only locally, but globally.

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Dipeptidyl Peptidase-4 Inhibitors and Gallbladder or Biliary Disease in Type 2 Diabetes : Systematic Review and Pairwise and Network Meta-analysis of Randomised Controlled Trials

Liyun He, Jialu W, Fan P, Na Y, Jingyue H, Wei L et al. BMJ. 2022;377:e068882.

This is a systemstic review. A total of 82 randomised controlled trials with 104 833 participants were included in the pairwise meta-analysis. Compared with placebo or non-incretin drugs, dipeptidyl peptidase-4 inhibitors were significantly associated with an increased risk of the composite of gallbladder or biliary diseases (Odds ratio 1.22 (95% confidence interval 1.04 to 1.43) risk difference 11 (2 to 21) more events per 10 000 person years) and cholecystitis (odds ratio 1.43 (1.14 to 1.79) risk difference 15 (5 to 27) more events per 10 000 person years) but not with the risk of cholelithiasis and biliary diseases. The associations tended to be observed in patients with a longer duration of dipeptidyl peptidase-4 inhibitor treatment. In the network meta-analysis of 184 trials, dipeptidyl peptidase-4 inhibitors increased the risk of the composite of gallbladder or biliary diseases and cholecystitis compared with sodium-glucose cotransporter-2 inhibitors but not compared with glucagon-like peptide-1 receptor agonists.

This review concluded that Dipeptidyl peptidase-4 inhibitors increased the risk of cholecystitis in randomised controlled trials, especially with a longer treatment duration, which requires more attention from physicians in clinical practice.

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Medicine Digest

Marine City Medical College Journal

New Application Prospect of Angiotensin Receptor Naprilysin Inhihitor

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Heart Failure (HF) is a global health issue. It affects 1-2 % of general population. In elderly cohorts the incidence is even higher. Fundamentally four types of drugs are used in heart failure. They are Angiotensin Converting Enzyme Inhibitor (ACEI) or Angiotensin Receptor Blocker (ARB) or Angiotensin Receptor Naprilysin Inhibitor (ARNI), a beta blocker, a Mineralocorticoid Receptor Antagonist (MRA) and a sodium-Glucose co-Transporter 2(SGLT2) inhibitor.

There was a paradigm shift of drugs used in heart failure (Fig 1).[1]

All these drugs act synergistically to reduce morbidity and mortality. ACEI, ARB and MRA are current Guideline directed heart failure drugs. ARNI, SGLT2 inhihibitors (Partly by renoprotection and sympatholytic and partly by reducing oxidative stress, inflammation and fibrosis) and sGC stimulators (Reduce oxidative stress by generating Nitric acid) like vericiruat are drugs with evidence of outcome benefit in heart failure (Prevent less hospitalization).

Novel therapeutic targets are Hypertrophy , fibrosis, cardiac metabolism . contractility and inflammation. PPAR (Peroxisome Proliferator-Activated Receptor) α antagonist (Trimetazidine) promotes shift to glucose metabolism by inhibiting fatty acid oxidation.

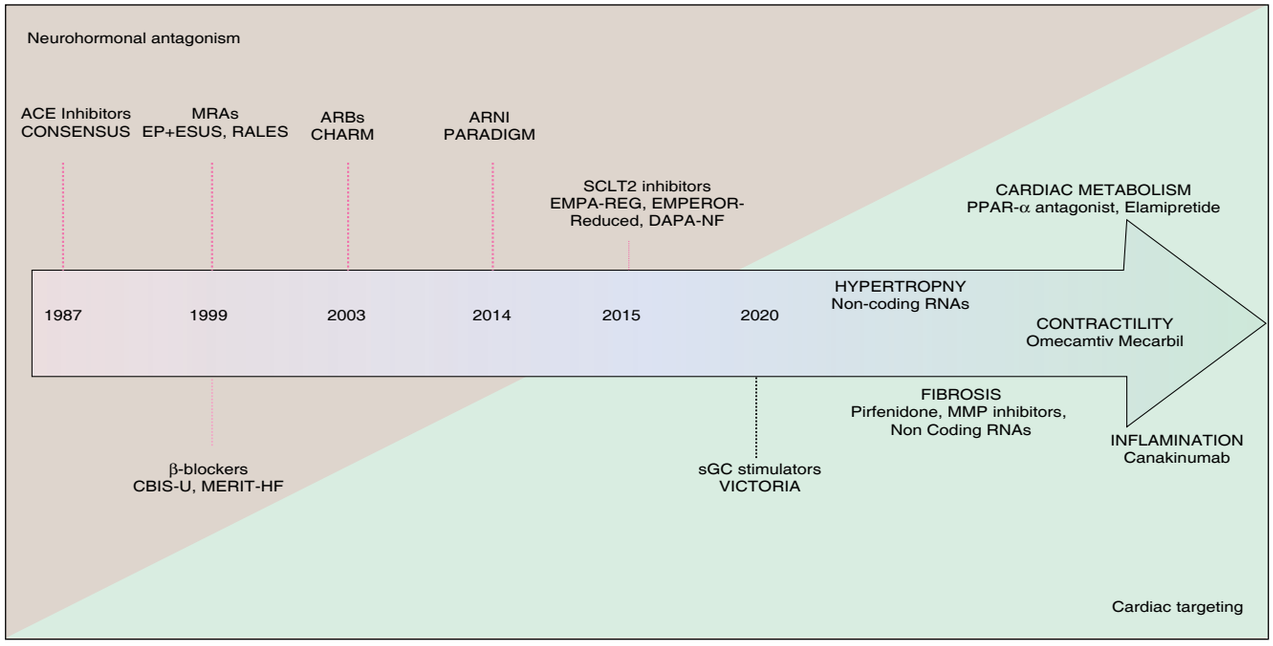

Figure 1 Chronologic development of drugs in heart failure, highlighting the shift from neurohormonal antagonism to specific cardiac targeting

ACE: Angiotensin Converting Enzyme, ARBs: Angiotensin Receptor Blocker, PPAR: Peroxisome Proliferator Activated Receptor, MMP : Metaloproteinase, sGC: soluble Guanylatecyclase[1]

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Volume 01 | Issue 01 | April 2022 | 8-12

Elamipretide, a cardiolipin-stabilizer, has been first tested on a canine model of HF showing improvements in LVEF (By myocardial membrane stabilizer) and reduction in circulating levels of NT-proBNP. Omecamtiv mecarbil (Myosin motor activator) and Canakinumab an interleukin-1beta blocker are also novel therapeutic approaches (Fig 1).

The blocking points in RAAS for each ARNI, ACEI, ARB and MRA are systemically demonstrated in Fig. 2.[2]

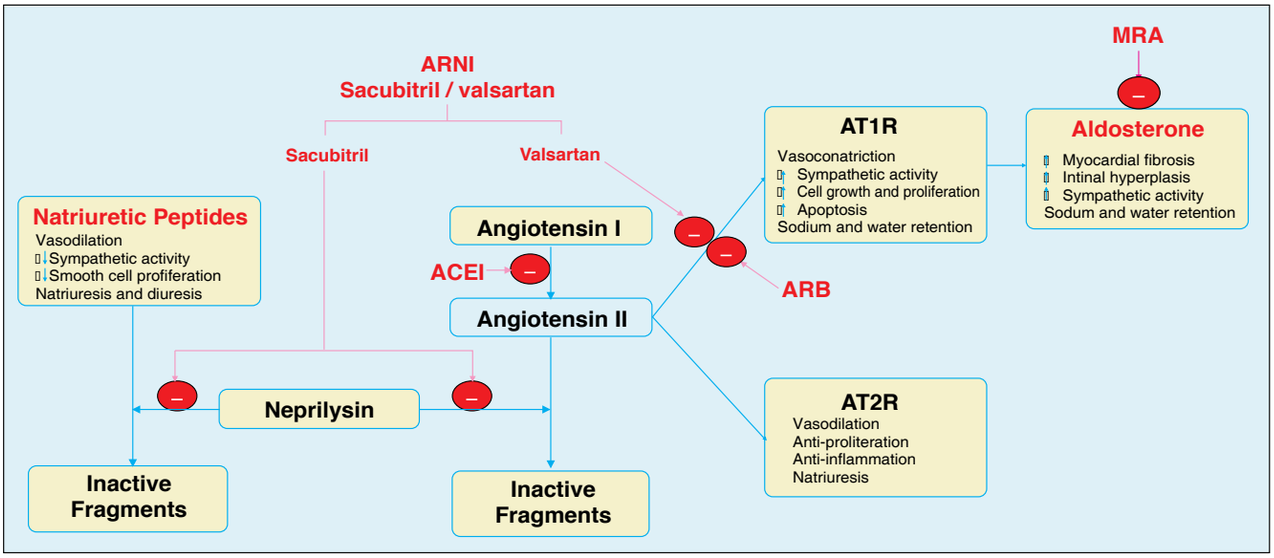

Figure 2 Blocking points for renin-angiotensin-aldosterone system inhibitors and a neprilysin inhibitor

ACEI : Angiotensin Converting Enzyme Inhibitor, ARB: Angiotensin Receptor Blocker, ARNI: Angiotensin Receptor Neprilysin Inhibitor, AT1R: Angiotensin II Receptor Type 1, AT2R : Angiotensin II Receptor Type 2, MRA, : Mineralocorticoid Antagonist.

Conventionally step wise sequential approach was adopted using one by one which require about 6 months to reach at peak target level with full combination. But now a days a more rapid evidence based sequencing is proposed.[3] Patients were started on all four drugs within 2-4 weeks. Initially a beta blocker and an SGLT2 inhibitor are started simultaneously followed 1-2 weeks later by Sacubitril/valsartan and 1-2 weeks later by a mineralocorticoid receptor antagonist (Fig 3).

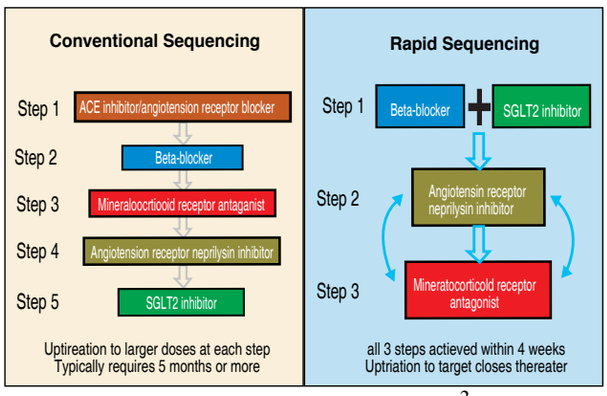

Figure 3 Rapid sequencing of Heart failure drugs[3]

Different RCTs showed that the efficacy of each fundamental drug is independent of treatment with other drugs. In each case when low starting doses of drugs is used, its therapeutic benefits is substantial. So, no drug is titrated to highest target dose and one drug increases tolerability of other drugs.[3] This accelerated sequencing acts to reduce morbidity and mortality very rapidly, i.e within 4 weeks of initiating therapy.

Previously Neurohumoral antagonism has not been shown to have any outcome benefit in Heart Failur with preserved EF (HFpEF). Only TOPCAT trial showed reduced mortality in HFpEF by aldosterone antagonist.[4] Recently new recommendation proposes use of ARNI may be of outcome benefit even in HFpEF (EF >50%) and Heart Failur with medium range EF (HF mrEF, EF 41-49%) in the lower end of the spectrum. It reduces hospitalization and cardiovascular motility.[5]

Another attractive feature is that in certain trial it was evident that ARNI has more potential benefit in HF of Asian population. It was postulated that unique characteristic of HTN in Asian population is that it is salt sensitive, nocturnal and systolic predominant (Fig 4).

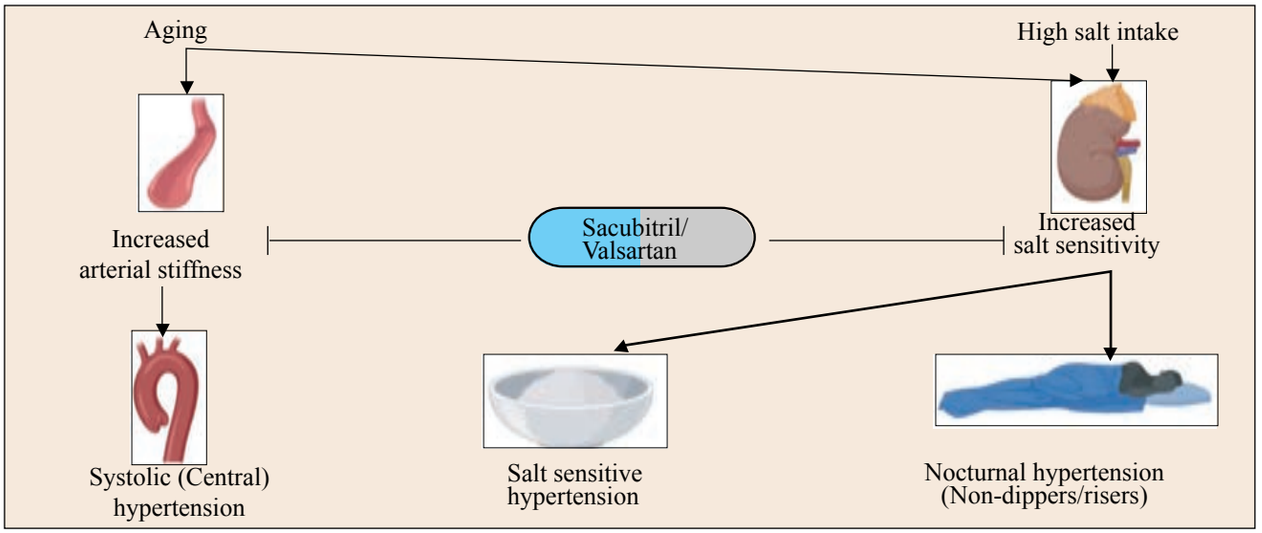

Figure 4 Characteristics of hypertension in Asians that are targets of sacubitril/valsartan[5]

Sacubitril inhibits Neprilysin. Naprylisin (Metallopeptidase) degrades Natriuretic Peptides (NPs). NPs exert sympatholytic, diuretic, natriuretic, vasodilatory and insulin-sensitizing effects mostly via cyclic Guanosine Monophosphate (cGMP)-mediated pathways. So sacubitril/valsartan combination besides Angiotensin II Receptor Type 1 Blockers (ARBs) with valsartan by stabilizing NPs causes additional reductions of office systolic blood pressures ranging between 5 and 7 mmHg. In addition elderly patients and Chronic Kidney disease patients tolerate this drug. Hence it is proposed that ARNI may be used as a first line a Antihypertensive.[6]

Recently the above quadruple therapy was also found to have cardiovascular benefit in CKD patients.[7] How these drugs modify renal haemodynamics were shown in Fig 5.

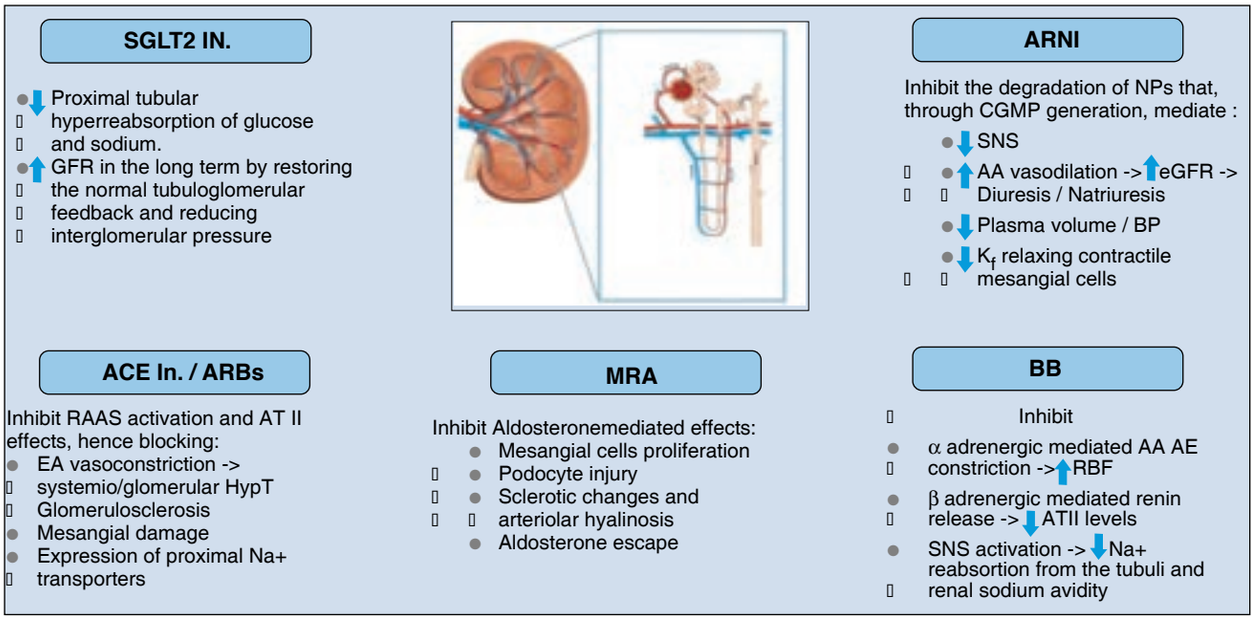

Figure 5 Probable mechanism of action of HF drugs over kidneys[6]

Drug adjustment in different stages of CKD was shown in Fig 6.

ARNI was tried in patients with moderate CKD (eGFR, 30–59 mL/min/1.73 m^2).[2] No dose adjustment is required at the start of sacubitril/ valsartan. However, the starting dose of sacubitril/ valsartan should be reduced in patients with severe CKD (eGFR, <30 mL/min/1.73 m^2).

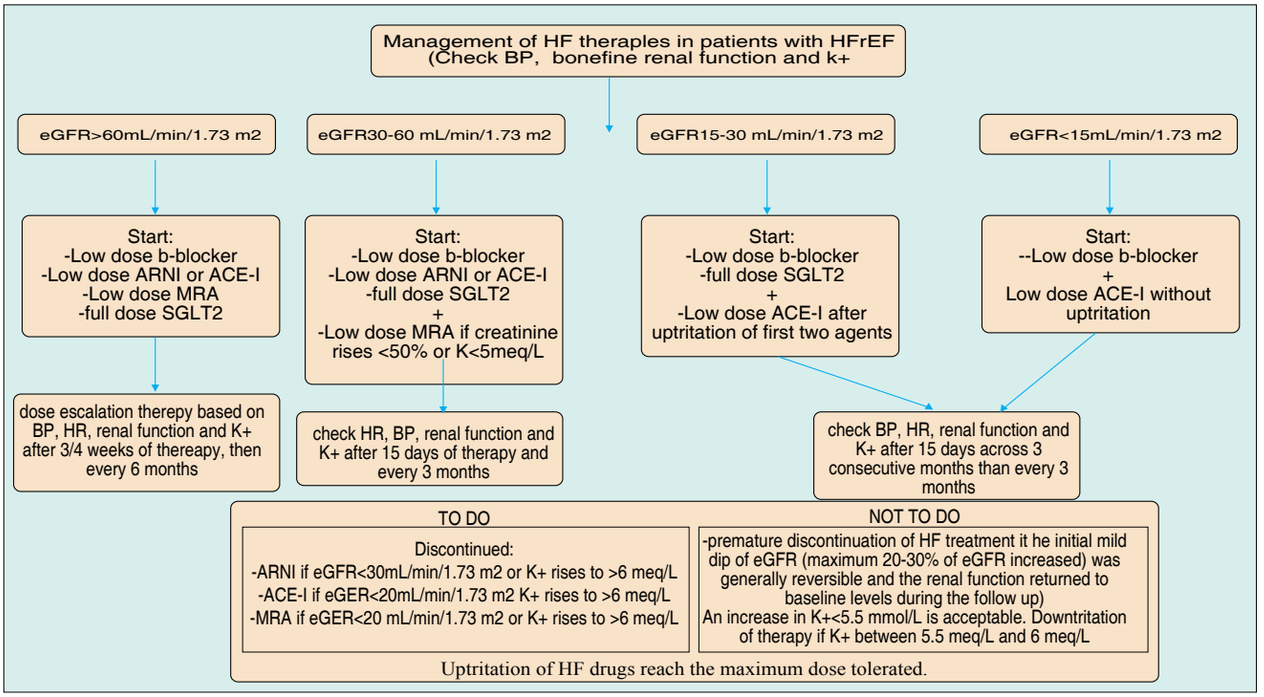

Figure 6 Drug adjustment according to eGFR

HFrEF: Heart Failure with reduced Ejection Fraction, ACE-I: Angiotensin Converting Enzyme Inhibitor, ARNI: Angiotensin Receptor Neprilisin Inhibitor, B-Blocker: Beta Blocker, BP: Blood Pressure, eGFR: estimated Glomerular Filtration Rate, HR: Heart Rate, K^+: Potassium, HF: Heart Failure, MRA: Mineralcorticoid Receptor Antagonist, SGLT2: Sodium Glucose Late Transporter 2 Inhibitors.[7]

The PARADIGM-HF study showed that if ARNI is used in Hf with CKD, dose of diuretic is to be reduced otherwise it may cause hypotension or deterioration of renal function by over diuresis.[8] Therefore Renal function and potassium levels are recommended to be evaluated within 1 to 2 weeks after ARNI initiation or dose escalation, subsequent follow up is ensured by the patient's kidney function and volume status. Usual recommended following intervals for renal function monitoring are monthly for the first 3 months and every 3 months thereafter.

Finally another potential role of ARNI combining ARB was recenlty elicited by some trials in diabetic kidney disease. ARNI increase natriuresis and reduces blood pressure, contributing to renoprotection in diabetic patients. It ameliorates inflammation, oxidative stress and renal dysfunction. It may also improve insulin resistance and blood glucose regulation via elevating neprilysin substrates such as NPs and GLP-1. Since GLP-1 is also a substrate of DPP-4, combining neprilysin inhibitor with DPP-4 inhibitor may offer better Diabetes control. However more research is needed to prove role of ARNI on proteinuria and albuminuria in diabetic kidney disease.[9]

DISCLOSURE

The author declared no competing interest.

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Review Article

Marine City Medical College Journal

Role of ARNI in the Treatment of Heart Failure

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ABSTRACT

Background: Heart Failure (HF) is a condition when the heart is unable to pump blood well enough to meet the body's demand properly. HF accounts for a tremendous burden on health care systems and the society.

Angiotensin Receptor Neprilysin Inhibitors (ARNI) has been shown to reduce cardiovascular mortality and morbidity with chronic HF and reduced left ventricular Ejection Fraction (HFrEF). This review article aims to rational for using ARNIs describes efficacy, summarizes the recent evidence of ARNI regarding patient-centered outcomes and recommendation from current guidelines and provides practical points about ARNI.

Methodology: This current study is a narrative review to published studies and articles by using Medline and Google. Structured search strategy using appropriate keywords and title.

Conclusion: In this systematic review it is concluded that the ARNI is found to be safe and well tolerated in the treatment of HF with reduced ejection fraction.

KEY WORDS

Chronic Heart failure; HFrEF; ARNI.

INTRODUCTION

Heart Failure (HF) is a major global public health problem. The estimated 45–67 million adult patients around the world suffer from HF and hospitalized. The staggering costs related to HF, which are mainly due to repeated hospitalizations and the loss of productivity in patients with HF, impose a severe economic burden on virtually every country around the world including Bangladesh. While therapeutic advances have improvedthe outlook for patients with HF, more work still needs to be done in order to deal with this global pandemic.[1,2]

SEARCH STRATEGY

Available studies and abstracts were identified through Medline data bases (1984-2018) and Google. Key search topics were "Treatment of Heart Failure & HFrEF". The following key words were used in various combinations. Bibliography was also searched of relevant full text.

DISCUSSION

Classification:

HF is classified based on Left Ventricular Ejection Fraction (LVEF) into HF with reduced EF (HFrEF) with an LVEF 40% and HF with preserved EF (HFpEF) with an LVEF ³50%.[3,4] An EF between 40% and 49% is considered an intermediate zone and is termed as HF with borderline EF or HF with mid-range EF. Epidemiologic data indicate that HFpEF and HFrEF contribute equally to the total HF population.

Neurohormonal Activation in HF

Approximately half of the worldwide HF population has HF with reduced Ejection Fraction (HFrEF). In these patients, neurohormonal activation is recognized as playing a critical role in the development and progression of their disease.[4-6] Systems such as the Renin Angiotensin Aldosterone System (RAAS) and Sympathetic Nervous System (SNS) are activated early in the course of the disease in response to myocardial injury or increases in load on the heart. As HF progresses, neurohormonal activation intensifies and circulating levels of the main effector molecules of these systems are increased in a step-wise manner.[7] Down-stream effects of Angiotensin II (Ang II) aldosterone and the catecholamines, the major signaling molecules of the RAAS and SNS, promote vasoconstriction and salt and water retention. They also stimulate maladaptive cardiac remodeling, a process characterized by increases in cardiac chamber volumes, muscle mass and interstitial fibrosis.[8] Understanding

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the importance of neurohormonal activation in the progression of HF resulted in the development of agents designed to inhibit this process. There is now abundant evidence that Angiotensin Converting Enzyme Inhibitors (ACEIs) Angiotensin Receptor Blockers (ARBs) Mineralocorticoid Receptor Antagonists (MRAs) and beta blockers all reduce morbidity and mortality and improve quality of life of patients with Stage C HFrEF.[9-16] As a result, these agents are widely recognized as being the cornerstones of HFrEF therapy and they are given the highest level of recommendation in contemporary guidelines for the pharmacologic treatment of HF.

Studies with ARNIs in Patients with HF

In PARADIGM-HF, treatment with sacubitril-valsartan resulted in a significantly greater reduction in levels of NT-proBNP than was seen with enalapril.[11] While NP levels have been used as surrogates for clinical outcomes, they are also related to LV wall stress which is a major factor in promoting maladaptive cardiac remodeling. Increased LV wall stress stimulates the production and release of B-type Natriuretic (BNP) in the heart.[12] A reduction in BNP or in NT-proBNP, which is a fragment of the BNP molecule, would be indicative of a reduction in LV wall stress. In the Prospective Study of Biomarkers, Symptom Improvement, and Ventricular Remodeling During Sacubitril/Valsartan Therapy for Heart Failure (PROVEHF) study, the association of change in NTpro-BNP following initiation of sacubitril-valsartan with change in cardiac structure and function was assessed in a population of 794 patients with HFrEF.[13] In this open label study, sacubitril-valsartan was started in a cohort of patients with HFrEF defined as LVEF £0.40. Blood samples for NT-proBNP were obtained at baseline and periodically over a year follow-up period and a Transthoracic Echocardiogram (TTE) was performed at baseline, 6- and 12-month. The TTE was interpreted by a core laboratory in a blinded fashion. The results showed that initiation of sacubitril-valsartan was associated with a rapid and significant reduction of NT-proBNP, with the majority of the reduction occurring within the first 2 weeks of initiating drug. Treatment with sacubitril-valsartan was also associated with reductions in LV End-Diastolic and End-Systolic Volume Indices (LVEDVI and LVESVI) of 12.25 and 16.25 mL/m^2, respectively (Both $p<0.001$) after 12 months of therapy, a 9.6% absolute increase in LVEF ($p<0.001$) and a reduction in Left Atrial Volume Index (LAVI). A shown in Figure 4, there was a modest but highly significant association between the changes in LVEF, LVEDVI, LVESVI and LAVI and reductions inNT-proBNP level.[14,15] Patients who hadexperienced the largest reduction in NT-proBNP and LVESVi by 6 months had lowest rates of subsequent death or HF hospitalization by 12 months. Biomarkers associated with profibrotic signaling including aldosterone, sST2, TIMP-1, MMP-9, procollagen type I N pro-peptide, and amino-terminal pro-peptide of type III collagen are increased in patients with HFrEF and are believed to be associated with the increase in cardiac fibrosis. A sub-study of PARADIGM-HF in which levels of these profibrotic biomarkers were measured at baseline and after 6 months of therapy in 2,067 patients reported that the levels of these biomarkers are significantly more decreased with sacubitril-valsartan than with enalapril.[16] Since elevation of many of these biomarkers is associated with clinical events in patients with HFrEF, these findings suggest that the reduction in their levels with sacubitril-valsartan is related to the reduction in clinical events seen in PARADIGM-HF.[17] It also possible that the combined effects of a reduction in profibrotic signaling along with a the reversal of the remodeling process resulted in the reduction in ventricular arrhythmias that has been reported with the use of sacubitril-valsartan.[18] Although the complex molecular mechanisms through which sacubitril-valsartan stimulates reversal of the remodeling process and brings about these favorable changes in cardiac structure and function have not been fully -defined, a systems biology approach provided evidence that the 2 drugs in the molecule work through separate pathways.[19] Valsartan was found to improve cardiac remodeling by inhibiting members of the guanine nucleotide-binding protein family, while sacubitril attenuated cardiomyocyte cell death, hypertrophy, and impaired myocyte contractility.[20]

In July 2015, the FDA approved the first of a new class of drugs for the treatment of heart failure, valsartan/sacubitril (Formerly known as LCZ696 and currently marketed by Novartis as Entresto).[10] Neprilysin is an enzyme that participates in the breakdown of biologically active natriuretic peptides and several other vasoactive compounds. The inhibition of neprilysin has been a therapeutic target forseveral drugs tested in cardiovascular disease, mainly for heart failure and/or hypertension.[21]

Dosage and Administration[22]

Sacubitril/valsartan should not be given in conjunction with another ARB or renin inhibitor (Because of the risk of renal impairment and hyperkalemia) or an ACE inhibitor (Risk of renal impairment, hyperkalemia and angioedema). Due to the potential risk of angioedema when used concurrently with an ACE inhibitor, sacubitril/valsartan must not be started for at least 36 half an hour after discontinuing an ACE inhibitor. Patients and carers should discard any remaining doses to reduce the risk of accidental dosing. The starting dose of sacubitril/valsartan is 49 mg/51 mg twice daily. This should be reduced in certain groups. The dose should be doubled every 2–4 weeks as tolerated by the patient to the maximum dose of 97 mg/103 mg twice daily. Patients should also be prescribed other evidence-based drugs (b- blocker, mineralocorticoid receptor antagonist, ivabradine and digoxin) and devices (CardiacRe-synchronization Therapy (CRT) Implantable Cardioverter Defibrillator (ICD) as appropriate.

Benefits of ARNI

Hypertension

The study concluded that sacubitril/valsartan + amlodipine combination could be an effective treatment for patients with systolic hypertension uncontrolled with Amlodipine.[23]

Post Myocardial Infarction

The sacubitril/valsartan group also had a lower left ventricular end-diastolic diameter, a higher left ventricular ejection fraction, and higher circular and diastolic wall strain, confirming improved left ventricular function 4 weeks after treatment.[23]

Renal Impairment

Better eGFR progression, a greater decrease in BP and serum creatinine levels in patients on sacubitril-valsartan when compared to valsartan.[23]

Diabetes

Those on sacubitril/valsartan were also less likely to start taking insulin or other meds for glycemic control and showed better improvements in HDL cholesterol. The significant improvement in HbA1c levels ($p = 0.0055$) over 3 years in the sacubitril/ valsartan group vsenalapril implies that heart-failure patients with diabetes who take the drug might benefit from and even require lower doses of any antidiabetic agents they may be taking.[22,23]

Contraindications

Sacubitril/valsartan is contraindicated: In pregnancy & lactation, in patients with hypersensitivity to any component, in patients with severe renal (eGFR<30 mL/min/1.73 m^2) or hepatic impairment (ChildPugh classification Class B and C, >7 points score), in patients with a history of angioedema related to previous ACE inhibitor or ARB therapy, with concomitant use of ACE inhibitors. Do not administer within 36 h of switching from or to an ACE inhibitor· with concomitant use of Aliskiren in patients with diabetes.[24]

Drug Interactions and Adverse Reactions

Use with an ACE inhibitor is contraindicated due to increased risk of angioedema. Concomitant use of potassium-sparing diuretics (e.g., Spironolactone, triamterene, amiloride) potassium supplements, or salt substitutes containing potassium may lead to increase in serum potassium concentrations. In patients who areelderly, volume-depleted (Including those on diuretic therapy) or with compromised renal function, concomitant use of NSAIDs, including COX-2 inhibitors, may result in worsening of renal function, including possible acute renal failure. These effects are usually reversible though periodic monitoring of renal function should be performed. Concomitant administration with lithium may result in an increase in serum lithium concentration and lithium toxicity. Clinically significant ADR include hypotension (18%), hyperkalemia (12%), cough (9%), dizziness (6%), orthostasis(2.1%), angioedema (<1%), impaired renal function (Reversible) dementia risk (Theoretical). 28 Mechanism of Action.[26,27]

Heart failure stimulates both the renin–angiotensin system and the natriuretic peptide system. LCZ696 is composed of two molecular moieties, the angiotensin receptor blocker valsartan and the neprilysin inhibitor pro-drug sacubitril. Valsartan blocks the AT1 receptor Sacubitril is converted enzymatically to the active neprilysin inhibitor LBQ657, which inhibits neprilysin, an enzyme that breaks down ANP, BNP and CNP, as well as other vasoactive substances. NTproBNP is not a substrate for neprilysin.[26]

CONCLUSION

Sacubitril/valsartan is unique in simultaneously blocking the renin angiotensin system while augmenting the body's intrinsic. natriuretic peptide system through neprilysin inhibition which may

represent an attractive and serendipitous therapeutic approach for a range of CV diseases, including hypertension and HF, in which vasoconstriction, volume overload and neuro- hormonal activation play a part in pathophysiology. The potential clinical benefits from neutral endopeptidase inhibition however can only be leveraged if the Renin– Angiotensin–Aldosterone System (RAAS) is inhibited concomitantly.

DISCLOSURE

The author declared no competing interest.

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Original Article

Marine City Medical College Journal

Evaluation of Aspartate Aminotransferase to Alanine Aminotransferase Ratio in Non-Alcoholic Fatty Liver Disease Patients

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ABSTRACT

Background: Non-Alcoholic Fatty Liver Disease (NAFLD) is a common cause of Chronic Liver Disease (CLD) worldwide and is becoming a major public health problem. NAFLD has been recognized as a hepatic manifestation of Metabolic Syndrome (MetS) linked with Insulin Resistance (IR) and is currently considered as the hepatic component of the Metabolic Syndrome (MetS). In a recent survey based on the National Health and Nutrition Examination Survey (NHANES) III, unexplained aminotransferase elevations, most likely due to NAFLD, were found in 5.4%of the general population. Aminotransferase (AST & ALT) levels may not correlate with fatty liver disease and can even be normal in advanced disease. The purpose of this study is to evaluate the Aspartate Aminotransferase to Alanine Aminotransferase (AST/ALT) Ratio in NAFLD Patients.

Materials and methods: A prospective hospital based cross sectional study was carried out in the Department of Biochemistry, Institute of Nuclear Medicine and Allied sciences (INMAS) and Chittagong Medical College Hospital (CMCH). One hundred & fifty (150) subjects aging between 18-60 years were included in this study by non probability consecutive sampling method. AST & ALT levels were measured in both the case and control groups. AST & ALT ratio of NAFLD patients were calculated.

Results: In this study aminotransferase levels were significantly higher in the NAFLD patients but there was no rise in the AST:ALT ratio

Conclusion: The findings of the current study suggest that independent variable such as AST and ALT were elevated in NAFLD subjects with normal AST:ALT ratio.

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Key words: Aspartate Aminotransferase; Alanine Aminotransferase; Non-Alcoholic Fatty Liver Disease.

INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) includes a wide spectrum of liver damage, ranging from simple steatosis to steatohepatitis and advanced fibrosis, with histological features of alcohol-induced liver disease in individuals who do not consume significant amounts of alcohol.[1,2] The cutoff limit of alcohol intake that distinguishes between alcoholic fatty liver disease and NAFLD is not known, although 20g/d for women and 30g/d for men is commonly used. One standard drink typically contains 10–20 g of alcohol.[3] In 1980, Ludwig et al published the first systematic description of what was then an "unnamed and poorly understood" condition.[4] On liver biopsy, findings resembled those of alcoholic hepatitis, but because the patients did not have a history of heavy drinking, the condition was named "nonalcoholic steatohepatitis". Around 90% of NAFLD patients had at least one component of MetS and around 33% of patients met the criteria for MetS.[5,6,7] NAFLD is also associated with extra hepatic manifestations such as Cardiovascular Disease (CVD) Chronic Kidney Disease (CKD) etc.[8,9] There are no evident clinical symptoms in its initial stage. Generally, absence of alcohol abuse or consumption of alcohol of < 20 g/day for prolonged periods, and negative serological tests for Hepatitis B and C should raise the suspicion of NAFLD.[10]

In a recent survey based on the National Health and Nutrition Examination Survey (NHANES) III, unexplained aminotransferase elevations, most likely due to NAFLD, were found in 5.4% of the general population.[1,2] Aminotransferase levels may not correlate with NAFLD and can even be normal in advanced disease.[1,11] An AST/ALT ratio of more than 1 may suggest advanced fibrosis or cirrhosis[1,12]. Paradoxically, a complete spectrum of NAFLD was reported in patients with normal ALT activity, even after the cutoff value was decreased to 19 U/L.[13]

Moreover, increased ALT not associated with fatty liver was observed frequently in obese participants.[14] ALT actually is a glucogenic enzyme, and increased ALT has been demonstrated to be an indicator of impaired insulin signaling, which might not necessarily be associated with liver injury due to hepatic steatosis.[15] To date, although an increased ALT concentration is considered a consequence of hepatocyte damage in NAFLD, it is unclear what underlies the relationship between ALT and NAFLD.[16] ALT and AST are indicators of hepatocellular injury.

Several cross-sectional studies have already demonstrated that higher ALT, even within the currently accepted normal reference interval, is associated with NAFLD.[17,18] A previous study also showed that ALT appears to have associations with hepatic insulin resistance and later decline in hepatic insulin sensitivity.[17,19] Several other studies have demonstrated that high ALT levels are correlated with a higher risk of NASH.[20,21,22] Some studies have shown that patients with a normal ALT level may also have histological features of NASH and are at risk of disease progression.[20,23] Additionally, some recent studies have introduced a new ALT upper limit for a healthy individual, which is ≤40 U/L for both sexes. Elevated ALT levels are sometimes associated with an underlying NAFLD.[20]

The aim of this study is to elucidate the relation between the AST:ALT ratio and elevated aminotransferases level in the NAFLD patients.

MATERIALS AND METHODS

A prospective hospital based cross sectional study was carried out in the Department of Biochemistry and Institute of Nuclear Medicine and Allied sciences, Chittagong Medical College Hospital, which included one hundred and fifty (150) subjects aged between 18-60 years over a period of one year from June 2017-June 2018. Subjects of both the sexes were evaluated sonographically and were divided into two groups as NAFLD cases (n=80) and Non-NAFLD controls (n=70). Subjects were excluded if they tested positive for hepatitis B virus surface antigen or anti -hepatitis C virus antibody or were suffering from liver cirrhosis, Acute or chronic hepatitis, history of alcohol abuse, Type II DM and Pregnancy.

Data was collected using a pre-tested structured questionnaire containing all the variables of interest after taking informed and written consent. Using standard phlebotomy procedures 5 ml of fasting venous blood was drawn from the median-cubital vein in between 8 and 9 am. Blood taken into clean and dry test tubes were kept for clot formation. After centrifugation serum was separated and taken into eppendorf which was then immediately transported to Biochemistry Laboratory for analysis. AST and ALT reagent is used to measure aspartate aminotransferase and alanine aminotransferase activity respectively by an enzymatic rate method.The rate of change in absorbance is directly proportional to the activity of aminotransferase which is used by the System to calculate and express aminotransferase activity.

Statistical analyses were performed using SPSS for Windows version 20.0. Statistical inference was based on 95% confidence interval and p value ≤0.05 was considered statistically significant. Data were expressed as mean ± Standard Error of Means (SEM) and comparison between two groups wasdone using student t-test. The summarized data were presented in the form of tables and figure.

RESULTS

Complete clinical profile, US data and serum samples were available for 150 subjects out of which, 80 (53%) were NAFLD cases and 70 (47%) were Non-NAFLD subjects taken as controls [Fig: 1]. In the gender distribution of the study population there was female predominance [Table: I]. Mean age was significantly higher in cases (35.05 ± 1.05 years) than controls (26.53 ± 1.02 years), p<.05. Among the NAFLD subjects, 66.3% were in age group 30-49 years [Table: II].Serum ALT (42.15±1.37 vs. 38.87±1.18) and AST (23.29±0.76 vs. 21.43± 0.73) were significantly higher in cases than that of controls, as P < 0.05 [Table: III].

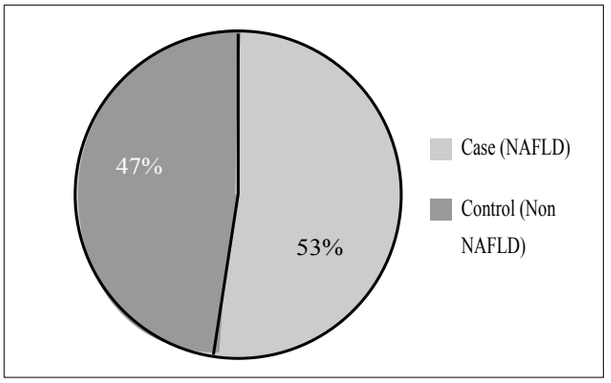

Figure 1 Pie chart showing distribution of study population by NAFLD status (n = 150)

Table I Distribution of gender among the study population (n = 150)

Gender	Cases (n = 80)		Controls (n = 70)		Total	
	n	%	n	%	n	%
Male	35	44	32	46	67	44.67
Female	45	56	38	54	83	55.33

Table II Age distribution among the NAFLD cases (n = 80)

Age category (Years)	NAFLD cases	Percentage (%)
<30	22	27.5%
30-39	28	35%
40-49	25	31.25%
50-59	4	5%
≥60	1	1.25%
Total	80	100%

Table III Comparison of serum hepatic enzymes (AST & ALT) amongst the study population (n =150)

Variables (U/L)	Cases (n=80) (Mean ± SEM)	Controls(n=70) (Mean ± SEM)	p value
Serum ALT	42.15 ± 1.37	38.87 ± 1.18	p = 0.037
Serum AST	23.29 ± 0.76	21.43 ± 0.73	p = 0.039

Table IV Evaluation of serum AST: ALT ratio amongst NAFLD patients (n =80)

Variables (U/L)	Cases (n=80) (Mean ± SEM)	AST:ALT ratio
Serum ALT	42.15 ± 1.37	0.552
Serum AST	23.29 ± 0.76	

DISCUSSION

NAFLD is a growing epidemic disease. Emerging data notes a high prevalence of NAFLD not only in the Western world but also in the South Asian population. NAFLD can progress to steatohepatitis which may further lead to Hepatocellular Carcinoma (HCC). NAFLD has become an increasingly serious public health problem worldwide. About 1/4th(22.10–28.65%) of the world's population suffers from NAFLD.[24] Compared with common chronic diseases such as HTN and DM, the epidemic scale of NAFL D is equally shocking and will continue to increase.[24-26] The impact of NAFLD is systemic. It is not only related to the development and deterioration of liver diseases but also to cardiovascular disease, metabolic disease, malignant tumors and other diseases.[27] Currently, NAFLD is the second leading indication for liver transplantation in the USA[24]. Clinically, obesity is closely associated with NAFLD, but there are still many people with a normal Body Mass Index (BMI) who are diagnosed with NAFLD. In the third National Health and Nutrition Inspection Survey of America, it was reported that liver steatosis could be detected by ultrasound in 7.4% of nonobese adults, and in Asia, the figure was as high as 8–19%.[24] AST and ALT are often used to indicate the quality of liver function. In previous studies, ALT has been shown to be associated with NAFLD. Even ALT values within the normal reference range have been associated with a risk of NAFLD.[28] The ALT/AST ratio can be used to evaluate the degree of hepatic fat infiltration and hepatic steatosis. In a recent Framingham study, it was shown that the ALT/AST ratio could identify hepatic steatosis more accurately than using ALT or AST alone.[24] Presently, there are limited studies that have reported on the association of the ALT/AST ratio with NAFLD risk. Only a few cross-sectional studies have found a positive correlation of NAFLD risk with the ALT/AST ratio.[24]

Complete clinical profile and US data with serum samples were recorded for one hundred and fifty (150) subjects. Among the subjects 80 were NAFLD and 70 were Non-NAFLD. In the gender distribution of the study there was female predominance.

Independent variables such as Serum ALT (p=0.037) and AST (p=0.039) were significantly higher in cases than that of controls.Though AST and ALT were raised in cases it did not provide evidence for prognosis of NAFLD to Chronic Liver Disease (CLD). Furthermore AST:ALT ratio was found to be less than one (<1). Henceforth it can be assumed that the NAFLD cases in this study were not progressing to CLD, rather it indicated the onset of the disease. The present study established an association between increased AST and ALT level in NAFLD patients and the observational findings were similar to other studies[20,24].

LIMITATIONS

The study has certain limitations which includes short duration of time, small sample size, cross sectional study and not assessing NAFLD by Liver biopsy.

CONCLUSION

The study revealed that although the AST:ALT ratio among the NAFLD patients were normal; individually all the Aminotransferases levels were elevated.

RECOMMENDATIONS

Further prospective multicenter study in large scale is necessary to better understand the biochemical strategy of inflammatory markers for the development of NAFLD.

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AUTHOR'S CONTRIBUTION

FH-Concept, design, data collection, manuscript writing and final approval of the draft.
PK-Data analysis, interpretation of the data, critical revision of the version & final approval of the draft.

DISCLOSURE

The authors declared no conflicts of interest.

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Original Article

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Perceived Stress and Associated Factors among the Doctors of Bangladesh Study

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ABSTRACT

Background: Stress is an inevitable part of life that cannot be avoided. Stress is more prevalent among doctors due to the heavy workload. This stress can result in harmful consequences for doctors themselves and the patients. The present studyaimed to assess perceived stress among doctors of different ages working in Bangladesh.

Materials and methods: A cross-sectional, survey was conducted in January and February 2022. The Perceived Stress Scale (PSS-10) was used to assess the level of stress. Data collected were analyzed using the Microsoft Excel spreadsheet (Version 2010) and all ethical considerations were followed.

Results: One hundred and forty-ninedoctors participated in the study, where 81 were male and 68 were female. Moderate stress was found predominantly in 67.11% of doctors, the low stress in 19.43%,and high stress in 13.42% of doctors. Statistically, a significantly higher stress level was found in the 36-40 years age group (p=.0117) and the doctors dissatisfied with their income (p=.0018).

Conclusion: Higher age group dissatisfaction with income, play major role in stress of doctors.

Key words: Doctor's; Perceived stress; Stree.

INTRODUCTION

Psychological distress like stress and depression has become a significant mental health issue in our working environment that could have the worst possible consequences. These include low productivity, absenteeism and job turnover.[1] The prevalence of stress and stress-related anxiety and depression in medical students, postgraduate trainees and qualified physicians is increasing in number day by day.[2] The complex environment of a modern medical workplace, such as hospitals and medical colleges, makes doctors respond differently, some find it exciting, whereas some feel stressed from the heavy workload.[3] In conclusion, this kind of psychological distress among doctors is harmful to their health and negatively influences their patients negatively.[4] Moderate and high emotional distress increases the likelihood of failure at work.[5] Thus, the topic of stress and mental health of doctors is a concern for both doctors and the health of other people.[6] Lower career satisfaction and lower-income compared to workload are likely associated with high-stress levels in our doctors.[1] In Bangladesh, some studies about mental health target specific doctor groups such as resident doctors. Still, there is little documentation about the overall doctor community's stress level, including doctors working in places like government hospitals, doctors at private hospitals, etc.The present study aims to identify how stressed our doctors are and their associated factors.

MATERIALS AND METHODS

A cross-sectional study was conducted over government hospitals, private hospitals and medical colleges. The sample size was 149. The selection of the sample was made by usinga convenient sampling technique. The study was conducted through a google form circulated through emails and messenger. After taking informed consent, the google form was divided into two sections. The first section carried the socio-demographical factors such as age, sex, marital status, current job, working hours, H/O mental illness, co morbidity,

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smoking, consumption of alcohol and satisfaction with current monthly income. Perceived Stress Scale-10 (PSS-10) was used to determine the doctors' stress levels based on their perceptions about their life according to their past 1 month experience in the second section. The inclusion criteria were doctors who responded and the exclusion criteria were doctors who did not answer.

Perceived Stress Scale (PSS) developed by Cohen, Kamarck, and Mermelstein, is one of the most widely used tools to measure psychological stress in the world.[7] Data collected were analyzed using the Microsoft Excel spread sheet (Version 2010). Demographic variables were mentioned in terms of percentages. PSS scores were obtained by reversing responses (e.g., 0 = 4, 1 = 3, 2 = 2, 3 = 1, and 4 = 0) to the four positively stated items (Items 4, 5, 7, and 8) and then summing across all scale items. Scores ranging from 0-to 13 would be considered low stress. ● Scores ranging from 14-26 would be considered moderate stress. ● Scores ranging from 27-40 would be considered high perceived stress.The Chi-square test was used to determine the association of stress with different demographic variables.

RESULTS

149 doctors participated in the study. Table I shows all age groups were represented, with most subjects from 36-40 years group 30.87%. More than 45 years were 5.36%, 41-45 years were 4.03%, 31-35 years were 29.53%, and 25-30 years was 30.20%. It also shows males were more predominant (54%) than females (46%) in the case of response. 82% were nonsmokers and only 18% were smokers, 94% did not consume alcohol and 6% consumed alcohol. 58% were dissatisfied with their monthly income and 42% were satisfied. Most of the doctors who responded were in government service (40%), whereas 35% were in private hospitals and 15% were in post-graduation courses. Most of the doctors (52%) had to work for 36-38 hours/week, 25% worked more than 48 hours/week, and 23% worked less than 36 hours/week.

Table I Frequency and percentage of different demographic variables

Variables		No	%
Age in years			
	25-30	45	30%
	31-35	44	29%
	36-40	46	31%
	41-45	6	4%
	>45	8	6%
sex	Male	81	54%
	Female	68	46%
Satisfied with monthly income	Yes	63	42%
	No	86	58%
Smoking	Yes	27	18%
	No	122	82%
Alcohol consumption	Yes	9	6%
	No	140	94%
Current job	Doctor in govt hospital/medical college	59	40%
	Doctor in private hospital/medical college	52	35%
	Post-graduation course	22	15%
	General practitioner	4	3%
	Temporary job	12	8%
Working hours	<36 hours/week	22	23%
	36-48 hours/week	77	52%
	>48 hours/week	38	25%

Figure 1 showed most doctors had moderate stress levels (67.11%) withlow-stress levels in second (19.43%) followed by high-stress levels (13.42%).

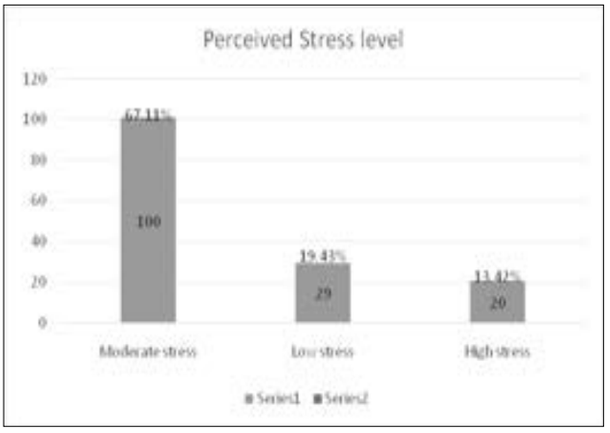

Figure 1 Total percentage of different perceived stress levels of doctors

Table II showed moderate stress was more common in 36-40 years (75.55%) and 41-45 years (71.42%). High stress was more in 41-45 years (14.28%), followed by 31-35 years (13.64%). > 45 years doctors were in low stress mostly (75%). Moderate stress was found in both males (67.90%) and females (66.18%), whereas High stress was markedly found in females (19.12%) compared to males (8.61%). Doctors of private hospitals were primarily under moderate stress (71.15%) followed by 68.18% of postgraduate students.

Table II Percentage of stress in different demographic variables

Variable	Stress					
	Low		Moderate		High	
	No	%	No	%	No	%
Age group (Years)						
25-30	7	15.55%	29	64.44%	9	20%
31-35	8	18.18%	30	68.18%	6	13.64%
36-40	7	15.55%	34	75.55%	4	8.88%
41-45	1	14.28%	5	71.42%	1	14.28%
>45	6	75.00%	1	12.5%	1	12.50%
Sex						
Male	19	23.46%	55	67.90%	7	8.61%
Female	10	14.70%	45	66.18%	13	19.12%
Marital status						
Unmarried	3	10.71%	19	67.85%	6	21.42%
Married	26	21.49%	81	66.94%	14	11.57%
Current job						
Gov. hospital/medical college	15	25.42%	39	66.10%	5	8.47%
Private hospital/medical college	9	17.30%	37	71.15%	6	11.53%
Post-graduation course	3	13.64%	15	68.18%	4	18.18%
General practitioner	1	25%	2	50%	1	25%
Temporary job	1	8.33%	7	58.33%	4	33.33%
Current working hour						
<36 hours/week	5	14.70%	24	70.58%	5	14.70%
36-48 hours/week	14	18.18%	54	70.13%	9	11.69%
>48 hours/week	10	26.31%	22	57.89%	6	15.79%
H/O mental disorder						
Yes	2	15.38%	8	61.54%	3	23.08%
No	27	19.85%	92	67.65%	17	12.5%
Co-morbidity						
Yes	8	22.22%	22	61.11%	6	16.66%
No	21	18.58%	78	69.03%	14	12.39%
Smoking						
Yes	4	14.81%	19	70.37%	4	14.81%
No	25	20.49%	81	66.39%	16	13.11%
Alcohol consumption						
Yes	1	11.11%	7	77.77%	1	11.11%
No	28	20%	92	65.71%	20	14.28%
Satisfied with monthly income						
Yes	19	30.16%	41	65.08%	3	4.76%
No	10	11.62%	59	68.60%	17	19.77%

Both the married and unmarried groups were under moderate stress mostly (66.94% % 67.85%).Doctors who had working hours<36 hours/week and 36-48 hours/week mostly showed moderate stress levels (70.58%, 70.13%), whereas 57.89% who worked for >48 hours/week had moderate 15.79% showed high stress. Those with a history of a mental disorder showed mainly moderate stress (61.54%) and 67.65% of doctors who had no history of mental illness had moderate stress. Doctors with co-morbidity showed mostly moderate stress (61.11%) the same as those who didn't have co-morbidity (69.03%). Moderate stress was found more commonly in smokers and nonsmoker doctors (70.37%, 66.39%). 77.77% of alcoholic doctors had moderate stress, whereas 65.71% of nonalcoholic doctors had the same. Both satisfied and dissatisfied doctors with their monthly income showed moderate stress levels (65.08%, 68.60%) but there was a high-stress level in dissatisfied doctors (19.77%) compared to satisfied (4.76%).

In table III, the result of the chi-square test is shown. The age group was significantly related to stress with a p-value of .0117, younger age groups were found tohave moderate stress, whereas the older group was on low stress. There were no significant correlations of stress level found with sex group (p value=.1057) marital status (p value=.2225), job (p value=.3961), working hour (p value=.6632), H/O mental illness (p value=.5552) or co-morbidity (p value=.6660), smoking (p value=.7922) and alcohol consumption (p value=.7449). But there was a significant correlation between stress level with satisfaction with the monthly income of a doctor, where p value=.0018. Doctors who were dissatisfied with their monthly earnings were more on stress.

Table III Chi-square test result between stress level and different variables

Variable		Stress		p-value
Age	low	moderate	high	
25-30 years	7 (8.76) [0.35]	29 (29.90) [0.03]	9 (6.34) [1.11]	.0117
31-35 years	8 (8.56) [0.04]	30 (29.23) [0.02]	6 (6.20) [0.01]	
36-40 years	7 (8.76) [0.35]	34 (29.90) [0.56]	4 (6.34) [0.87]	
41-45 years	1 (1.36) [0.10]	5 (4.65) [0.03]	1 (0.99) [0.00]	
>45 years	6 (1.56) [12.68]	1 (5.32) [3.50]	1 (1.13) [0.01]	
Sex				
Male	19 (15.77) [0.66]	55 (54.36) [0.01]	7 (10.87) [1.38]	.1057
Female	10 (13.23) [0.79]	45 (45.64) [0.01]	13 (9.13) [1.64]	
Marital status				
Unmarried	3 (5.45) [1.10]	19 (18.79) [0.00]	6 (3.76) [1.34]	.2225
Married	26 (23.55) [0.25]	81 (81.21) [0.00]	14 (16.24) [0.31]	
Current job				
Gov. doctors	15 (11.48) [1.08]	39 (39.60) [0.01]	5 (7.92) [1.08]	.3961
Private doctors	9 (10.12) [0.12]	37 (34.90) [0.13]	6 (6.98) [0.14]	
Postgraduate students	3 (4.28) [0.38]	15 (14.77) [0.00]	4 (2.95) [0.37]	

General practitioner	1 (0.78) [0.06]	2 (2.68) [0.17]	1 (0.54) [0.40]	
Temporary job	1 (2.34) [0.76]	7 (8.05) [0.14]	4 (1.61) [3.54]	
Working hours				
<36 hours	5 (6.62) [0.40]	24 (22.82) [0.06]	5 (4.56) [0.04]	
36-48 hours	14 (14.99) [0.06]	54 (51.68) [0.10]	9 (10.34) [0.17]	.6632
>48 hours	10 (7.40) [0.92]	22 (25.50) [0.48]	6 (5.10) [0.16]	
H/O mental disorder				
Yes	2 (2.53) [0.11]	8 (8.72) [0.06]	3 (1.74) [0.90]	.5552
No	27 (26.47) [0.01]	92 (91.28) [0.01]	17 (18.26) [0.09]	
Co-morbidity				
Present	8 (7.01) [0.14]	22 (24.16) [0.19]	6 (4.83) [0.28]	.6660
Absent	21 (21.99) [0.04]	78 (75.84) [0.06]	14 (15.17) [0.09]	
Smoking				
Yes	4 (5.26) [0.30]	19 (18.12) [0.04]	4 (3.62) [0.04]	.7922
No	25 (23.74) [0.07]	81 (81.88) [0.01]	16 (16.38) [0.01]	
Alcohol consumption				
Yes	1 (1.75) [0.32]	7 (5.98) [0.17]	1 (1.27) [0.06]	.7449
No	28 (27.25) [0.02]	92 (93.02) [0.01]	20 (19.73) [0.00]	
Satisfaction with monthly income				
Satisfied	19 (12.26) [3.70]	41 (42.28) [0.04]	3 (8.46) [3.52]	.0018*
Dissatisfied	10 (16.74) [2.71]	59 (57.72) [0.03]	17 (11.54) [2.58]	

DISCUSSION

Among 149 participants, males (54%) were more than females (46%), similar to the study of West Bengal.[8] But the similar research of Sidhu TK et al had more female participants (54.7%).[3] The present study's most common age group was 36-40 years. However, in another same type of study, the common age group was 25-35 years.[9 10] In our study, stress levels were assessed using the PSS-10 scale. The majority (67.11%) of the participants had moderate stress levels. A similar result was found in Sidhuet al study.[3] But a study among resident doctors of Mumbai showed the stress of only 37.3%.[11] Significant statistical stress was seen in 36-40 years age group of doctors p= .0117, which was consistent with Sidhu et al. But a study where stress levels of doctors were compared with nurses significant lower stress levels as compared to the age group of 31–40 years conducted by Sathiya et al.[12] Male (67.9%) and female (66.18%) doctors showed slightly different moderate stress levels which were statistically not significant p=.1057 which was not consistent with the study of Chatterjee et al Sidhu TK who found female were more stressed than males,they had more female participantsthat might be the explanation of it.[10,3] Our study found correlations of marital status, type of jobs, working hours, history of mental disorder, and co-morbidity were all statistically insignificant, the same as those conducted in South Africa.[13] But in the study of Chatterjee et al., unmarried doctors were more under stress.[10] A study in Jordan showed that general practitioners had more stress than others, and an analysis in Mumbai identified heavy workload with long working hours as a vital factor of stress.[14 11] We found no statistically significant correlation between smoking (p=.7922) and alcohol consumption (p=.7449) with stress, whereas Logra et al found a relation between stress with smoking and alcohol consumption.[15] In the present study, stress was statistically significant between the doctors satisfied with monthly income and dissatisfied with monthly income. 58% of doctors were dissatisfied with a monthly incomep-value was .0018. A study conducted in BIRDEM also showed that low monthly income significantly affected doctors' mental conditions, although this study comprised only postgraduate trainee.[16] Another study in Southwest Ethiopia noted that sex, age and monthly salary were essential factors for stress in doctors.[17]

LIMITATIONS

There were some limitations to the study. The sample size was not that large. It was an online study, so only doctors who had access to smartphones, laptops or computers participated. Convenient sampling was done, so there might be sampling bias.

CONCLUSION

It can be said that young and dissatisfied doctors with income are more liable to perceive stress.The mental health of a doctor is as important as the physical. It should be addressed appropriately, and doctors who are under stress need proper counseling and medication if necessary to alleviate their stress.

RECOMMENDATION

Further study with large sample size has recommended.

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AUTHORS CONTRIBUTION

JD-Conception, design, critical revision and final approval of the draft.

SC-Design, acquisition of data, manuscript writing and final approval of the draft.

SDS-Data collection, interpritation of data, drafting and final approval of the draft.

DD-Data analysis, critical revision and final approval of the draft.

DISCLOSURE

All the authors declared no competing interest.

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Original Article

Marine City Medical College Journal

Diagnostic Utility of Fine Needle Aspiration Cytology and Cell Block in Evaluation of Palpable Thyroid Swellings

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ABSTRACT

Background: Fine Needle Aspirations Cytology (FNAC) of the thyroid is practiced worldwide for thyroid nodule diagnosis. Cell Block (CB) prepared from residual tissue fluid and FNAC can be useful for establishing a more definite cytopathological diagnosis. The aim of this study is to establish increase the acceptance of CB and FNAC on thyroid swelling diagnosis in single setting by taking the histological findings as the gold standard.

Materials and methods: This cross sectional comparative study carried out in the Department of Pathology, Chittagong Medical College, Chattogram, Bangladesh over a period of one year from 1st July 2016 to 30th June 2017 on 146 consecutive cases who fulfilling the criteria of this study. FNAC and CB were performed for each case. Association of both test with histopathology were assessed by Chi-square test and comparison also seen by Z test.

Results: The mean age of the patients was 36.83± 13.43 and female was predominance (84.25%). In FNAC and CB accuracy were 96.43% & 96.36% respectively. There is no significant difference between FNAC and CB in diagnosis of thyroid swellings.

Conclusion: The combined effort of these two procedures have beneficial effect in diagnosis of palpable thyroid swellings in single setting. FNAC and CB can fulfil the preoperative proper diagnosis the thyroid swelling and it can be easily performed in many centers even in peripheral areas of Bangladesh.

Key words: Cell block; FNAC; Histopathology; Thyroid swelling.

INTRODUCTION

Neck swelling is a common clinical presentation all over the world and thyroid lesions are more common in many countries. The prevalence of thyroid swelling ranges from 4% to 10% in the general adult population and from 0.2% to 1.2% in children.[1] Thyroid enlargement or goiter is a common clinical problem of Bangladesh. According to Bangladesh country health system profile WHO, 2004, total visible goiter rate is 8.8%.[2] A multitude of noninvasive and invasive diagnostic tests like ultrasound, thyroid scan and FNAC is available to the clinician for the evaluation of thyroid swellings.[3] FNAC of thyroid gland is now firmly established as a first line diagnostic test for evaluation of thyroid swelling and can be safely performed on an outpatient basis.[4] FNAC has few limitations to define malignant lesions and in order to overcome these problems, CB mimics the histopathological sections, thus help in sub classifying various neoplastic lesions.[5] CB technique combines the advantages of FNAC in being fast and safe method and providing with a precise diagnostic architecture similar to a histological diagnosis.[6] During the microscopic examination as well, CB technique poses less difficulty for observation as lesser dispersal of the cells occurs with this technique.[7] Special stains can be done on CB preparations for better diagnostic accuracy of thyroid nodules. Confirmation of malignant thyroid conditions, can be done by immunohistochemistry studies on CB.[8] CB has been increasingly used in addition to FNAC to improve diagnostic accuracy. In Bangladesh, CB is not a routine procedure in the diagnosis of thyroid lesion.

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FNAC and CB can be performed easily in a single setting which may fulfill the preoperative proper diagnosis the thyroid swelling and it can be easily performed in many centers even in peripheral areas of Bangladesh.

MATERIALS AND METHODS

This cross-sectional study was conducted among 146 patients with palpable thyroid swelling in Department of Pathology, Chittagong Medical College, Chattogram, during the period of one year from 1st July, 2016 to 30th June, 2017. All the patients, included in the study, were informed and explained about the nature of study. Informed written consent was taken from all the subjects after full explanation of nature, purpose and potential risks of all the procedures was taken out for the study. All patients were evaluated by FNAC followed by CB who has palpable thyroid swelling and given written informed consent for study and previously diagnosed, treated patient were not included in this study. The thyroid lesions were aspirated by 10 ml disposable syringe and after smear preparation fixed in 95% alcohol and for CB the residual material of the needle hub was pushed in 10 ml of 10% formalin in the test tube and centrifuged at 2500/rpm for 10 minutes. The formed cell button was allowed to fix in 10% formalin for overnight and processed as routine biopsy specimens. After processing and sectioning, slides were stained by Haematoxylin and Eosin (H&E) stain. CB section were interpreted and results recorded. Out of 146 patients histopathological diagnosis was available in 57 patients and rest of all patients were reassured and followed up. Data was analyzed by Microsoft Excel for data processing and statistics. Proportions were compared by using Chi square test. Sensitivity, specificity,diagnostic accuracy, positive and negative predictive values were calculated by using respective formulas. Kappa coefficient was used to find out the reliability and comparison in between test also seen by Z test. Statistical significance and confidence interval were set at $p<0.05$ and 95% level of all analysis.

RESULTS

The mean age of was 36.83± 13.43 in the patients age groups 10 to 70 years. Out of 146 patients most of the patients were female 123 (84.25%) and male to female ratio was 1:5. Most of the patients was in the age range 31-40 years (32.19%) and came from rural area which were 80 (54.79%). Frequent patients came with the complaints of single nodular lesion which was 120 in number, 117(80.14%) have negative family history and only 5(3.42%) have positive radiation (X-ray, CT scan, Thyroid scan) exposure history. Most of the patients were euthyroid state 117(80.14%) and 129 (88.36%) had no history of taking drug for thyroid disease. Regarding size of the lesion most were up to 4 cm in diameter (52.05%), 99.32% lesions were mobile and 86.99% lesions were firm in consistency. On FNAC findings, benign follicular nodule consistent with nodular goiter was found in 125 cases followed by benign follicular lesion consistent with thyroiditis was found in 13 cases. Female was predominant in both types of lesions.On CB findings, nodular goiter (Fig. 1) was found in 108 cases followed by colloid goiter and thyroiditis (Fig. 2) were found in 14 cases in each. Female was predominant in all types of lesions.

Table I Diagnosis by histopathology of thyroid specimen (n=57)

	Diagnosis	Male n (%)	Female n (%)	Total n (%)
Benign	Multinodular goiter	05(8.77)	37(64.91)	42(73.68)
	Lymphocytic thyroiditis	00(00)	04(7.02)	04(7.02)
	Hashimoto thyroiditis	00(00)	03(5.26)	03(5.26)
	Follicular adenoma	00(00)	01(1.75)	01(1.75)
Malignant	Papillary carcinoma	00(00)	05(8.77)	05(8.77)
	Follicular carcinoma	01(1.75)	00(00)	01(1.75)
	Anaplastic carcinoma	01(1.75)	00(00)	01(1.75)

Table II Association between FNAC and Histopathology (With χ^2 test)

FNAC	Histopathology			Kappa coefficient	χ^2 test significance
	Benign (n)	Malignant (n)	Total (n)		
Benign	50	2	52	0.78	χ^2= 35.70835
Malignant	0	4	4		p= <0.001
Non-diagnostic	0	1	1		Highly
Total	50	7	57		significant

Table III Association between cell block and Histopathology (With χ^2 test)

Cell block	Histopathology			Kappa coefficient	χ^2 test significance
	Benign (n)	Malignant (n)	Total (n)		
Benign	50	2	52	0.78	χ^2= 39.14835
Malignant	0	3	3		p= <0.001
Non-diagnostic	0	2	2		Highly
Total	50	7	57		significant

Table IV Comparison in between FNAC and cell block of thyroid lesion biopsy available in 57 cases

Findings	FNAC diagnosis n (%)	CB diagnosis n (%)	Histological diagnosis n (%)	Z- test value	p value
Nodular goiter	48(84.21)	41(71.93)	41(71.93)		
Colloid goiter	00(00)	05(8.77)	01(1.75)		
Thyroiditis	04(7.02)	06(10.53)	07(12.28)		
Follicular adenoma	00(00)	00(00)	01(1.75)		
Papillary carcinoma	03(5.26)	03(5.26)	05(8.77)	1.38	0.0735
Follicular carcinoma	01(1.75)	00(00)	01(1.75)		
Anaplastic carcinoma	00(00)	00(00)	01(1.75)		
Non-diagnostic	01(1.75)	02(3.51)	00(00)		

In FNAC and CB χ^2 value are respectively 35.71 and 39.15 along with $p<0.001$ represent both were highly significant. Kappa coefficient interpretation is 0.78 which showed good agreement (Table II, Table III). In validity testsensitivity of both FNAC and CB were 66.67% and 60% respectively and specificity 100% in both. Diagnostic accuracy of FNAC and CB were 96.43% and 96.36% respectively. Comparison in between FNAC and CB showed test statistic (1.38) is less than critical value (1.96) (Table IV). So, $p>0.05$ and there is no difference between FNAC and CB in diagnosis of thyroid swelling and standard error of FNAC and CB is 7.23.

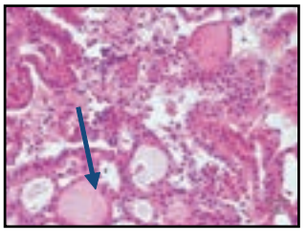

Figure 1 Nodular Goitre (Arrow mark showed benign follicle) Cell Block (H&E stain) 100X

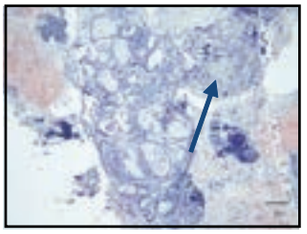

Figure 2 Lymphocytic thyroiditis (Arrow mark showed lymphocytes iniltration) Cell Block (H&E stain) 400X

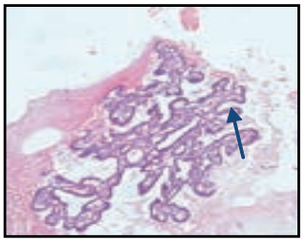

Figure 3 Papilary carcinoma (Arrow mark showed Papillary pattern) Cell Block (H&E stain) 400X

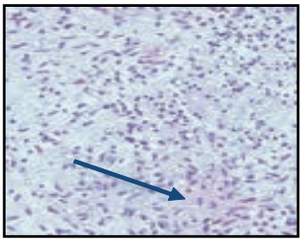

Figure 4 Granulomatous thyroiditis (Arrow mark showed epithelioid cells) Cell Block (H&E stain) 100X

DISCUSSION

Thyroid nodule represent a very common clinical problem and the differential diagnosis includes thyroid cancer. Thyroid enlargement or goiter is a common problem of Bangladesh. CB preparation of FNA specimens has been shown to be a valuable additional technique to direct smear and has been increasingly used in addition to FNA to improve diagnostic accuracy. The main advantages of the CB technique are preservation of tissue architecture and obtaining multiple sections for special stains and immunohistochemistry.[9] In this study, maximum number of cases in 31-40 years age group 47(32.19%) cases. Shetty et al and Borgohain et al showed maximum number of cases of thyroid lesion was in 21-40 years.[10,1] Regarding analysis of nature of lesion high frequency of malignancy was found in the age group 21-40 years of age group. Similar observations were reported by Borgohain et al and others study.[1,4,11] However, Qureshi et al observed maximum number of cases between age group 41 to 50 years.[12] In the present study, maximum number of cases 117(80.14%) had no positive family history which is similar with the observation of Ahmed where 88(97.78%) cases had negative family history of thyroid swelling.[13] Among 146 cases unsatisfactory smears were obtained in 5 cases initially and 1 case showed necrotic material were in this study. Repeat FNAC was done in all unsatisfactory smears for obtaining adequate materials, in only one case it was not possible due to operation already done due to clinically suspected malignancy. For this reason there was 1 unsatisfactory smear in this study. FNAC on thyroid swelling were classified according to the Bethesda system. On the histopathological examination, among 7 malignant cases 4 were diagnosed by FNAC as malignant. Two cases were falsely diagnosed as benign by FNAC and 1 case was malignant but undiagnosed by FNAC due to necrotic material. Among CB of all cases, 136(93.15%) cases were found benign, 4(2.74%) cases were malignant and 6(4.11%) cases were non-diagnostic due to inadequate material. On the histologic examination, among 7 malignant cases, 3 cases were correctly diagnosed by CB as malignant and 2 cases were falsely diagnosed benign along with 2 cases were undiagnosed by CB due to inadequate material. Both false negative were diagnosed as nodular goiter in both FNAC and CB. The false negativity was probably due to missing the nuclear features or cystic or degenerative changes in papillary carcinoma or the needle missing the target site

of the lesions. The statistical evaluation of this study was based on histologically confirmed 57 cases. In the present study FNAC was diagnostically accurate in 96.43% cases where true positive were 4 cases, true negative were 50 cases, no false positive case and false negative were 2 cases. CB was diagnostically accurate among 96.36% cases where true positive 3 cases, true negative 50 cases, no false positive case and false negative were 2 cases. FNAC has been used as a first test for distinguishing benign and malignant thyroid lesion. This test has been successful in detecting early malignancy and selecting patient for surgical treatment but is not entirely reliable because of false positive and false negative diagnosis. So in this study, both FNAC and CB were taken as a diagnostic test for thyroid lesions. Diagnostic accuracy and sensitivityof FNAC respectively 96.43% and 66.67% compared with other studies showed almost similar with Santosh et al and Qureishi et al.[3,12] However, Hirachand et al. and others studyshowed more sensitivity in comparison to present study due to large sample size.[1,14-16] Comparison of CB in this study with previous other studies showed diagnostic accuracy almost similar with Rajib et al. and others[2,5,13,16]. Ahmed et al and Cristo et al studies had no case of false negative and all unsatisfactory cases, indeterminate cases, follicular lesions cases, papillary thyroid microcarcinoma cases were excluded from Cristo et al.study and for that sensitivity of this study not similar with other studies.[13,16] The present study of CB showed that sensitivity and specificity were same as FNAC. Diagnostic accuracy more or less similar with other observations. The results of comparative study of FNAC and CB with histopathology were statistic significant and showed no difference in both diagnostic test in thyroid swelling diagnosis. All the findings of the present study were not always consistent with the findings of the other investigations. This study was done in a small sample, the study period was short. But many findings of the present study were more or less similar to other investigators. It was noted that there were wide disparity of findings among the observations by different authors. Probably this might be the reason behind inconsistent findings with others. In spite of these reasons the present study showed more or less acceptable findings with consideration of the observations by others but no study showed that those two diagnostic tests separately was suitable for thyroid nodule on the ground of missing and over diagnosis of cancer. It had been observed that there was possibility of missing diagnosis of cancer by FNAC also in CB. It mostly occurred in the diagnosis of papillary carcinoma in multinodular goiter where false negative result were found in both FNAC and CB. Despite this there was an inter-observer variation in diagnosis among different pathologists. To minimizing the small fault of this technique a second diagnostic technique should be applied. For this purpose USG guided FNAC may be helpful for aspiration from the lesion site properly. The CB technique has added advantage that multiple sections of the same material can be obtained for special stains and immunohistochemistry. Apart from these, morphological details can also be obtained with CB method, which include preservation of the architectural pattern like cell ball and papillae and three dimensional clusters, excellent nuclear and cytoplasmic details, and individual cell characteristics. On the other hand, fragments of tissue can easily be interpreted in a biopsy-like fashion. CB are not routinely prepared in addition to the smears. The tissue architecture can be better appreciated in the CB and additional CB analysis can decrease the number of needle passes by increasing diagnostic accuracy.

LIMITATION

Cross sectional study, small sample size and short duration of period.

CONCLUSION

In this study it was found that, both FNAC and CB are reliable and less invasive procedure to diagnose thyroid nodule either benign or malignant along with a good guide to decide for further operative procedure and can be easily performed in many centers even in peripheral areas of Bangladesh.

RECOMMENDATION

Both FNAC and cell block are acceptable method for diagnosis of thyroid nodule. Pre-operative differentiating benign from malignant thyroid lesion cell block can be used in a single setting during FNAC.

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AUTHOR'S CONTRIBUTION

TK-Concept, design, data collection, data analysis, manuscript writing and final approval of the draft.
RA-Acquisition of data, critical revision and final approval of the draft.

SK-Acquisition of data, critical revision and final approval of the draft.
MB-Acquisition of data, critical revision and final approval of the draft.
RM-Acquisition of data, critical revision and final approval of the draft.
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DISCLOSURE

All the authors declared no conflicts of interests.

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Original Article

Marine City Medical College Journal

Complications Following Thyroid Surgery

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ABSTRACT

Background: Different types of complications may occur following Thyroid surgery. The purpose of the study was to find out the incidence and types of complications after thyroidectomy and to analyse the factors related to the complications of thyroid surgery.

Materials and methods: This prospective study was carried out at Marine City Medical College an Private Hospital from July 2019 to June 2020. Fifty patients were selected for the study who were treated by thyroidectomy. The mean patient's age at the time of surgery was 40.9±9. 1 years ranged from 10 to 60 years. Data were collected in a prescribed data collection sheet. Then all data were compiled and analysed.

Result: 14% of the patients had complications. Out of them 2% had transient hypoparathyroidism, 4% had haemorrhage, 2% had temporary Recurrent Laryngeal Nerve (RLN) palsy and 2% had permanent recurrent laryngeal nerve palsy, 2% had Superior Recurrent Nerve (SRN) palsy & 2% had wound infection.

Conclusion: Surgery of thyroid gland can be performed safely in the majority of patients. Hyperthyroidism and Goitre size are the two independent risk factors for the development of complications.

KEY WORDS

Thyroidectomy; Recurrent laryngeal nerve palsy; Hypoparathyroidism; Hypocalcemia.

INTRODUCTION

Thyroid surgeries are the most common endocrine surgeries performed now a day. In spite of improved techniques, every thyroid surgeon has come across complications associated with this surgery. This study aims to understand various complications after thyroid surgeries and the factors responsible for complications and discuss management techniques for those complications in brief. Abnormalities of the thyroid gland are extremely common affecting approximately 11% of the general population.[1] Surgery for thyroid gland abnormalities is quite common.[2] Thyroidectomy is one of the commonest operations for the Otolaryngology and Head-Neck Surgeons, General Surgeon and Endocrine Surgeon. Following thyroidectomy complications may develop, these are immediate and late complications, such as haemorrhage, dyspnoea, seroma, haematoma, recurrent laryngeal nerve paralysis, thyroid crisis, wound infection and hypoparathyroidism. The complication which is most feared is trauma to the recurrent laryngeal nerve estimated to occur in between 1 and 10% of operations.[3-4] The nerve may be out stretched or burnt, usually as a result of failure to recognize or dissect it properly. In unilateral paralysis of the RLN results in immobile vocal cord in the paramedian position which causes weak, cracked and breathy voice. Bilateral paralysis leads to severe airway obstruction necessitating an urgent tracheostomy in the majority of patients. The nerve is more prone to be injured on the right side for it's anatomical variability. The external laryngeal nerve is traumatized more often than one supposes. Its close relationship to the superior vascular pedicle and an occasionally aberrant course predispose it to damage.[6] Diathermy of the small vein which passed from the superior thyroid vein to the lateral part of cricothyroid muscle is a further cause of damage to this nerve. Therefore it is suggested to clamp the upper pole of Thyroid gland after proper identification of superior laryngeal nerve or at least close to the gland in case of nonidentification of nerve. Hypocalcaemia

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which is uncommon after thyroidectomy may be the result of rough handling of the posterior aspect of the thyroid lobes or interruption of the terminal branches of the main divisions of the inferior thyroid artery. Hypocalcaemia is very common in total thyroidectomy.

MATERIALS AND METHODS

This prospective study was carried out at Marine City Medical College and Private Hospital July 2019 to June 2020. Fifty patients were selected for the study who were treated by thyroidectomy. The mean patient age at the time of surgery was 40.9±9. 1 years ranged from 10 to 60 years. Data were collected in a prescribed data collection sheet. The data of each patients included age, sex, symptoms, signs, provisional diagnosis, preoperative investigations such as T3, T4, TSH, FNAC, ultrasonogram of thyroid gland, Thyroid scan, Cytological study, operative notes, histopathological examination and follow up. Then all data were compiled and analysed. Statistical analysis was done by using appropriate statistical test. Necessary permission has been taken from proper authorities before commenceing the study.

RESULTS

Table I Age distribution of the study

Age in Year	Number of Patient	Percentage
10-20	04	8
21-30	14	28
31-40	16	32
41-50	09	18 51-60
07	14	

Table II Sex distribution of the study

Sex	Number of Patient	Percentage
Female	44	88
Male	06	12

Table III Types of Thyroid Disease in study population

Thyroid pathology	Number of patient	Percentage
Solitary nodular goitre	28	56
Multi nodular goitre	12	24
Thyroiditis	2	4
Papillary carcinoma	3	6
Medullary carcinoma	1	2
Follicular Neoplasm	4	8

Table IV Types of Thyroid surgery among study group

Disease	*HT	**ST	***TT	#NT	##LT
Solitary Nodular Goitre	26				2
Multi Nodular Gotre		2	8	2	
Thyroiditis				2	
Papillary carcinoma				3	
Medullary carcinoma				1	
Follicular Lesion		2		2	

*HT-Hemithyroidectomy, **ST- Subtotal Thyroidectomy, ***TT-Total Thyroidectomy, #NT-Near Total Thyroidectomy, ##LT- Lobectomy.

Table V Postoperative complication following thyroid surgery

Complication	Number of patient	Percentage %
Haemorrhage/haematoma	2	4
Airway Obstruction	0	0
Temporary Recurrent Larygeal Nerve palsy	1	2
Permanent Recurrent Laryngeal Nerve Palsy	1	2
Superior Laryngeal Nerve Palsy	1	2
Hypoparathyroidism	1	2
Wound infection	1	2
Total	7	14

DISCUSSION

In this study the age of the patient at the time of surgery ranged from 10 to 60 years. We observed in our study the maximum incidence is in third and fourth decade. Doriarajan and Jatashree, mentioned in their study that the peak incidence is in third decade.[5] In this series, out of 50 cases, 44 patients (88%) were female and 12 patients (24%) were male, with a female to male ratio was 7.33: 1. There was a female preponderance in this series but it was higher than that of the study of Sinna & Ezzat.[6] The incidence of thyroid diseases were quite higher in female patient in all age group. Twenty eight patients in this study presented with solitary nodular goitre (56%) twelve patients with multinodular goitre (24%) two patients with Thyroiditis (04%), 04 patient were diagnosed cytologically as Follicular lesion (04%) and Four patients with thyroid carcinoma without metastasis. Out of Four patients of thyroid cancer 03 had papillary carcinoma (75%) and 01 (25%) had Medullary carcinoma. Papillary carcinoma is the commonest thyroid malignancy, constituting 50% of all

thyroid cancer with a male to female ratio is 1:36 . In this series, commonest thyroid disorder was solitary nodular goitre with an overall incidence of 56%. Hemithyroidectomy was performed in 26 patients and Lobectomy were done for 02 Patients. Subtotal thyroidectomy was carried out in 02 patients of multinodular goitre. Total thyroidectomy was done in 08 cases of thyroid cancer and near total thyroidectomy was done in 02 case of multinodular goitre. Total thyroidectomy were carried out in 02 cases of Thyroiditis. For carcinoma thyroid cases total Thyroidectomy with Selective central neck dissection was carried out as there were no evidence of metastasis. For Follicular lesions hemithyroidectomy was done in 02 cases and total thyroidectomy was done in 02 cases. Out of 50 cases, 07 cases (14%) developed post operative complications. Of these, 02 patients developed post operative haematoma due to oozing from remaining thyroid tissue and wound surface which was managed by cauterization and ligation after exploration of wound. During operation, substantial blood vessels in the operative field should be tied with fine silk ligature, whereas small vessels can be managed with the bipolar diathermy.[7] Khaky et al, in his study showed that the overall complication rate for combined surgeries was 14.2% with Recurrent Laryngeal Nerve (RLN) injury more common than hypoparathyroidism.[8] On the contrary Delbridge et al in a series of 3089 thyroidectomy patients reported 0.5% Permanent RLN injury, 0.4% hypoparathyroidism and 0.9% definitive complication.[9] In this series 02 patients had unilateral recurrent laryngeal nerve paralysis. Among 02 patients, 01 patient showed gradual improvement of voice in subsequent follow up and after 6 months his voice was almost normal by compensation of the opposite vocal cord. One other patient did not show significant improvement even after an average period of 6 months follow up. Transient paralysis may result from pressure on the nerve by oedema in which cases recovery can be anticipated. Iqbal et al found only one recurrent laryngeal nerve damage out of 111 cases of Thyroidectomy (0.9).[10] Lalida et al, found the incidence of recurrent laryngeal nerve paralysis among 361 patients was 6.09%.[11] on the contrary Kraimps JL et al 1.8% patient presented with vocal cord alternation with a normal voice following surgery.[12] Transient paralysis occurs in about 03% of nerve at risk and recovers in 3 weeks to 3 months[2]. The intra-operative nerve monitoring with the purpose of identification of the recurrent laryngeal nerve is a safe and reliable method. Lalida found that, the failure in identifying the nerve did not show significant correlation with incidence of permanent recurrent laryngeal nerve paralysis.[11] The incidence of hypoparathyroidism is as high as 20 percent when total thyroidectomy and neck dissection is performed and as low as 0.9 percent for subtotal thyroidectomy.[13] But in this series only one patient (2%) developed transient parathyroid insufficiency on 2nd post operative day which was improved later on. It is rarely the result of inadvertent removal of all parathyroid gland but more commonly due to disruption of their blood supply. Devascularization can be minimized by careful ligation of branches of inferior thyroid artery on the thyroid capsule distal to their supply of parathyroid glands i.e maintaining sub-capsular dissection. Parathyroid glands usually situated in the posterior border of the thyroid gland but Clark et al reasoned that parathyroid glands situated anterior to the thyroid gland are at highest risk of injury.[14] Injury to the gland during dissection is usually accompanied by a change in colour of the gland from tan to black purple. If the gland needs to removed during surgery it must be sliced and should be transplanted into sterno-mastoid muscle or the forearm.[14] The incidence of hypoparathyroidism is also directly related to the surgeons experience with thyroidectomy. The incidence of permanent hypoparathyroidism following total thyroidectomy ranges from 0.6 to 17% in reports Bhattacharyy N et al observed in their study, postoperative hypocalcaemia is the most common immediate surgical complication of total thyroidectomy.[14-16] Out of 50 patients, 01 patient developed wound infection which was managed by exploration, wound debridement and secondary stitch. There was no death in this series.

LIMITATIONS

The study has certain limitations like only two centres study, small sample size and short study period.

CONCLUSION

Surgery of thyroid gland can be performed safely in the majority of patients. Hyperthyroidism and Goitre size are the two independent risk factors for the development of complications.

RECOMMENDATION

Large samples size with multicentre study is to be recommended .

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AUTHORS CONTRIBUTIONS

S D- Concept, design, data collection, manuscript writing and final approval of the draft.
S H- Data analysis, interpretation of the data, critical review of the version and final approval of the draft.
T S- Critical revision of the version, manuscript writing and final approval of the draft.

DISCLOSURE

All the authors declared no competing interest.

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Original Article

Marine City Medical College Journal

Prevalence of Anemia in Children Aged Six Months to Sixty Months : A Hospital Based Study

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ABSTRACT

Background: Anemia is a major public health problem in Bangladesh, affects all age groups, but children aged 6 months to 60 months are the most vulnerable. Overall, 43.1% of children aged 6-60 months are anemic in Bangladesh. The study aims to analyze the prevalenceand associated factors of anemia among hospitalized children aged 6 months to 60 months in Bangladesh.

Materials and methods: It was a cross sectional study was conducted on children 6 months to 60 months aged who were admitted to Marine City Medical College & Hospital due to some acute illness, were enrolled from January 2021 to December 2021. Children were classified as anemic when Hb level was <11gm/dl.

Results: A total of 418 patients were included and analyzed in this study. The result is described in two groups 1st is children with anemia (354) and 2nd is children without anemia (64). Among them 111(86.05%) were Iron Deficiency Anemia (IDA) 11(8.53%) were undetermined, 6(4.65%) were beta thalassaemia trait and one patient was beta thalassaemia major. Representing anemia type or haemoglobin levels, 234(55.98%) patients were from 7-9.9 g/dl (Moderately anemic), 119(28.47%) patients were from 10-10.9 g/dl (Mildly anemic), 63(15.07%) patients were from ≥11 g/dl (Normal) and only 2 patients were from <7 g/dl (Severely anemic).

Conclusion: A large fraction of hospitalized children under 60 months were found anemic. Raising awareness of the problem and providing health care education in this age group will be the key strategies to prevent and control this massive public health problem in Bangladesh.

KEY WORDS

IDA; Thalassaemia; Children (6 to 60 months).

INTRODUCTION

Anemia is one of the most serious and common nutritional deficiency disorders of public health concern in developing countries.[1] Anemia is a condition in which the reduction of red blood cell volumes or hemoglobin concentration is below the range. values occurring in a healthy person or 2 SD below the mean for the age and sex.[2,3] The most vulnerable population suffering from anemia is children <5 years, especially those in the first 2 years of life. Data from World Health Organization (WHO) showed that the anemia prevalence among children aged 6–59 months was 42.0% globally in 2019.[4] In Bangladesh 43.1% of children aged <5 years are anemic. Anemia diagnosis is classified as mild (Hb=10.0-10.9 g/dl), moderate (Hb=7.0-9.9 g/dl), severe (Hb<7.0g/dl) and normal (Hb 11.0 g/dl) Hb level concentration for children aged 6 to 59 months.[2] Despite anemia being preventable, it has caused a lot of morbidity and mortality in children under five years.[5] Anemia has adverse effects on children, especially in the first two years of life, such as behavioral delay, reduced cognitive development (Impaired learning and decreased school achievement), low immunity and growth failure, fatigue, difficulty with concentration, lethargy, increased mortality, and susceptibility to infection.[2,6,7] Common signs and symptoms of anemia in children are dizziness, fatigue,

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Volume 01 | Issue 01 | April 2022 | 37-41

general body weakness, loss of appetite, low body weight, paleness of the skin, eyes, and palms, under severe conditions-Heart failure, unconsciousness, and finally death.[8] However, the nutrition status of children has been significantly improved along with the rapid socio-economic development in Bangladesh and the extensive implementation of children's nutrition improvement projects in recent 10 years. Childhood anemia will adversely affect children's health, including physical development, and may cause irreversible damage to motion, cognitional and behavioral development.[9,10,11] The age from 0 to 5 years old is the critical period for children's growth and development, and it is also a high age group for anemia. According to the world health organization, IDA affects 43% of the world's children and according to UNICEF report.1.62 billion people suffer from anemia worldwide and most of them have IDA, especially in underdeveloped / developing countries, where 40-50% of children under age 5 are iron deficient.[12] This study was designed to determine the prevalence of anemia in 6 months to 60 months old hospitalized children who were admitted due to some acute illness.

MATERIALS AND METHODS

This was a cross sectional study conducted in Department of paediatrics, Marine City Medical College & Hospital Chattogram over a period of January-2021 to December 2021, Age six months to sixty months who were admitted during this period due to an acute illness like- acute respiratory tract infection, acute gastroenteritis, Enteric fever, UTI, Diarrhoeaetc and whose parent or guardian provided informed consent, were eligible for enrolment. Children who have been suffering from chronic illnesses such as JIA, hematological and renal disorders, severe malnutrition, persistent diarrhea and who received a blood transfusion before admission due to any cause were excluded from the study. At enrolment, a detailed case history was taken and a thorough physical examination was performed and recorded on standard case record forms. Laboratory investigation : Complete Blood Count (CBC), Peripheral Blood Film (PBF) was done in all cases on enrollment. A blood sample (2ml) was collected by venipuncture into an Ethylene Diaminete Traacetic Acid (EDTA) coated tube. The cell counter machine was used for values of Hemoglobin (Hb), erythrocyte count and mean corpuscular count. Peripheral blood film showed microcytic hypochromic RBC, further investigation for S ferritin (2ml blood collected in a plain test tube for the measurement of serum ferritin by immune enzymatic examination) routine and microscopic examination of stool, hemoglobin electrophoresis and CRP were performed. Iron deficiency anemia was defined when concentration of S ferritin was less than 12 Microgram/L. Serum iron and Total Iron Binding Capacity (TIBC) could not be performed due to financial reason. The data were entered and analyzed using SPSS version 12.0 for Windows (SPSS Inc, Chicago, IL, USA) software. The standard test for significance using Chi-square (Ç2) test and multivariate predictor analysis were performed. Ap-value of <0.05 was considered statistically significant.

RESULTS

This was a retrospective study, a total of 418 patients were included and analyzed in this study. The result is described in two groups 1st is children with anemia (354) and 2nd is children without anemia (64). Figure-1 shows the age distribution; from the 1st group, males were 218(61.58%) and females were 136(38.42%) and from the 2nd group, the male was 40(62.5%) and the female was 24(37.5%). The living area of the study is described in Table-I from the 1st group, 18(5.08%) patients were from the municipal area, 85(24.01%) patients were from the urban area, and from the 2nd group 251(70.90%) patients were from the rural area, 52(81.25%) patients were from the municipal area, 8(12.50%) patients were from the urban area, 4(6.25%) patients were from the rural area and the p-value was 0.438628 which is not-significant. Table II conveys the age distribution of the study, the height number of patients were from the 12-23 months' age range from both groups. The mean±SD was 70.8±48.48 of the 1st group and 12.8±10.42 of the 2nd group, 6-60 months is the minimum-maximum age range of the study and it's same for both two groups and the p-value was 0.00805 which is significant. Causes of microcytic hypochromic anemia are described in Table III, 111(86.05%) patients were from IDA, 11(8.53%) patients were from undetermined, 6(4.65%) patients were from beta thalassaemia trait and one patient were from beta thalassaemia major. Table IV is representing anemia type or haemoglobin levels, 234(55.98%) patients were from 7-9.9 g/dl (Moderately anemic) 119(28.47%) patients were from 10-10.9 g/dl (Mildly anemic), 63(15.07%) patients were from ≥11 g/dl (Normal) and only 2 patients were from <7 g/dl (Severely anemic).

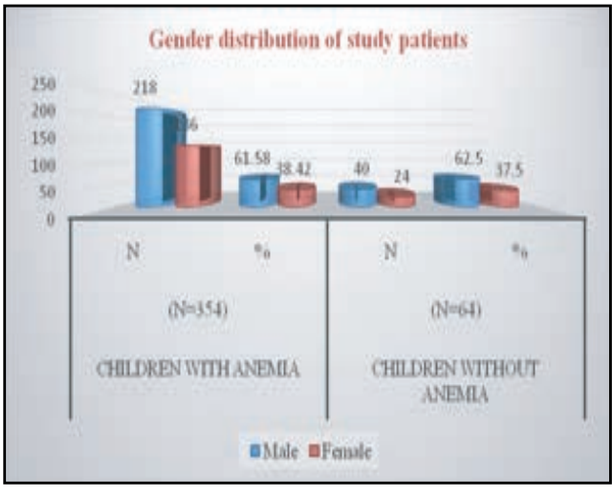

Figure I Gender distribution of study patients (n=418)

Table I Distribution of living area of study patients (n=418)

Living area	Children with anemia (n=354)		Children without anemia (n=64)		p-value
	n	%	n	%	
	Living area				
Municipal area	18	5.08	52	81.25	0.438
Urban area	85	24.01	8	12.50	
Rural area	251	70.90	4	6.25	

Table II Distribution of age according to anemia of study patients (n=418)

Age in month	Children with anemia (n=354)		Children without anemia (n=64)		p-value
	n	%	n	%	0.00805
6-11 months	102	28.81	16	25.00	
12-23 months	135	38.14	27	42.19	
24-35 months	67	18.93	16	25.00	
36-47 months	32	9.04	3	4.69	
48-60 months	18	5.08	2	3.13	
Mean±SD	70.8±48.48		12.8±10.42		
Range (Min-Max)	(6-60)		(6-60)		

Table III Causes of microcytic hypochromic anemiain study patients (n=129)

Causes of microcytic hypochromic anemia	Frequency	Percentage
IDA	111	86.05
Beta Thalassaemia Trait	6	4.65
Beta Thalassaemia Major	1	0.78
Undetermined	11	8.53

Table IV Anemia (Haemoglobinlevels) type of study patients (n=418)

Anemia (Hemoglobin value)	Frequency	Percentage (%)
<7 g/dl (Severely anemic)	2	0.48
7-9.9 g/dl (Moderately anemic)	234	55.98
10-10.9 g/dl (Mildly anemic)	119	28.47
≥11 g/dl (Normal)	63	15.07

DISCUSSION

The prevalence of anemia varies widely between the countries. Different surveys in the past have shown that anemia is a severe problem in Bangladesh among all ages, populations and geographic groups.[13-15] The variations in the prevalence of anemia in different studies could be due to heterogeneity of the studied population, dietary habits, different nutritional status and incidence of worm infestation in a defined geographical area. The prevalence of anemia, in this study, 354(84.68%) children had anemia, overall 68% of children aged 6-60 months had anemia. The prevalence of anemia in India was 74.35% for the 6-35 months age group, Nepal had 78% for the 6-59 months age group and in Kazakhstan, it was 73.7% for the 0-23 months age group.[16] The prevalence of anemia in preschool children (0-4 years) of WHO countries of Africa, south-east Asia and the eastern Mediterranean were 67.6%, 65.5% and 46.7% cases respectively.[17] The prevalence of anemia is much lower in developed countries such as in America 29.3% and Europe 21.7%.17 According to the WHO/UNICEF/UNN classification in this study, we found that 234(55.98%) children had moderate anemia, 119(28.47%) children had mild anemia and 2(0.48%) children had several anemia (Table IV). In a study done in Nigeria showed that 70.5% (n=400) children had varying degrees of anemia. Among the anemic cases, mild, moderate and severe anemia was 38.0%, 31.8% and 0.8% respectively. The most affected age group was 6-23 months (76.12%). In a study done in Bangladesh in 1994, the prevalence of anemia was 92% among the 6-11month age group and 85% among the 12-23 month age group. The most affected group was 6-23 months (87%).[15] In this study, the prevalence of anemia in males was higher 218(61.58%) than in females 136 (38.42%) and the 234(55.98%) children had moderate anemia 7-9.9 g/dl and only 2(0.48%) children had several anemia <7 g/dl. These findings are similar to a study in Bangladesh where boys (n=641) were more anemic than girls

(n=586).[18] Among 129 patients having microcytic hypochromic anemia, IDA, beta Thalassaemia trait, ß Thalassaemia major and the undetermined were 111(86.05%), 6(4.65%), 1(0.78%) cases respectively and 11(8.53%).

LIMITATIONS

This was a cross sectional, single centre, and small population study. All causes of anemia was not investigated due to unavailable logistic facility. Chronically ill children were also not included which might have undermined the values.

CONCLUSION

A large proportion of hospitalized children under 5 years were found anemic. Among all anemic children, IDA was high. This result emphasizes the importance of identifying the risk factors of anemia in this age group.

RECOMMENDATION

Further studies, to know the etiology of anemia and appropriate interventions including awareness among people about a diet rich in iron, folate and other micronutrients are needed.

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AUTHORS CONTRIBUTION

MSU-Conception, acquisition of data, manuscript writing & final approval of the draft.
BRM-Interpritation of data, critical revision, drafting & final approval of the draft.
LA-Data analysis, drafting & final approval.
BAS-Acquisition of data, critical revision & final approval of the draft.
MNAS-Interpritation data, manuscript writing & final approval of the draft.

DISCLOSURE

All the authors declared no competing interest.

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Name of Reviewers (April 2022)

Editorial Review

- **Professor Dr. Pradip Kumar Dutta**
  Head, Department of Nephrology
  Marine City Medical College, Chattogram.

Peer Review

- **Professor Dr. Asok Kumar Dutta**
  Head, Department of Medicine (Retired)
  Chittagong Medical College, Chattogram.

- **Professor Dr. Mahmood A Chowdhury Arzu**
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  Chattogram Maa-O-Shishu Hospital Medical College
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- **Professor Dr. Prabir Kumar Das**
  Head, Department of Cardiology (Retired)
  Chittagong Medical College, Chattogram.

- **Professor Dr. Md Hafizul Islam**
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  Chittagong Medical College, Chattogram.

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- **Professor Dr. Md Mahbubul Alam Chowdhury**
  Head, Department of Otolaryngology
  Institute of Applied Health & Sciences (IAHS)
  Chattogram.

- **Dr. Rajat Sanker Boy Biswas**
  Associate Professor & Head
  Department of Medicine
  Chattogram Maa-O-Shishu Hospital Medical College
  Chattogram.

MARINE CITY
MEDICAL COLLEGE

Marine City Medical College Journal (MCMCJ)

Information to Authors

Marine City Medical College (MCMC) started its historical and memorable journey in the year 2013. MCMC is one of the famous and reputed Medical College among the Private Medical Colleges in Bangladesh. It is situated in port city, Chattogram. The aim of the MCMC is to attain a standard level in Health & Medical education at home and abroad.

Marine City Medical College is affiliated under Chittagong Medical University & approved by the Ministry of Health & Family Welfare, Government of People's Republic of Bangladesh. A very good number of academicians, researchers and skill professionals are performing in this institute.

Marine City Medical College inaugurated to publish a double blinded, peer reviewed scientific journal from April 2022.

The "Marine City Medical College Journal (MCMCJ)" is a half yearly published eg. April & October accorded with a view to translation of current research into clinical practice. It is the official publication of the Marine City Medical College.

MCMCJ publishes article of authors from any part of the globe, but has a special interest in publishing research articles of authors from Bangladesh and of relevance to developing countries. It publishes Editorial, Original (Research) article, Special article, Review article, Short communication, Case report and Letters on new findings of Medical Science.

MCMCJ follows the recommendations made by International Committee of Medical Journal Editors (ICJME) (http://icmje.org/).

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Manuscript (Papers) are submitted to the Managing Editor or authorised persons or by Email at any time. Papers accepted for publication are subjected to peer review and editorial revision. Manuscript should be typed in English (Font size and style: 10, Times New Roman) on one side of white bond paper of A4 size with margins of at least 2.5 cm, using double space throughout. With full title (Title should be concise and informative) accompanied by a cover letter signed by Principal and Co-authors including name, academic degrees, designation, the departmental and institutional affiliation. Complete address, Cell number including Email address of Corresponding author should be mentioned. Not more than 6 (Six) authors will be accepted for all manuscripts.

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Abstract

A structured abstract should not be of more than 250 words. It should be a factual description of the study performed organized with the heading of Background (Includes aim or Objectives) Methods (Includes patient population, procedures and data analysis) Results and Conclusion. The abstract should contain the data to support the key findings or conclusions of the study and this should be self explanatory without references to the text. the first time an abbreviated term is used it should be spelled out in full form and follow with the abbreviation in parentheses for example:- CHD (Coronary Heart Disease). Please do not cite any references in the abstract.

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- Disclosure

Single digit numbers used in the text should be in words except datas and reference numbers. Maximum length of text may be with in 2000-2500 words (Excluding references). The total number of reference should not be less than 15 (Fifteen) for the original article.

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