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EDITORIAL

BREAKING DOWN THE WALLS OF OSTEOPOROSIS: A CALL TO ACTION

RUBINA YASMIN

Osteoporosis is a silent epidemic affecting millions worldwide, poses a significant public health challenge. It is a skeletal disorder characterized by decreased bone mass and micro architectural deterioration of bone tissue resulting in less bone tension and strength and increased risk of fragility fracture.A report suggests that 10 million Americans aged 50 or over have an active diagnosis of osteoporosis, with another 34 million in the "at-risk" category. Every year, 1.5 million Americans suffer from osteoporosis-related fractures which are predicted to triple in the USA by 2025 because of a lack of focus on bone health and prevention. Besides high-income countries, the high prevalence of osteoporosis and risk of osteoporosis is also reported for middle and low-income countries of Southeast Asia. However, early diagnosis and appropriate prevention methods and treatment significantly reduce the prevalence of osteoporosis, and fracture.

With an aging global population, the burden of osteoporosis-related fractures is expected to rise substantially. Fractures of the hip, vertebrae and distal forearm are considered as osteoporotic fractures with common epidemiologic characteristics with fracture incidences are higher in women compared to men. Important risk factors of osteoporosis are inadequate nutritional absorption, lack of physical activity, weight loss, cigarette smoking, alcohol consumption, air pollution, stress, older age, family history of osteoporosis, prolonged corticosteroid use, vitamin D deficiency and diabetes mellitus. The impact of osteoporosis-related fractures can lead to increase pain, disability, nursing home placement, total health care costs, and death.Evidence suggests that fifty percent of patients with osteoporotic fracture have failed to return to their pre-fracture functional ability level. Furthermore, it has a very high economic burden because of higher treatment costs, extended hospital stays, and the need for special care at home after discharge from the hospital.

One of the key challenges in tackling osteoporosis is its asymptomatic nature until a fracture occurs. This lack of early warning signs often results in delayed diagnosis and intervention, allowing the disease to progress unchecked. It's time to break the silence surrounding osteoporosis and raise awareness about the importance of bone health throughout the lifespan. To reduce the risk of fracture and economic burden in the health sector, it is crucial to assess bone health at an early age.The diagnosis of osteoporosis is primarily determined by measuring bone mineral density (BMD) using noninvasive dual-energy x-ray absorptiometry.

To stop the epidemic of osteoporosis paramount measures should be prevention of osteoporosis measuressuch as patient education, understanding the risk factors and adopting a bone-healthy lifestyle can significantly reduce the likelihood of developing osteoporosis.

First and foremost, regular physical activity is recommended in all age groups to maximize peak bone mass and maintain bone strength. Physical activity has been suggested as a non-pharmacologic intervention for increasing bone density in youth and preventing bone loss in the elderly. Both aerobic exercise and resistance training, the best forms of weight-bearing exercise, increase the rate of bone remodeling in postmenopausal women. However, resistance exercise training induces more effective favorable changes in BMD status than aerobic exercise

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training in postmenopausal women. A 10% increase in peak bone mass was predicted to delay the development of osteoporosis by 13 years and reduce the risk of fragility fractures after menopause by 50%. Adequate daily calcium and vitamin D is required to maximize bone mass and for the subsequent maintenance of bone health.Along with regular weight-bearing exercise, avoiding tobacco and excessive alcohol consumption, fall prevention strategies into patient care plans is essential for optimizing outcomes.

We have to play a crucial role in the early detection and management of osteoporosis. Incorporating bone density testing into routine healthcare assessments for at-risk populations can aid in early diagnosis and the implementation of preventive measures. Additionally, healthcare providers should prioritize educating patients about osteoporosis risk factors and the importance of adherence to prescribed treatments.

By integrating bone health education into public health initiatives, we can empower individuals to take proactive steps toward maintaining strong and resilient bones.

Institutional support is vital to create a comprehensive approach to osteoporosis prevention and management. Governments, healthcare organizations, and advocacy groups must work together to allocate resources for public awareness campaigns, educational programs, and research initiatives. By fostering a united front against osteoporosis, we can reduce the burden on healthcare systems and improve the quality of life for those affected.

Moreover, there is a need for increased research and development of innovative treatments for osteoporosis. While current medications exist to manage the condition, ongoing efforts to discover new therapies with fewer side effects and broader efficacy are essential.

Osteoporosis may be a silent threat, but its consequences are loud and clear. It's time for a collective effort to shatter the silence and build a foundation of awareness, prevention, and treatment. By prioritizing bone health education, early detection, and ongoing research, we can break down the walls of osteoporosis and pave the way for a healthier, more resilient future.

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REVIEW ARTICLE

EVOLUTION OF MANAGEMENT OF DIABETES MELLITUS

KHWAJA NAZIM UDDIN

Introduction:

Diabetes is an ancient disease and for centuries extreme diets and herbal remedies were used to treat diabetes symptoms. The discovery of insulin in 1921 transformed the landscape of diabetes treatment and was followed by the discovery of several new therapies which improved glycemia and increased patient life span.

In the 1990s, the DCCT and the UKPDS trials demonstrated that tight glucose control reduced the microvascular complications of diabetes, but had marginal effects on cardiovascular disease, the leading cause of death in patients with diabetes. In 2008, the FDA directed that all new diabetes medications demonstrate cardiovascular safety.

Developments in diabetes technology like continuous glucose monitoring systems, insulin pumps, telemedicine and precision medicine have advanced diabetes management.

Today type 2 diabetes is preventable and long-term remission of diabetes is possible.Progress continues in the field of islet transplantation, perhaps the ultimate frontier in diabetes management.

Epidemiology: According to the World Health Organization (WHO) approximately 537 million adults (ages 20–79 years) are living with diabetes today, and this number is predicted to rise to 643 million by 2030 and 783 million by 2045[1].

History:

The first description of a polyuric state resembling diabetes has been attributed to Hesy Ra, chief physician to the Egyptian Pharoah Djoser, nearly 5000 years ago[2]. The presence of sweetness in the urine was initially noted by the ancient Hindu physicians Charaka and Sushruta around 400–500 BC[2]. The term "diabetes" (from the Greek for siphon) has been attributed to Apollonius of Memphis in ancient Greece (around 250 BC).John Rollo, a Scottish military surgeon is said to have first used the word "mellitus" (from the Latin for honey) in 1797[2].

Treatment of diabetes in preinsulin era:

3000 BC to 1920:The treatments in ancient time were empirical and included Herbs,chemicals,Opium,meat diets and starvation "Keto"diet.[2] In the mid-1600s, Thomas Willis introduced carbohydrate-restriction and limited his patients to a diet of milk and barley water boiled with bread. In the 1700s, the "Meat Diet" was popularized by John Rollo.[2.] The French physician Apollinaire Bouchardat (1809–1886), considered the "Father of Diabetology," became the first to implement individualized therapy for patients, introducing exercise, and advocating daily urine testing "to keep track of the tolerance and to guard against a return of sugar without the patient's knowledge[3,]Around the end of the nineteenth century, Sir William Osler (1849–1919), the "Father of Modern American Medicine," recommended that diabetes patients consume a diet of 65% fat, 32% protein, and 3% carbohydrate, and abstain from "all fruits and garden stuff"[3,]At the dawn of the twentieth century, Frederick Allen of The Rockefeller Institute introduced a diet that involved fasting for up to 10 days to clear glycosuria, followed by a restricted-calorie diet that provided mainly fat and protein (especially eggs) with the smallest amount

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of carbohydrates (mostly vegetables) necessary to sustain life. This regimen essentially starved people with severe diabetes to control the disease. Elliot P. Joslin, the pioneer of diabetes care in the United States (US), embraced the Allen approach, but also used a treatment that began by withdrawing only fat and then protein after 2 days followed by a progressive lowering of carbohydrates in the diet to 10 g a day or until the patient's urine was free of sugar!.

Discovery of insulin and the era of Glucose
Lowering drugs:
20th century
Insulin: In 1921: Banting, Best, Macleod and Collin discovered insulin.In 1940s: Longer acting insulin introduced .Iincluded among these was NPH insulin (1946), still in use today,other one is Lente insulin

Oral agents:
In 1955, the first oral anti-diabetic medication,secretagogues the sulfonylurea (SU) carbutamide was introduced, followed by others in the same family including chlorpropamide, tolbutamide, glipizide, glyburide and glimiperide among others[5]. The first insulin sensitizer, the biguanide Metformin was introduced in Europe in 1957 and in the US in 1995. In the mid-1990s, several oral anti-diabetic agents were introduced including the alpha-glucosidase inhibitors (Acarbose, Miglitol and Voglibose), followed by the meglitinides (Nateglinide and Repaglinide)[5],, secretogogues ,structurally different from SUs and of shorter duration action. The late 1990s and early 2000s saw the introduction of the thiazolidinediones (TZDs), which are PPARᾱ agonists and potent insulin sensitizers[5].Rosiglitazone was withdrawn but Pioglitazone is still available, with proven benefits for stroke prevention and diabetes prevention

21st century:

With the turn of the twenty-first century, the range of anti-hyperglycemic options broadened to include the first human insulin analogs followed by several other short- and long-acting analogs, pramlintide (an injectable amylin analog) in 2005, and the dipeptidyl-peptidase inhibitors (DPP-4 inhibitors) which are oral agents in the incretin class of drugs in 2006. These medications (Sitagliptin Vildagliptin Saxagliptin Linagliptin, Alogliptin) inhibit DPP 4 activity, increase endogenous incretin levels, and thereby promote glucose-dependent increases in insulin and inhibit glucagon secretion. Other drugs launching in the late 2000s include colesevelam (a bile acid sequestrant which activates liver farnesoid receptors, lowers glucose by increasing incretin secretion and improving beta cell function) in 2008.Bromocriptine which activates

and reset hypothalamic dopamine receptors was introduced in 2009.

Drugs with (cardiovascular)CV benefit:
2008 FDA directate all diabetes drugs should demonstrate CV safety[9,8]Perhaps the most important classes of drugs to be introduced in the 2000s are the GLP-1 receptor agonists (GLP1-RA), the SGLT2-inhibitors (SGLT2i) and the dual GLP-1 receptor and GIP receptor agonists (GIP/GLP1-RA)[5]. The GLP1RA (Exenatide Liraglutide, Lixisenatide, Albiglutide, Dulaglutide and Semaglutide) directly act on the GLP-1 receptor to stimulate glucose-dependent insulin secretion and inhibit glucagon secretion. Their effects are far more potent than those of the DPP-4 inhibitors. In addition, they also reduce postprandial glucose excursions by slowing gastric motility and act centrally to increase satiety, leading to weight loss[5]. In 2022, the FDA approved the first combined GIP and GLP-1RA for the treatment of adults with type 2 diabetes (T2DM), with initial studies demonstrating superiority in both glycemic control and weight loss compared to GLP1-RA alone[7]. The SGLT2i drugs act through a novel mechanism to inhibit SGLT2 transporters in proximal renal tubules promoting glucosuria and lowering of blood glucose[5]. The robust cardio-renal benefits of these medications have transformed the landscape of diabetes treatment[8], and led to these agents being recommended for cardio-renal risk reduction in high risk patients with T2DM[9].

Antidiabetic drugs and their efficacy:
Insulin and the GLP-1RA and dual GLP-1RA/GIP-RA have *very high efficacy; TZDs, SUs and metformin high efficacy; SGLT2i intermediate to high efficacy; and DPP-*4i, AGI and colesevelam *intermediate efficacy[9]*

Cardiovascular Outcomes Trial (CVOT)s and Cardio-renal Protection:
In the 1990s, the DCCT and the UKPDS trials demonstrated the benefits of tight glucose control on the microvascular complications of diabetes such as retinopathy, nephropathy and neuropathy.· However, tight glucose control had marginal effects on macrovascular disease. FDA guidance in 2008, directing that any new diabetes therapy be evaluated for CV safety[6]. Following the FDA guidance, several large cardiovascular outcomes trials (CVOTs) were conducted and results with the GLP-1RA and SGLT2i have transformed the landscape of diabetes treatment[10]. In 2015, the EMPA-REG OUTCOME trial demonstrated that empagliflozin, compared to placebo, significantly reduced the incidence of major adverse cardio-vascular events (MACE) comprising non-fatal MI, stroke and CV death in patients with T2DM and

established CV disease[12]The first positive CV results with GLP-1RA were reported in the LEADER trial with liraglutide[13]and have been subsequently confirmed as a class effect with albiglutide (HARMONY study) and dulaglutide (REWIND study). In the CVOTs to-date, the GLP-1RA have consistently demonstrated reduction in atherosclerotic cardiovascular disease (ASCVD)[11] events in patients both with and without established ASCVD, however, their effect on renal disease is confined to improvements in albuminuria without preventing progression to end stage kidney disease (ESRD—dialysis/kidney transplant) ESRD[14]. Further, the GLP-1RA do not have beneficial effects on HF in diabetes (REF). In contrast, the SGLT2i have modest benefits on atherosclerotic MACE confined to patients with established ASCVD[14] but have robust benefits on reducing hospitalization for HF and progression of renal disease, regardless of existing ASCVD or a HF history. More importantly, unlike GLP-1RA, SGLT2i reduce hospitalization for HF and progression to ESRD in those with and without diabetes, as seen in the DAPA HF, DAPA CKD, CREDENCE and the EMPEROR PRESERVED/REDUCED studies.[12.] The above cardio-renal benefits have led to a major shift in international treatment guidelines. Both the American Diabetes Association (ADA) and the European Society for the Study of Diabetes (EASD) now recommend the use of SGLT2i and GLP-1RA as first-line treatment to reduce the risk of cardiorenal complications in individuals at high risk of CV disease, irrespective of metformin use and baseline/target glucose control[13]. The European Society of Cardiology (ESC) guidelines also recommend either a SGLT2i or a GLP-1RA as first-line treatment in people with T2DM at high CV risk, ahead of metformin[14]. However, it is important to note that in the CVOTs, most participants with diabetes were on at least one glucose-lowering medication (primarily metformin) at baseline[15].

Prevention of Diabetes mellitus:

1. Da Qing study :The first large study to demonstrate that T2DM can be prevented was the Da Qing study from China published in 1995[16]. The authors randomized 577 men and women with impaired glucose tolerance (IGT) to the active intervention (n=438) or control (n=138). At 6 years, the cumulative incidence of diabetes was 67.7% in the control group compared with 43.8% in the diet group, 41.1% in the exercise group, and 46.0% in the diet-plus-exercise group (P<0.05).

2. Finnish Diabetes Prevention study :The next large study which evaluated diet and lifestyle in diabetes prevention was the Finnish Diabetes Prevention study (2001) which randomized 522 subjects with IGT (172 men and 350 women; mean age, 55 years; mean BMI 31 kg/m2) to either the intervention or the control group[17]. The intervention group received individualized counseling aimed at reducing weight and dietary fat intake, and increasing fiber intake and physical activity. The cumulative incidence of diabetes after four years was 11% in the intervention group and 23% in the control group, with a relative risk reduction of 58% (p <0.001).

3. US Diabetes Prevention Program (DPP, 2002) also evaluated the role of metformin in diabetes prevention[17]. In this study, pre-diabetic individuals (68% women, mean age 51 years, mean BMI 34 kg/m2) were randomized to placebo, metformin (850 mg twice daily), or a lifestyle-modification program targeting a minimum 7% weight loss and 150 min of physical activity per week. After an average follow-up of 2.8 years, as compared to placebo, lifestyle intervention reduced the incidence by 58% compared to only 31% with metformin.

4. Indian Diabetes Prevention-1 (IDDP -1) study, in which 531 subjects with IGT (421 men, 110 women, mean age 45.9 years, BMI 25.8 kg/m2) were randomized into four groups[17,18.] Group 1 was the control, Group 2 was given advice on lifestyle modification (LSM), Group 3 was treated with metformin (MET) and Group 4 was given LSM plus MET. After 3 years, the cumulative incidences of diabetes were 55.0%, 39.3%, 40.5% and 39.5% in Groups 1–4, respectively. Thus, in this study, although both lifestyle and metformin significantly reduced the incidence of diabetes in Asian Indians with IGT, surprisingly, there was no added benefit from combining them.

The Concept of Diabetes Remission:

It is well known that intensive diet and lifestyle measures can lead to significant weight loss which may be sustained for long periods of time and lead to a regression from overt diabetes to normal glucose regulation in individuals with T2DM[19].

Remission should be defined as a return of HbA1c to < 6.5% (<48 mmol/mol) that occurs spontaneously or following an intervention and that persists for at least 3 months in the absence of usual glucose-lowering pharmacotherapy

Intensive Weight Management & Diabetes Remission
1. *Intensive weight management in routine primary care*: The DiRECT study in the UK assessed whether intensive weight management within routine primary

care increased remission of T2DM in patients diagnosed within the past six years and not on insulin[20]. In an open-label, cluster-randomized trial, 306 individuals (20–65 years) were randomized to an intervention group (n = 157) that underwent total diet replacement (825–853 kcal/day formula diet for 3–5 months), progressive food reintroduction (2–8 weeks), and structured support for long-term weight loss maintenance, or a control group (n =149). Mean bodyweight by 10.0 kg versus 1.0 kg and diabetes remission was achieved in 46% vs 4% of participants in the intervention versus control group, respectively.

2. *Bariatric Surgery and Diabetes Remission*: compared to intensive diet/lifestyle, more robust rates of diabetes remission are achieved after bariatric surgery, with Roux-en-Y gastric bypass (RYGB) being associated with greater remission rates than sleeve gastrectomy. In a large retrospective, observational study of 5928 patients with T2DM at the time of surgery, over an average follow-up of nearly 6 years, 71% of patients experienced remission of T2DM (mean time to remission 1.0 year), with weight loss after bariatric surgery being strongly associated with initial T2DM remission up to a threshold of 20% total weight loss.

3. *Pharmacologic Treatment and Diabetes Remission*:. In the SURPASS-1 trial 705 individuals with short duration T2DM (mean 4.7 years, mean HbA1c~8.0%) were randomized to placebo or escalating doses of tirzepatide a novel "twincretin" with glucagon-like peptide 1(GLP-1) and glucose-dependent insulinotropic polypeptide (GIP)receptor agonist activity, recently approved by the FDA for the treatment of type 2 diabetes[21]. After 40 weeks of treatment, the mean HbA1c decreased from baseline by ~
 2.0% in the tirzepatide group, along with weight loss of 7 to 9.5 kg from a baseline of 5.5 kg. Notably, more participants on tirzepatide than on placebo met HbA1c targets of <7·0% (~ 90% vs 20%) and 6·5% or less (81–86% vs 10%) and 31–52% of patients on tirzepatide versus 1% on placebo reached an HbA1c of less than 5·7%, which is in the normal range.

Technology and Diabetes Management

1.*Advances in Glucose Monitoring and Insulin Delivery*
CGM and Insulin pump: introduction of sophisticated continuous glucose monitoring systems (CGMS) which not only provide near-real-time glucose readings, but also communicate with state-of-the-art insulin pumps which correlate insulin delivery with glucose trends.

***Insulin pump*:** Hybrid closed-loop systems partially automate insulin dosing, requiring only manual mealtime boluses and occasional correction boluses.

This has led to significant improvements in glucose control and reductions in hypoglycemia.

TIR(Time in range):Is a new diabetic metric that express the percentage of time of a person wit diabetes spend within their target of glycemic range. In registry and case–control longitudinal data, pump use has been associated with fewer CV events and reduction of CV disease and all-cause mortality.

***Artificial pancreas*:** Studies on bi-hormonal (insulin and glucagon) systems are also ongoing.

 Insulin pumps and CGMS are expensive and primarily used in patients with type 1 diabetes mellitus (T1DM). The goal in this field is to develop long term, implantable glucose sensors and fully automated insulin delivery systems which use artificial intelligence to seamlessly maintain glucose in the normal range without the need for human intervention.

The Advent of Telemedicine:
Telemedicine can be useful for the management of diabetes mellitus and can also be cost-effective[23]. However, it must be remembered that although telemedicine can be used to deliver effective diabetes care and complement current diabetes management strategies, it cannot replace all in-person consultations. Patients with complex health needs, and those who require a physical examination are not suitable for telemedicine.

AI(artificial intelligence):Together with diabetes technology and telemedicine, the use of artificial intelligence (AI)[22] is slowly coming of age and may soon present a paradigm shift in diabetic management through data-driven precision care

 Precision Medicine:
Precision medicine [24]is an emerging approach for disease prevention and treatment that considers how individual variability in genes, environment, and lifestyle impact disease. This is in contrast to a one-size-fits-all approach, in which disease treatment and prevention strategies are developed with less consideration for the differences between individuals.. Compared with oncology, the role of precision medicine in diabetes management is less clear given the heterogeneous nature of T2DM, and the fact that diabetes medications are usually selected based on comorbidities, cost and side effects, rather than on the specific pathophysiology underlying disease in the individual patient.

The Last Frontier- Islet Transplantation in Diabetes Management

Islet Transplantation

A promising avenue is â-cell replacement through whole pancreas or islet cell transplantation[25]. This approach not only restores physiologic insulin secretion but also reduces hypoglycemia risk by partially restoring glucagon secretion.. Unfortunately, donor shortage hinders the widespread implementation of these therapies.

Stem cell technology:

The advances in stem cell technology may be able to bridge this gap of donor shortage in transplantation technology in the future.[25,26]

Conclusion:

Treatment of Diabetes was started with starvation .With advent of breakthrough discoveries of Insulin, oral antidiabetic agents and technologies diabetes treatment has been revolutionized. The improvements in glycemic control with medical therapy and lifestyle measures have clearly ameliorated polyuric symptoms and increased the life span of patients with diabetes. However with increased life expectancy, patients are more prone to manifest the classic microvascular and macrovascular complications of diabetes, broadening the goal of diabetes treatment to include prevention of these long-term complications. Drugs Dietary adjustment & Discipline in life remains at the centre of diabetes management .Individualized good compliance and surveillance by the care giver can only help to achieve this.14 th November has been promulgated as" World diabetes day(WDD)" by UN resolution 61/225 in 2006.WDD is the world's largest diabetes awareness campaign reaching a global audience of over 1 billion people in more than 160 countries. The campaign draws attention to issues of paramount importance to the diabetes world and keeps diabetes firmly in the public and political spotlight.

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ORIGINAL ARTICLE

RISK FACTORS, CLINICAL PRESENTATION IND IN-HOSPITAL OUTCOME OF ACUTE MYOCARDIAL INFARCTION IN ELDERLY PATIENTS

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Abstract:

Background: Coronary artery disease (CAD) is the leading cause of mortality, morbidity in the developed and developing country. Ageing is important risk factor for coronary artery disease. The role of conventional cardiovascular risk factors in older persons is incompletely understood because only fragmentary and inadequate data are available in most instance and manifestations of acute myocardial infarction are generally believed to be atypical in the elderly. The aim of the study was to find out the clinical presentation, common risk factors and In-hospital Outcome of Acute Myocardial Infarction in Elderly Patients. **Methods:**: An observational study in tertiary level hospital. Study protocol was approved by ethical review committee of Sir Salimullah Medical College & Mitford Hospital, Dhaka.Sample was selected from the population by purposive sampling technique. Detail demographic data were collected from the subject and recorded in structured case report form. Researchers make contact with patient and patient's caregiver, and describe them about study aim-objective, and then informed consent was taken. All collected questionnaire checked very carefully to identify the error in the data. Data processing work were consisting of registration of schedules, editing, coding and computerization, preparation of dummy tables, analysis and matching data. **Results**: In this series, the maximum number of patients (57.0%) was between 60-69 years age group, with mean value 67.21 ± 9.05 years. Out of 100 cases (62%) cases were male and (38%) were female (Figure 1). Male – female ratio was 1.63:1. Large numbers of respondents came from urban area (58%). Among the patients the poor class (44%) comprising the major percentage of the myocardial infarction patients. In this study majority (58%) of the patients had sedentary lifestyle before the onset of myocardial infarction. Among all the risk factors hypertension was the most common risk factor, present in 62% cases; next common risk factors were Diabetes mellitus 56%, dyslipidemia 32%, obesity 22%, smoking 40%. In this study majority of patients (56%) presented with shortness of breath as predominant symptoms. Besides typical chest pain others important atypical symptoms were atypical chest pain (31%), upper abdominal pain (18%), giddiness (4%) and confusional state (3%). In this study many of the patients had developed acute LVF (34%), arrhythmia (17%), cardiogenic shock (8%).**Conclusion:** We concluded that the manifestations of AMI are more subtle in the elderly, with different risk factors. The elderly subjects are under thrombolysed and have higher complication rate.

Key words: Acute myocardial infarction, elderly, AMI, Arrhythmia, Dyspnoea, Aging, Ischemic heart disease, Congestive heart failure

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Introduction:

The global demographic shift toward an aging population has brought to the forefront the increasing prevalence of cardiovascular diseases, particularly among the elderly. Heart disease, being the leading cause of mortality in this demographic, presents unique challenges owing to physiological changes and prevalent comorbidities associated with aging[1].

A study has highlighted that among the elderly, the most encountered cardiac disorders are ischemic heart disease, congestive heart failure, and atrial fibrillation. The hospitalization rates for ischemic heart disease exponentially rise in the 75-84 age group compared to younger individuals[2]. However, the impact of cardiovascular disease in this demographic is compounded by reduced homeostatic reserves, increased comorbidities, polypharmacy, and complex social issues like social deprivation and age-related devaluation.

Myocardial Infarction (MI) stands as a leading cause of mortality and morbidity among the elderly, often manifesting with a broader range of clinical presentations beyond chest pain. Symptoms may encompass chest pain, dyspnea, giddiness, vomiting, and sweating[3].Understanding the risk factors for cardiovascular diseases, primarily atherosclerosis, categorizes them into modifiable and non-modifiable factors. Hypertension, diabetes, smoking, unhealthy diet, physical inactivity, obesity, and raised cholesterol are among the modifiable risk factors, while age, race, ethnicity, and genetic factors constitute the non-modifiable ones[4].

The aging process in the cardiovascular system involves progressive loss of cardiac myocytes, hypertrophy of remaining cells, and increased connective tissue accumulation. Structural and functional changes in cardiomyocytes (CMs) precede alterations in heart anatomy. The aged heart experiences diminished compensatory capacity, with changes in maximal heart rate, end-systolic volume (ESV), end-diastolic volume (EDV), contractility, and altered sympathetic signaling. Atherosclerosis, a common disorder in the elderly, entails the accumulation of lipids, inflammatory cells, and plaque formation. Aging-induced endothelial dysfunction contributes to stroke, with modifications in brain microvasculature and white matter increasing vulnerability to myocardial infarction[5,6].

The research hypothesizes and investigates the risk factors, clinical presentations, and in-hospital outcomes of acute myocardial infarction in elderly patients (≥60 years). The objectives encompass evaluating sociodemographic characteristics, identifying risk factors, understanding clinical presentations, and assessing complications and in-hospital outcomes of MI in this specific demographic.This study endeavors to fill the knowledge gap by providing insights that could contribute to better care and outcomes for elderly patients experiencing acute myocardial infarction.

Methods:

The study was designed as a cross-sectional observational study and was conducted at the in-patient department of Cardiology and Medicine at Sir Salimullah Medical College & Mitford Hospital in Dhaka. This hospital is one of the largest tertiary care facilities in the country, comprising eight units in the Medicine department and a well-equipped cardiology department. Patients admitted to the hospital primarily reside in urban and semi-urban areas around Dhaka city, with some being transferred from rural hospitals across the country. The study took place from May 21, 2018, to November 20, 2018.

The study population included patients clinically diagnosed with acute myocardial infarction and evidenced through noninvasive tests such as ECG or laboratory profiles. The sampling technique used was purposive, and the sample size was estimated considering the statistical formula, resulting in 100 patients being included in the study.

Data collection was carried out using a preformed structured questionnaire that was developed considering the research questions, objectives, and variables of the study. Prior to the study, the questionnaire was pretested among 15 patients to ensure clarity, accuracy, and validity of the questions.

Various demographic and clinical variables were considered, such as age, sex, socio-economic status, occupation, clinical presentations of myocardial infarction (including symptoms like shortness of breath, chest pain, sweating, etc.), risk factors (hypertension, diabetes, obesity, smoking, physical inactivity, etc.), and in-hospital outcomes (recovery without complications, complications, death).

The selection criteria involved the inclusion of elderly patients (aged 60 years or above) diagnosed with acute myocardial infarction based on typical ECG patterns and elevated cardiac biomarker levels. Patients with valvular heart disease, stable or unstable angina, and those unwilling to provide informed consent were excluded from the study.

The methodology employed included consecutive sampling, detailed history taking, physical examination, investigations, and the collection of

patient data using the structured questionnaire. The data was entered into a computerized database for analysis.

Ethical measures were strictly adhered to, with informed consent obtained from both patients and their guardians before their inclusion in the study. Patients were informed about the aims, procedures, benefits, and any potential drawbacks of participating in the study, with the freedom to withdraw at any time.

The data collection procedure involved a cross-sectional observational study conducted over a six-month period. It included the enrollment of eligible patients, collection of demographic and clinical information, and close supervision of patients' conditions with appropriate management and record-keeping of any adverse events.

Data analysis was conducted using SPSS version 21, and the results were presented through tables, graphs, percentages, and charts. The statistical significance was determined with a threshold set at a "P" value of less than 0.05.

A quality assurance strategy was implemented, which included the development of a standard questionnaire, pretesting, and careful data collection to maintain the quality of the study.

Operational definitions for various parameters were established, such as defining the elderly population, risk factors of myocardial infarction, hypertension, diabetes mellitus, acute myocardial infarction, and other relevant clinical terms. These definitions were essential for consistency and understanding among researchers involved in the study.

This methodological approach ensured the systematic collection, analysis, and interpretation of data, in line with ethical considerations and maintaining a high standard of quality for the study.

Results:

In this cross-sectional observational study involving 100 patients aged 60 years and above with clinically diagnosed acute myocardial infarction (MI), several significant findings were observed.

Table-I
Age distribution of the patients (n=100)

Age (years)	Number of patients	Percentage	Mean ± SD
60-69	57	57.0	67.21 ± 9.05
70-79	31	31.0	
≥80	12	12.0	

Table-II
Life style pattern of study cases (n=100)

Life style pattern	Number of patients				p-value
	60-69 yrs.	70-79 yrs.	≥80 yrs.	Total	
Active	31	10	1	42.0	*0.018*
Sedentary	26	21	11	58.0	

The age distribution of the patients revealed that the majority (57.0%) fell within the 60-69 years age group, followed by 31.0% in the 70-79 years age group, and 12.0% aged 80 and above, with a mean age of 67.21 ± 9.05. The study also indicated a higher prevalence of sedentary lifestyle among patients aged 80 and above, with statistical significance (p < 0.05).

Table-III
Risk factors profile of the study subjects (n=100)

Risk factors	Number of patients			Total
	60-69 yrs.	70-79 yrs.	≥80 yrs.	
Hypertension	24	28	10	62 (62%)
Diabetes mellitus	23	24	9	56 (56%)
Obesity	15	5	2	22 (22%)
Dyslipidemia	11	10	11	32 (32%)
Smoking	23	12	5	40 (40%)
Physical inactivity	26	21	11	58 (58%)

The risk factors profile of the study subjects demonstrated that hypertension was the most common risk factor (62%), followed by diabetes mellitus (56%), dyslipidemia (32%), obesity (22%), and smoking (40%). Additionally, 45% of patients had three or more risk factors, emphasizing the multifactorial nature of acute coronary syndrome.
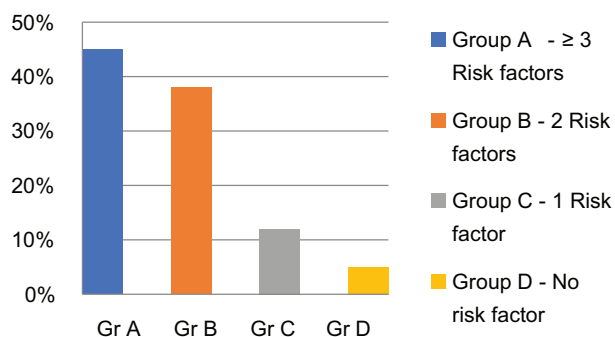
Fig.-1: *Number of risk factors of the study subjects (n = 100)*

(Risk factors are - Hypertension, diabetes mellitus, dyslipidemia, obesity, smoking, physical inactivity).

Table-IV
Clinical presentation of MI patient (n=100)

Presentation	Number of patients	Percentage (%)
Shortness of breath	56	56.0
Typical chest pain	42	42.0
Sweating	40	40.0
Palpitation	40	40.0
Vomiting	36	36.0
Restlessness	32	32.0
Atypical chest pain	31	31.0
Upper abdominal pain	18	18.0
Giddiness	4	4.0
Confusional state	3	3.0

In this study majority of patients presented with respiratory distress (56%) as a predominant symptom. Though typical chest pain was common, but 31% of patients presented with atypical chest pain and among 27% patients there was no chest pain at all. Others atypical presentation was upper abdominal pain, giddiness and confusional state.It was evident that typical chest pain was common (e.g., 42%), although 31% of patients presented with atypical chest pain and 27% patients with no chest pain at all.

Table-V
Time interval between symptoms and hospital admission (n=100)

Duration (hrs.)	Number of patients			Total
	60-69 yrs.	70-79 yrs.	≥80 yrs.	
Within 6 hrs.	13	4	1	18
Within 12 hrs.	14	5	3	22
More than 12 hrs.	30	22	8	60

The time interval from the onset of symptoms to presentation revealed that 60% of patients were admitted to the hospital more than 12 hours after symptom onset, mainly due to atypical presentation and the absence of typical chest pain in the elderly.
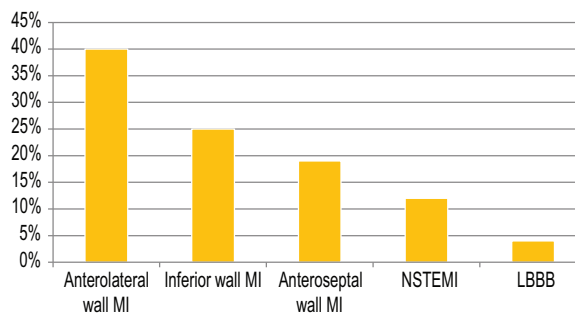
Fig.-2: *Types of acute myocardial infarction (n=100)*

Types of acute myocardial infarction indicated that anterolateral wall MI was the most common (40%), followed by inferior wall MI (25%), anteroseptal MI (19%), and NSTEMI (12%).

Table- VI
Assessment of different complications of the patient (n=100)

Complications	Number of patients			Total
	60-69 yrs.	70-79 yrs.	≥80 yrs.	
Uneventful	18	5	1	24
Acute LVF	19	11	4	34
Arrhythmia	12	4	1	17
Cardiogenic shock	3	4	1	8
Pericarditis	2	2	0	4
Thromboembolism	0	0	1	1
LBBB	2	1	1	4
RBBB+LAHB	0	1	0	1

Amongst the complications noted during hospital stay the commonest were acute LVF (34%), arrhythmia (17%) and cardiogenic shock (8%). Frequency of complications was more in advanced age group.

Table-VII
Various arrhythmias observed during in-hospital stay (n=17)

Arrhythmia	Number of patients	Percentage (%)
Premature ventricular contraction	4	23.5
Atrial fibrillation	2	11.8
AV block	9	52.9
1st degree	2	11.8
2nd degree	1	5.9
Complete heart block	6	35.3
Ventricular fibrillation	2	11.8

Complete heart block (35.3%) was the most common arrhythmia occurring elderly. Other arrhythmias were premature ventricular contraction (23.5%), AF (11.8%) and VF (11.8%).Out of the 100 patients, only 25% of patients were thrombolysed. The main reason for notthrombolysing the patients were delayed presentation to the hospital due to atypical presentation.In this study, total 24 patients recovered without any complications during hospital stay, but 69 patients developed some sort of complications and 7 patients expired during hospital stay.

Table - X
Outcome of the patient (n=100)

Outcome	Number of patients			Total
	60-69 yrs.	*70-79 yrs.*	*≥80 yrs.*	
Recovered without complications	18	5	1	24
Complications	38	23	8	69
Death	1	3	3	7

Discussion:

The demographic characteristics of the studied group revealed a higher prevalence of AMI in the age group of 60-69 years followed by the age group of 70-79 years indicating a notable burden of AMI in these age brackets. The male-female ratio was approximately 1.63:1. The majority of patients hailed from urban areas (58%). The study corroborates findings from previous research, reflecting an increased prevalence of angina with age in both sexes, highlighting the rise in angina cases as individuals grow older. The prevalence of angina increases sharply with age in both sexes from 0.1–1% in women aged 45–54 to 10–15% in women aged 65–74 and from 2–5% in men aged 45–54 to 10–20% in men aged 65–74[1]. In another study with a male, female ratio of 5.3: 4.7, 45.90% patients were over 55 years and 69.62% patients had come from urban area[7].

The study's observations align with other research, indicating that hypertension, diabetes mellitus, obesity, smoking, and dyslipidemia are among the common risk factors contributing to the development of AMI in the elderly[8].

Regarding the clinical presentation, the study pointed out that while typical chest pain was common, a substantial percentage of patients presented with atypical symptoms like respiratory distress, atypical chest pain, and in some instances, no chest pain at all. Findings consistent with result of other study[8]. In an analysis of symptomatology revealed that atypical chest pain, sweating, dyspnoea and giddiness were observed predominantly in the elderly group. In that study, typical chest pain was (48%), dyspnea (40%), atypical chest pain (29%) and in 21% there was no chest pain. In Worcester Heart Attack Study, chest pain was reported in less than half of the patients over age 75 years (45.5%) while dyspnea or cough (22%) and other symptoms like dizziness, syncope, sweating, palpitations, nausea were more common[9,10].

One significant finding was the delay in hospital presentation after the onset of symptoms, with nearly 60% of patients arriving at the hospital more than 12 hours after symptom onset. This delay in seeking medical care among the elderly might be due to societal neglect or lack of health awareness.Complications during hospital stay were noted, with acute left ventricular failure (LVF) being the most common, followed by arrhythmias and cardiogenic shock. Findings accordance with the result of other studies. Assessment of complications of AMI revealed that 45 (70.2%) cases presented with congestive cardiac failure, 37 (57.8%) cases had arrhythmias, and AV block was seen in 16 (28.6%). The complications like arrhythmias, CCF, cardiogenic shock, re-infarction, CVE and mortality were commonly seen in elderly population[8]. In a study among the complications noted during hospital stay commonest were acute pulmonary oedema (18%), cardiogenic shock (16%) and arrhythmias (13%). Arrhythmias noted were varying degrees of heart block (8%), atrial fibrillation (3%) and ventricular tachycardia (2%). Severe LV dysfunction which contributes to the development of pulmonary edema and cardiogenic shock was reported in 15% of patients[3].

The study also noted a mortality rate of 7%, with a higher mortality rate observed among patients aged 80 years or older, aligning with the understanding that mortality tends to increase with advancing age in AMI cases.In other study[3], mortality rates were 20%. In that study, 4 out of 9 patients died in the age group e" 80 yrs. So, like other study, with the advancement of age, the rate of mortality is also increased.

Overall, these findings underscore the diverse clinical presentation, varied risk factors, delayed presentation to hospitals, and notable complications and mortality rates associated with AMI in the elderly. These insights are crucial for better understanding and addressing the unique challenges and healthcare needs of this demographic group, thereby facilitating improved management and care for elderly patients suffering from AMI.

Conclusion:

This cross-sectional study of 100 elderly patients with acute myocardial infarction highlighted the prevalence of sedentary lifestyles, with a significant association in those aged 80 and above. The most common risk factors were hypertension, diabetes, and smoking, contributing to the majority having three or more risk factors. Respiratory distress was the predominant presentation, with atypical chest pain noted in 31%. Delayed hospital presentation occurred due to atypical symptoms, influencing treatment decisions. Complications, notably acute LVF and arrhythmias, were more frequent in advanced age groups. The study emphasizes the complexity of managing myocardial infarction in the elderly, requiring tailored interventions for optimal outcomes.

Limitations:

This is a small study; only patients of acute MI admitted in the Department of Medicine &Cardiology, SSMC MH were taken for the study. So, this will not reflect the overall picture of the country. A large scale, preferably, nationwide survey should be conducted to reach to a definitive conclusion.Sample were taken by purposive method in which question of personal biasness might arise.

Conflict of Interest:

The authors stated there is no conflict of interest in this study.

Funding:

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Ethical Consideration:

Ethical measures were taken throughout the study period to maintain a high standard of confidentiality and anonymity of the participants. Formal approval was taken from the ethical committee of Sir Salimullah Medical College Mitford Hospital.

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ORIGINAL ARTICLE

ASSOCIATION OF HYPERTENSION WITH BODY MASS INDEX IN NORTHERN DISTRICTS OF BANGLADESH

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Abstract:

Background: Body Mass Index is one of the significant determinant associated with many disease process particularly hypertension. There is positive association between Body Mass Index (BMI) and blood pressure (BP). Lowering BMI with weight reduction significantly reduces blood pressure (BP). The main purpose of this study was to find out the association of BMI with hypertension. The aim of the study is to find out any association between BMI and hypertension in a particular area of Bangladesh. **Methods:** This is a retrospective study which involves review of written medical records for adults diagnosed with hypertension aged 18 years and above. This study was conducted at hypertension and research centre, Rangpur. A total of 14137 hypertensive patients were included in this study. Hypertension was defined by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7). BMI was calculated by a person's weight in kilograms divided by his height in meters squared. **Results:** Majority (42.1%) of hypertensive patients were within 41 to 50 years of age. Among 14137 participants 4.6% were underweight, 46.5% were healthy weight, 38.7% were overweight and 10.2& were obese. The mean values of systolic and diastolic blood pressure were144.9, 145.2, 148.3, 152.7 and 89.8, 90.4, 91.2, 92.8 respectively with increasing BMI. **Conclusion:** Increasing BMI increases the risk of HTN.

Key words: Retrospective study, obesity, overweight, BMI, blood pressure, hypertension

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Introduction:

Hypertension is common in day to day practice. Many patients with hypertension are obese. Many studies were done to see correlation between obesity and hypertension. Few were done in patients residing in northern districts of Bangladesh. There was a positive correlation between Body mass index (BMI) and blood pressure (BP); this association has critical implications. In countries like China, where high blood pressure and obesity is increasing[1].Blood pressure can be reduced significantly with control of obesity[2]. Obesity is not only a factor associated with high BP but also a cause[3]. Hypertension has prevented to be a recognized cause of morbidity and deaths worldwide[4]. In developing countries like Bangladesh hypertension is an emerging major publichealth problem[5].One quarter of world adult population is already hypertensive and most of them are in developing countries[6]. According to an extensive survey on non-communicable disease conducted in 2010; prevalence of hypertension is 17.9%[7]. Exact prevalence of HTN in Bangladesh was not known. One meta-analysis and a population-based survey found the prevalence 11.3% and 18.6% respectively[8]-[9]. In another survey the prevalence was 20.1%[10]. 'Prevention is better' this is particularly true for hypertension. We tried to see if there was association between BMI and hypertension. So finding the association between BMI and HTN might help prevent HTN and its many complications. Though Bangladesh is a small country it has nearly 200 million populations. Out of them many suffers from hypertension and its complications. Bangladesh is a developing country with overwhelming impact on healthcare system. Once hypertension developed it requires long term medication with increased cumulative cost. Northern districts of Bangladesh are relatively poor compared to other parts. Many are not able to continue the treatment of hypertension due to financial constraints. Many study found clear association between increased BMI and hypertension. Very few studies done in this particular area. Hypertension and research centre covers wide areas of northern districts of Bangladesh including Rangpur, Kurigram, Gaibandha, Lalmonirhat, Nilphamari, Dinajpur, Thakurgaon and Panchagarh. This centre has a rich, huge data of patients from these districts. Our rationale for this study is to find any association between BMI and hypertension among people living in this area.

Methods:

This retrospective study was conducted at hypertension and research centre, Rangpur. Data collected from 2008 till December 2021 was enrolled for study. A total of 28000 participants were considered initially, out of them 14143 were finally selected. Rest was excluded due to missing information or lack of complete data. Participants were included by purposive sampling method.

According to The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) HTN is diagnosed when systolic and diastolic blood pressure equals to or more than 140 and 90 respectively[11].Blood pressure was recorded through pre-checked and reliable aneroid sphygmomanometer. Patients were seated on comfortable chairs calm and quiet for at least 5 minutes prior to measurement. Three consecutive readings of BP were recorded at 3 minutes interval in between measurements and mean were calculated.

Weight and height were measured without shoes and wearing light clothes. Height was measured with patients stood upright with head in[1]Frankfort plane done by stadiometer. Height was recorded to the nearest 0.5 cm. Weight was measured by asking the patient standing straight in a digital weighing scale. Weight was recorded to the nearest 100 grams. Body mass index is calculated using a person's height and weight. The formula is BMI = kg/m^2 where kg is a person's weight in kilograms and m^2 is their height in meters' squared.

BMI interpretation[12]. BMI less than 18.5: Underweight, BMI between 18.5 and 24.9, Healthy weight, BMI between 25 and 29.9: Overweight, BMI of 30 or higher: Obese

Patients with HTN were allocated to different groups on the basis of age, sex, educational qualification, occupation, residence, family history of HTN etc. Alldata were recorded systematically in Semi-structured questionnaire.

Patients with HTN attending the 'hypertension and research centre Rangpur' were registered by registered doctor. Then registered patient was referred to the investigator. Written consent was taken from the patient. Detailed history was taken and clinical examination was done systematically. A pre-set data form was filled up for every patient. Patients with serious co-morbidities and patients who refuse to give consent were excluded from the study. Information on certain socio-demographic variables was obtained from the patients and/or their caregivers.

Results:

The study was intended to find any association between BMI and hypertension. The findings were presented

below which were derived from this study.Among 14143 participants 7366 (52.1%) were males and 6771 (47.9%) were females (Fig 1). Socio-demographic data demonstrated that majority (52.1%) of the study subjects were female. Most of them resided in rural areas (70.1%), 42.3% were housewife and 32.9% were service holders. Of our study subjects 11.1% had no institutional qualification, 23.8% & 37.9% completed primary and secondary education respectively, and 26.7% completed bachelor/post O graduation (Table-1). BMI distribution revealed underweight, healthy weight, overweight & obese 4.6%, 46.5%, 38.7% & 10.2% respectively (figure 2). From the bar chart it was obvious that a significant proportion (49%) of study population were either overweight or obese. Mean value of SBP (144.91, 145.23, 148.39, 152.71) & DBP (89.83, 90.48, 91.21, 92.84) were found to be increasing as the BMI increased (Table-II). The association of BMI with SBP & DBP revealed significant positive correlation with $p<0.005$ and $r=0.689$ (SBP) and $p<0.005$ and $r=0.705$ (Table III).

Table-II

Socio-demographic characteristics of the study subjects (n=14137)

Variables		Frequency	Percent
Sex	Male	6771	47.9
	Female	7366	52.1
Residence	Rural	9910	70.1
	Urban	4147	29.3
	Suburban	80	0.6
Occupation	Housewife	5986	42.3
	Service holder	4644	32.9
	Businessman	1934	13.7
	Farmer	1573	11.1
Qualification	Primary	3366	23.8
	Secondary	5350	37.9
	Bachelor/ postgraduate	3776	26.7
	Illiterate	1645	11.6

Fig.-1: *Distribution of male and female participants*
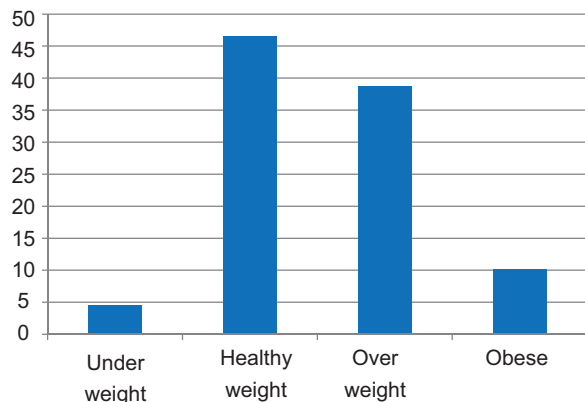
Fig.-2: *BMI distribution*

Table II

Mean BP in each BMI category

BMI	Mean SBP	Mean DBP
Underweight (<18.5)	144.91±9.28	89.83±7.52
Healthy weight(18.5-24.9)	145.23±10.34	90.48±7.88
Overweight(25-29.9)	148.39±9.82	91.21±6.78
Obese (≥30)	152.71±11.52	92.84±9.27

Table III

Pearson correlation between BMI & BP

	SBP		DBP	
	P value	r value	P value	r value
BMI	0.000	0.689	0.000	0.705

Correlation was significant at 0.01 level

Discussion:

Our study provided an idea of association between BMI and BP in general population residing in a particular area of Bangladesh. To date there are no published studies to see if this is true for the population living in greater Rangpur area of Bangladesh. Our study revealed strong association between BMI and SBP or DBP among participants. Both SBP and DBP increased significantly as the BMI increased.

Overweight or obese subjects were more likely to have higher SBP or DBP compared to healthy weight subjects. Underweight subjects were less likely to have high BP than healthy subjects with normal BMI. Our findings were similar to a study done by Esha Shrestha et al. where BMI was a strong predictor of hypertension[13]. Humayun et al. found BMI is more associated HTN compared to age[14]. Another study done by Kumanyika et al found BMI was more strongly associated with HTN compared to race[15]. One study conducted in adolescent population found strong relation between BMI and both SBP & DBP[16].

The Frahingham study demonstrated SBP increased 4 mmHg for every 4.5 kg of increased weight[17]. In our study higher BMI participants had 7 mmHg mean high SBP and 3 mmHg mean high DBP compared to normal BMI participants.

Overweight/obesity among the participants might be due to less physical activity, high fat intake, sweetened beverages, familial obesity, less fruits and vegetables intake. Various studies revealed diet, physical activity and self-discipline are major factors influencing obesity and HTN. The prevalence of HTN and obesity are significant public health problem and the trend is increasing globally. It is important that there is a need for nationwide campaign for control of weight and obesity. There is specification that measurement of blood pressure and BMI and timely diagnosis and control are essential for all particularly overweight/obese people.

Conclusion:
There was a positive correlation between HTN and increased BMI. So, we recommended measures to reduce overweight or obesity to prevent HTN and its negative consequences. The limitation of our study was that data were collected from a single centre. Further multi-centrestudy was recommended for validation of present study.

Limitations:
This is a study; only patients at hypertension and research centre, Rangpur were taken for the study. So, this will not reflect the overall picture of the country. A large scale, preferably, nationwide survey should be conducted to reach to a definitive conclusion. Sample were taken by purposive method in which question of personal biasness might arise.

Conflict of Interest:
The authors stated there is no conflict of interest in this study.

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ORIGINAL ARTICLE

DELIRIUM ON ADMISSION: PATTERNS IN A MEDICINE UNIT OF A TERTIARY CARE HOSPITAL IN BANGLADESH

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Abstract:
Background: Delirium, a complex neuropsychiatric syndrome, poses challenges in clinical settings due to its varied aetiology and under diagnosis. This study aimed to explore the prevalence, demographic characteristics, and contributing factors of delirium as a presenting feature in the population admitted to a tertiary care hospital in Bangladesh. Limited studies on delirium in low- and middle-income countries necessitate a comprehensive investigation to inform healthcare practices in diverse settings. Methods: A prospective observational study was conducted on 102 patients diagnosed with delirium among a total of 2599 patients admitted to the medicine unit over six months. Delirium was assessed using the Confusion Assessment Method (CAM) score, with demographic variables and comorbidities analyzed. Results: The study identified a delirium prevalence of 3.8%, with stroke and poisoning as major contributors. Females (56.8%), individuals above 50 years (69.8%), and those with comorbidities (67.6%) exhibited higher susceptibility to delirium. The multifactorial aetiology included stroke (49.3%), poisoning (1.42%), electrolyte imbalance (0.76%), and others. Sedative poisoning predominated (45.9%) among poisoning cases.Conclusion: This study highlights the demographic and etiological dimensions of delirium. The significant impact of stroke, the underexplored realm of poisoning-related delirium, and the influence of age and comorbidities underscore the need for targeted interventions and increased awareness.

Keywords: *Delirium, prevalence, demographic characteristics, contributing factors, tertiary care hospital, Bangladesh.*

Introduction:

Delirium is a complex neuropsychiatric syndrome and often considered the most common one in a medical setting[1]. Delirium constitutes a grave alteration in cognitive function that extends beyond the typical oscillations in attention and alertness. It is characterized by altered consciousness, cognitive impairment, and inattention fluctuating over time and have an abrupt onset as a defining feature[2]. This condition is not an isolated entity but rather a symptom

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of an underlying medical issue or external precipitating factor. These can range from infections, such as RTI or UTI to metabolic disorders like electrolyte imbalances, liver or kidney failure. Adverse reactions to medications, abrupt substance withdrawal, and traumatic insults to the brain, whether through injury or surgery, are also common instigators.

Although frequently encountered, delirium is still not well established in terms of its etiology and remains under diagnosed. It is often recognized as a geriatric disease as certain populations, notably older adults (those aged 65 and older) are particularly susceptible to delirium[3.] Moreover, regardless of age, past cognitive ability, or comorbidities, it is associated with adverse outcomes like longer hospital stays, higher mortality rate and increased healthcare costs[4]. It is reported in one study that for every additional 48 hours of active delirium, mortality increases by 11%, emphasizing the need for prompt diagnosis and intervention[5]. According to a different study, people who have delirium lose an average of 13% of a year of life and have a 62% increased risk of mortality[6]

Though a number of studies have been found measuring the prevalence and incidence rates of delirium in hospitalized patients in medical wards, there were discrepancies in the findings. As it is difficult to conduct clinical trials and systemic studies, getting the right results is often challenging[7]. The prevalence of delirium in the general population is estimated to be 0.4% worldwide, increasing to 1% in the population above 55 years of ageby Soenke et al[8].

Despite its high prevalence, delirium often remains inadequately managed during patient admission in a hospital[9]. We have found no research that investigated the presence of delirium in the whole adult population of a hospital, especially in any of the low-and-middle-income countries. The limited study that is conducted on delirium solely comprises of the findings from the intensive care units and after surgeries.

Our study aims to shed light to this issue by investigating the extant of delirium on patient admission in the medicine unit at a tertiary care hospital. The Confusion Assessment Method (CAM) score is used for diagnosis and assessment of delirium[10]. Employed during clinical examinations, a CAM score exceeding 3 confirmed the presence of delirium in eligible patients, ensuring a standardized and objective evaluation. Studying delirium as a presenting feature in a country like Bangladesh is crucial for optimizing healthcare resource allocation and improving patient outcomes. Understanding the nuances of delirium during patient admission is imperative for tailoring effective diagnostic and intervention strategies, ultimately contributing to healthcare system efficiency.

Methods:

Study design and sample size:

This prospective observational study was conducted in the indoor unit of the medicine department at Sir Salimullah Medical College Mitford Hospital, Dhaka.The study was conducted over a period of six months, from January to June 2022. A total of 2599 patients who were admitted within the time frame were assessed and 102 patients with delirium were included in the study.

Data Collection:

Data was collected from the patients with the informed consent from their attendants. Necessary permission from the authorities concerned was taken to review the medical files of the patients. Patients were assessed according to the CAM score. The Inclusion criteria constituted of patients aging 14 and above, admitted to the medicine unit of the tertiary care hospital during the specified time frame of our study, presence of delirium as a primary presenting feature upon admission, confirmed through clinical examination. The patients aged below 13 years, patients with pre-existing severe cognitive impairment (e.g., dementia), patients admitted for psychiatric reasons with delirium as a secondary feature and the patients or attendants who refused to participate or provide informed consent were excluded from the study. Stroke was excluded by CT or MRI.

Data Analysis:

The study employed a prospective observational design wherein data pertaining to delirium as a presenting pattern were meticulously collected, stratified based on age, sex, and underlying causes. The data set was systematically entered into Microsoft Excel for subsequent analysis. Utilizing SPSS version 24, the acquired data were subjected to statistical examination, with results articulated in terms of percentages and proportions. This methodological approach facilitated a comprehensive exploration of the demographic and etiological dimensions of delirium, offering valuable insights into its distribution within the studied population.

Results:
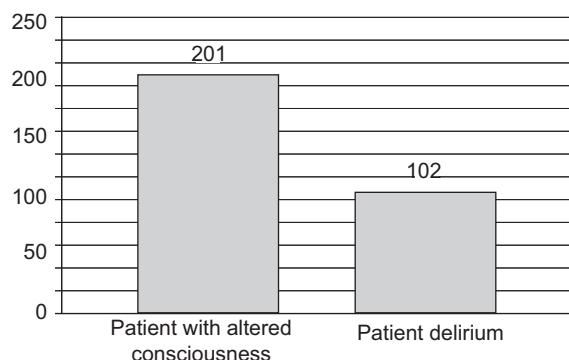
Fig 1: *A total number of 2599 patients were assessed as the sample of our study with 201 patients having altered level of consciousness as a presenting feature during admission. Among them, 102 patients were found fitting the criteria of delirium according to CAM score.*
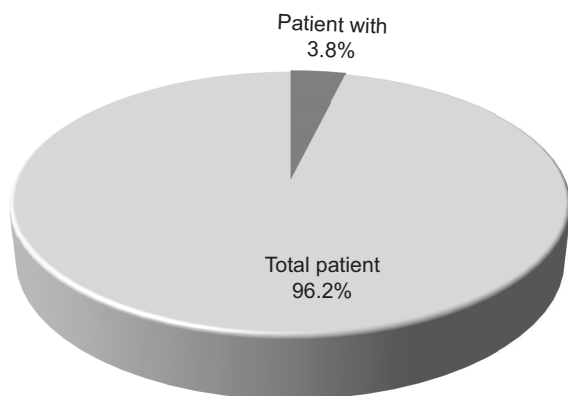
Fig.-2: *Among 201 patients with altered consciousness, 102 patients were diagnosed with delirium according to CAM score, which consisted of 3.8% of the total admitted patients.*
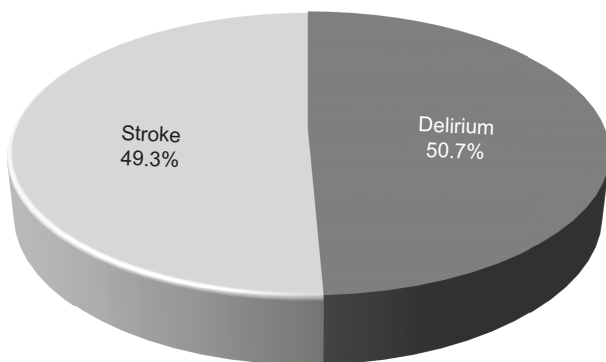
Fig.-3: *Causes of altered level of consciousness consisted of stroke as a major cause for 99 patients (49.3%) and delirium for 102 patients (50.7%).*

Table I
Demographic variables of the patients presented with delirium as a presenting feature during hospital admission.

Variable	Category	Number	Percentage
Gender	Male	44	43.1%
	Female	58	56.8%
Age	≤50 years	41	40.2%
	>50 years	61	59.8%
Co-morbidities	Co-morbidities	69	67.6%
	No co-morbidities	33	32.4%
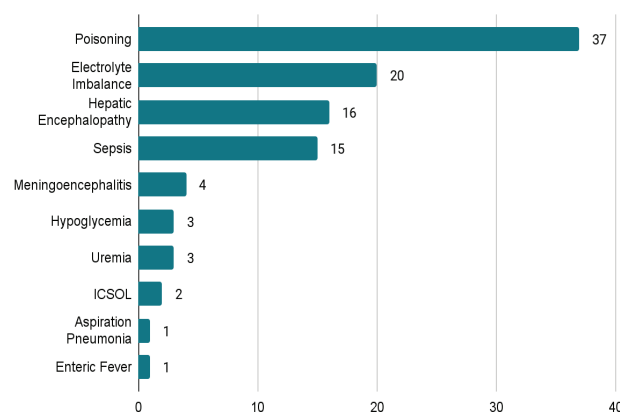
Fig.-4: *Etiology of delirium is described with poisoning (36.3%) as the leading cause with a maximum number of patients, followed by electrolyte imbalance (19.6%), hepatic encephalopathy (15.7%), sepsis (14.7%), meningo-encephalitis (3.9%), hypoglycemia (2.9%), uremia (2.9%) and ICSOL (2%).*
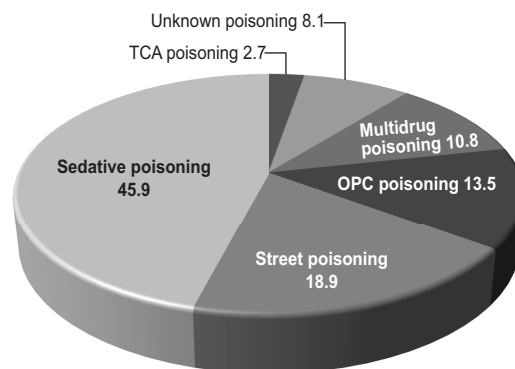
Fig 5: *Causes of poisoning are shown with sedative poisoning as a leading cause (45.9%) of all types of poisoning, followed by street poisoning (18.9%), OPC (13.5%), multidrug (10.8%), unknown poisoning (8.1%) and TCA (2.7%).*

Discussion:

In our comprehensive study aimed at exploring statistical disparities in delirium as a presenting feature during admission to a medical unit, we first delved into the prevalence of delirium during patient admission. The prevalence of delirium exhibits variability among diverse populations, with recent research indicating incidence rates ranging from 10% to 60% in hospitalized patients [11,17]. According to another systematic research, the prevalence of delirium in acute hospitals ranged from 11 to 42%[3.] While our observed prevalence (3.8%) may appear lower in comparison, it is crucial to consider the unique characteristics and demographic composition of our study population, as well as potential variations in healthcare settings.

Demographic variables, specifically gender, age, and the presence of comorbidities, were systematically examined in our study. Our findings indicated a higher incidence of delirium among females compared to males (56.8% vs. 43.1%), with approximately 69.8% of affected individuals being aged over 50 years. This gender-related study findings aligns with previous observations of a separate study where the majority of delirium cases were also reported among females (57.29%)[12].

Advanced age emerged as a significant correlate of delirium, with individuals older than 50 years demonstrating a heightened susceptibility compared to their younger counterparts[8]. Our finding was supported by evidence from studies from Ethiopia[13], Ireland[14] and India[15].

Multiple studies have consistently highlighted the correlation between delirium prevalence and the presence of comorbid conditions [16,17]. Our study reinforces this trend, revealing that a substantial 67.6% of patients diagnosed with delirium in our study exhibited concurrent comorbidities. This underscores the pervasive influence of comorbidities on the manifestation of delirium in our patient population.

Our study identified stroke and delirium as the primary contributors to altered consciousness, revealing a substantial prevalence of 49.3% attributed to stroke. This finding diverges from a previous systematic analysis in 2019, reporting a comparatively lower prevalence of altered consciousness in acute stroke conditions at 25%[18]. This highlights the importance of considering the specific context and characteristics of the studied population when interpreting and comparing prevalence rates, highlighting the potential impact of population demographics on study outcomes.

The multifactorial etiology of altered consciousness encompasses a broad spectrum, including hypoglycemia, toxic ingestion, trauma, seizures, infections, metabolic disturbances, electrolyte disorders, encephalopathy, overdose, intoxication, uremia, stroke, and hypo-hyperglycemia [19,20,21]. Our findings align comprehensively with this diverse range, revealing stroke as the predominant cause (3.8%), followed by poisoning (1.42%), electrolyte imbalance (0.76%), hepatic encephalopathy (0.61%), sepsis (0.57%), meningoencephalitis (0.15%), hypoglycemia (0.11%), uremia (0.11%), ICSOL (0.07%), aspiration pneumonia (0.038%), and enteric fever (0.038%). Sepsis and metabolic abnormalities were identified to be the most common causes of delirium in hospital patients in medical wards by Khurana et al, which also supported our findings[22]. Our detailed breakdown emphasizes the nuanced landscape of causes contributing to altered consciousness in our patient population.

The scarcity of existing literature on the types of poisoning causing delirium in patients emphasizes the novelty of our study's exploration into this critical domain. Though few studies have been conducted on delirium caused by drug induced toxicity[23], substance abuse[24] and anticholinergic poisoning[25], this side is still greatly unexplored. Our findings illuminate a complex landscape of poisoning etiology, with sedative poisoning emerging as the predominant cause, constituting 45.9% of all poisoning cases. Street poisoning follows at 18.9%, while other significant contributors include organophosphorus compound (OPC) poisoning at 13.5%, multidrug poisoning at 10.8%, unknown poisoning at 8.1%, and tricyclic antidepressant (TCA) poisoning at 2.7%. This information not only contributes substantially to the area of poisoning-related delirium but also emphasizes the diverse array of toxicological agents influencing altered mental status in the hospitalization of our patients.

Conclusion:

In conclusion, our study provides valuable insights into the demographic, etiological, and clinical dimensions of delirium in a tertiary care hospital in Bangladesh. The significant impact of stroke, the underexplored realm of poisoning-related delirium, and the influence of age and comorbidities underscore the need for targeted interventions, increased awareness, and comprehensive patient management strategies.

Limitations of the Study:

The single hospital-based study did not reflect the exact scenario of the whole community. Patients from all

socioeconomic statuses and all parts of the country did not come to seek medical attention in the study place.

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ORIGINAL ARTICLE

BASELINE HAEMATOLOGICAL EVALUATION IN INDIVIDUALS PRIOR TO INITIATING ANTIRETROVIRAL THERAPY FOR HIV

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Abstract:

Background: Human immunodeficiency virus (HIV) was discovered in 1983, while acquired immunodeficiency syndrome (AIDS) was first detected in 1981. Since then, it continues to be a public health problem. The phenomenon of HIV/AIDS is best viewed as a pandemic affecting almost all countries of the world. The first case of HIV/AIDS in Bangladesh was documented in 1989.This study was conducted to evaluate the baseline haematological characteristics in individuals prior to initiating antiretroviral therapy for HIV. **Methods:** This study was a cross sectional analytical study conducted among one hundred and fifty-four HIV positive patients attending at ART center, Bangabandhu Sheikh Mujib Medical University. Patients were included as per inclusion and exclusion criteria from April 2019 to October 2022. Co-morbid conditions were excluded mostly by self-reporting and clinically relevant investigations. **Results:** The study revealed that HIV infected patients were predominantly middle-aged and young comprising > 70% of the patients with the mean age of the patients being 35.5 ± 9.5 years (range: 20-60 years). A male preponderance was observed in the study with a male-to-female ratio being 3:1. The majority (92.2%) of patients received first-line ART. The red cell indices like Hct, MCV, MCH, and MCHC were also low at the initiation of therapy but changed to normality after treatment. **Conclusion:** From the findings of the study, it can be concluded that HIV infected individuals are predominantly male, middle-aged, and young. The most common haematological abnormality is anaemia which is significantly reduced in percentage after a mean treatment period of nine and a half months with ART.

Key words: Haematological changes, Antiretroviral therapy, ART regimens, HIV, Immune system response.

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Introduction:

Human immunodeficiency virus (HIV) was discovered in 1983, while acquired immunodeficiency syndrome (AIDS) was first detected in 1981. Since then, it continues to be a public health problem [1,2]. The phenomenon of HIV/AIDS is best viewed as a pandemic affecting almost all countries of the world [3]. The first case of HIV/AIDS in Bangladesh was documented in 1989 [4,5].The total population of individuals living with HIV (PLHIV) in Bangladesh is 14,000 across all age groups. Among them, fewer than 500 are in the 0-14 age range, while 4,800 are women aged 15 and above and 8,700 are men aged 15 and above. HIV incidence per 1000 population is 0.01 and HIV prevalence (15-49 years) is <0.1[6].There were total 580 (all ages) AIDS related death in 2018[6].HIV can spread through the exchange of a range of body fluids, including blood, breast milk, sperm, and vaginal secretions, from infected people. During pregnancy and delivery, HIV can be passed from a mother to her child [7]. HIV is an enveloped virus that predominantly affects the immune system by targeting T-lymphocytes. It replicates by exploiting the deoxyribonucleic acid of CD4+ T cells, decreasing their numbers and putting the patient at risk of opportunistic infections over months to years, finally leading to death [8,9]. HIV is classified into HIV-1 and HIV-2 with HIV-1 being the predominant cause of AIDS worldwide [10,11,12,13]. When HIV enters the body, it spreads quickly to cells and tissues, insidiously destroying the lymph node's architecture and prompting the immune system to soar a defense against it via CD4+ and CD8+ T cells, which are then killed by the virus, allowing free HIV replication and eventually full-blown AIDS. The World Health Organization (WHO) has classified AIDS into four stages based on symptoms, clinical signs, and opportunistic infections, starting with Stage I, which is asymptomatic, then Stage II, which is mildly symptomatic, Stage III, which is moderately symptomatic, and Stage IV, which is HIV wasting syndrome [14].Based on the stage of infection, HIV may have different symptoms. Although persons living with HIV are most infectious in the first few months following infection, many do not feel they are infected until later [15]. Peoplemay have no symptoms or an influenza-like sickness, such as fever, headache, rash, or sore throat, in the first few weeks following infection. They may develop other signs and symptoms when the virus impairs their immune system, including swollen lymph nodes, weight loss, fever, diarrhea, and cough [16,17]. They could acquire serious illnesses like tuberculosis (TB), cryptococcal meningitis, severe bacterial infections, and malignancies like lymphomas and Kaposi's sarcoma if they don't get treatment [7]. Haematological abnormalities commonly found in HIV-infected individuals are anaemia, granulocyte disorders, thrombocytopenia, lymphomas, coagulopathies, and vascular malignancies. Although these abnormalities are detected in the majority of cases in the middle or advanced stages of HIV infection, anaemia and thrombocytopenia may occur in the early stages of HIV infection [18,19,20]. The origin of haematological disorders in HIV infection remains incompletely understood but has been attributed to several factors causing dysfunctional haematopoiesis in the bonemarrow[21].

Methods:

This study was a cross sectional analytical study conducted among one hundred and fifty-four (154) HIV positive patients attending at antiretroviral-therapy centre, Bangabandhu Sheikh Mujib Medical University from April 2019 to October 2022. Patients were included by Laboratory confirmation of HIV infection through serological testing and Inability to provide informed consent for treatment excluded. Co-morbid conditions were excluded mostly by self-reporting and clinically relevant investigations. Study purpose was explained to the study subjects and informed written consent was taken. All demographic characters like age, sex, address, and education level, and occupation, marital and socio-economic status were documented in a structured form after the patient's registration. History related to risk factors and sexual patterns was asked face-to-face to the patients and documented in the datasheet. Reports were collected on a day-to-day basis and entered into Microsoft Office 2010 Excel worksheet.

Data collection

All participants signed informed written consent before entering the study. Before study enrolment, all individuals were informed of the voluntary nature of participation and confidentiality as well as the use of their data for research purposes only.

Sampling method

Purposive sampling as per inclusion and exclusion criteria was applied to collect sample.

Ethical consideration

Prior to the commencement of this study, the research protocol was approved by the Institutional Review

Board (IRB) of BSMMU, Dhaka. The purpose of the study along with its procedure, methods, risks, and benefits were explained to the patients in an easily understandable local language and then informed consent was taken from those who voluntarily agreed to participate in the study. Informed consent was obtained.

Statistical analysis

Data were processed and analyzed using the statistical software SPSS (Statistical Package for Social Sciences), version 24.0. The level of significance was set at 5% and p-value < 0.05 was considered statistically significant.

Result
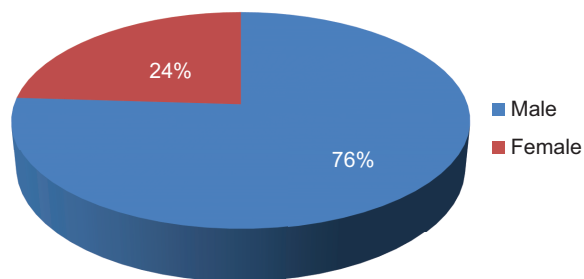
Fig.-1: *Gender distribution of our study patients (n = 154)*

Figure 1 show in terms of gender distribution, more than three-quarters 117 (76.0%) were male and 37 (24.0%) were female with male-to-female ratio being roughly 3:1.
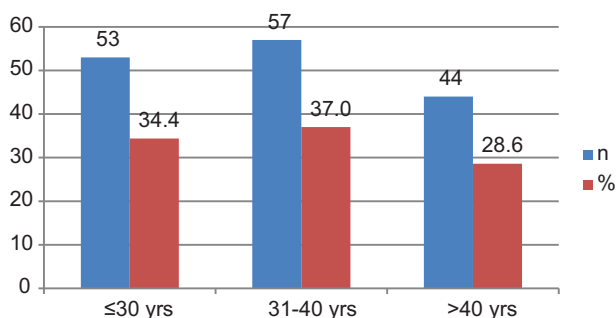
Fig.-2: *Age distribution of our study patients (n =154)*

In Figure 2 age distribution shows that more than one-third 57 (37.0%) of the HIV positive patients were 31-40 years old, 53 (34.4%) were d" 30 years old and 44 (28.6%) were > 40 years old with mean age of the patients being 35.5 ± 9.5 years (range: 20-60 years).

Table-I

Distribution of our study patients by Education (n = 154)

Education	n	%
Illiterate	04	2.6
Primary	49	31.9
Secondary	61	39.6
Higher Secondary	19	12.3
Graduate	21	13.6
Total	154	100

In Table 1 we found more than one-third 61 (39.6%) of the patients were secondary level educated, 49 (31.9%) were primary level, 19 (12.3%) higher secondary, 21 (13.6%) graduate-level educated and 4 (2.6%) patients were illiterate respectively.

Table II

Distribution of our study patients by occupation (n = 154)

Occupation	n	%
Service	42	27.3
Unemployed	37	24.0
Housewife	34	22.1
Business	22	14.3
Others	19	12.3
Total	154	100

In Table II over one-quarter 42 (27.3%) patients were service-holder, 37 (24.0%)1 unemployed, 34 (22.1%) housewife, 22 (14.3%) were businessman and 19 (12.3%) patients were connected with others occupation.

Table III

Distribution of the study patients by types of ART received during study period (n = 154)

ART	n	%
First-line	142	92.2
Second-line	12	7.8
Total	154	100

In Table III out of 154 study patients, 142 (92.2%) received first-line ART. On the other hand, second-line ART was received by 12 (7.8%) patients respectively.

Table IV

Changes in selected haematological parameters before and after ART for 7-8 months (n = 50)

Haematological parameters	Before ART	After ART	p-value
Haemoglobin (gm/dl)	12.3 ± 2.1	13.2 ± 1.5	0.0154
ESR (mm in 1sthr)	33.5 ± 17.7	14.3 ± 6.5	<0.0001
TC of WBC (/cmm)	6934 ± 2125	7530 ± 2225	0.1739
N (%)	58.5 ± 12.4	55.5 ± 12.6	0.2330
L (%)	31.2 ± 11.5	34.5 ± 10.6	0.1389
Platelet count (10^9 /L)	265 ± 83	287 ± 67	0.1479
Hct (%)	37.3 ± 6.3	41.3 ± 4.6	0.0005
MCV (fl)	84.3 ± 8.1	93.5 ± 10.0	<0.0001
MCH (pg)	27.7 ± 2.7	29.8 ± 3.7	0.0016
MCHC (gm/L)	31.8 ± 1.3	32.9 ± 1.4	0.0001

Table IV shows the changes in haematological parameters before and after 7-8 months of ART. The level of haemoglobin improved significantly from 12.3 gm/dl to 13.2 gm/dl (p = 0.0154), while ESR decreased abruptly from 33.5 ± 17.7 mm in 1st hr to 14.3 ± 9.1 mm in 1st hr at the end-point of study (p = <0.0001). Neutrophil decreased and lymphocyte increased to some extent, although the difference was statistically not significant (p = 0.2330 and p = 0.1389 respectively). The haematocrit (Hct), MCV, MCH, and MCHC changed significantly from their before ART figures to the end-point of the study (p = 0.0005, p = < 0.0001, p = 0.0016 and p = 0.0001 respectively).

Table V shows the changes in haematological parameters before and after 9-10 months of ART. The level of haemoglobin responded well (p = 0.0491) and ESR decreased appreciably from 40.0 ± 13.9 mm in 1st hr to 19.6 ± 17.2 mm in 1st hr at the end-point of the study (p < 0.0001). The total count of WBC did not show a significant response. However, neutrophil decreased insignificantly at the end-point of the study (p = 0.0279). All the red-cell indices like Hct, MCV, MCH, and MCHC improved significantly from their before ART figures to the end-point of the study (p = 0.0017, p = < 0.0001, p = < 0.0001 and p = 0.0001 respectively).

Table V

Changes in selected haematological parameters before and after ART for 9-10 months (n = 50)

Haematological parameters	Before ART	After ART	p-value
Haemoglobin (gm/dl)	12.7 ± 1.9	13.4 ± 1.7	0.0491
ESR (mm in 1sthr)	40.0 ± 13.9	19.6 ± 17.2	<0.0001
TC of WBC (/cmm)	6540 ± 2158	7190 ± 1606	0.0907
N (%)	60.6 ± 11.6	55.4 ± 11.7	0.0279
L (%)	30.6. ± 10.2	34.7 ± 10.5	0.0505
Platelet count (10^9 /L)	262 ± 69	278 ± 81	0.2903
Hct (%)	38.3 ± 5.4	41.6 ± 4.8	0.0017
MCV (fl)	84.9 ± 8.3	96.5 ± 9.3	<0.0001
MCH (pg)	28.0 ± 3.2	30.9 ± 3.5	<0.0001
MCHC (gm/L)	31.9 ± 1.6	33.1 ± 1.3	0.0001

Table VI

Changes in selected haematological parameters before and after ART for 11-12 months (n = 54)

Haematological parameters	Before ART	After ART	p-value
Haemoglobin (gm/dl)	12.8 ± 1.7	13.5 ± 1.6	0.0297
ESR (mm in 1st hr)	40.0 ± 17.1	18.0 ± 4.7	<0.0001
TC of WBC (/cmm)	6798 ± 1699	6462 ± 1040	0.2179
N (%)	58.4 ± 11.0	54.7 ± 11.5	0.0905
L (%)	32.6 ± 9.6	36.5 ± 10.2	0.0432
Platelet count (10^9 /L)	247 ± 68	302 ± 81	0.0002
Hct (%)	39.3 ± 5.0	42.3 ± 5.2	0.0028
MCV (fl)	84.6 ± 5.6	95.0 ± 12.7	<0.0001
MCH (pg)	27.8 ± 2.2	30.2 ± 4.4	0.0005
MCHC (gm/L)	31.8 ± 1.6	32.6 ± 1.5	0.0085

Table VI depicts the changes in haematological parameters before and after 11-12 months of treatment with ART. The level of haemoglobin increased significantly from 12.8 gm/dl to 13.5 gm/dl (p = 0.0297). The ESR decreased well from 40.0 ± 17.1 mm in 1st hr to 18.0 ± 4.7 mm in 1st hr at the end-point of the study (p = < 0.0001). Lymphocyte increased significantly during the same period of time (p = 0.0432). Platelet count also increased significantly (p = 0.0002). All the red-cell indices like Hct, MCV, MCH, and MCHC improved significantly from their before ART figures to the end-point of the study (p = 0.0028, p = < 0.0001, p = 0.0005 and p = 0.0085 respectively).

Discussion:

The study revealed that HIV infected patients were predominantly middle-aged (31-40 years) and young (d" 30 years old) comprising > 70% of the patients with the mean age of the patients being 35.5 ± 9.5 years (range: 20-60 years). The mean age was 34.5 ± 9.6 years among 250 HIV positive patients in a study by Parinitha and Kulkarni in India [3]. The mean age was 35.3 ± 9.5 years in another study in Bangladesh by Rahman et al. [22]. A male preponderance was evidenced in the study with the male-to-female ratio being roughly 3:1. In India, a study by Kathuria et al. [23] reported a male-to-female ratio of 1.5:1. Similar study in Bangladesh by Rahman et al. [22] reported male-to-female ratio roughly 2:1.

Majority (92.2%) of patients received first-line ART. However, 12 patients were switched to second-line ART due to virological, immunological or clinical failure. In the present study, there was significant improvement in haematological parameters (like haemglobin, ESR, neutrophil, platelet count and red cell indices) is noted after 7- 12 months of treatment with ART. There was significant change in haemoglobin level in all patients who received ART for 7-8 months, 9-10 months and 11-12 months. Although the significant level of neutrophil, lymphocyte and platelet count varies in different groups and this might be due to the different factors such as the difference in the study population, sample size, study design and anti-retroviral drug formulations. While many medications used to treat HIV-related disorders are myelosuppressive, the use of zidovudine is the most common cause of severe cytopenia[24, 25]. After initiation of ART the mean value of red cell indices (Hct, MCV, MCH and MCHC) increased significantly in overall and as well as in 7-8 months, 9-10 months and 11-12 months group, which act as evidences of step up of haemoglobin level following ART. These findings are consistent with other studies [15, 26, 27].

Although significant changes in haematological parameters are noted after 7-12 months of treatment with ART, no significant differences in changes were observed among the three different durations (7-8 months, 9-10 months, and 11-12 months) of treatment concerning these variables, indicating that duration of treatment does not have an impact on these haematological parameters. There is an impact of treatment, but not in the duration of treatment. Besides this, different ART does not have significant differences in changes in haematological parameters.

Limitations of the study:

Present study is not without limitation. The sampling method was purposive that might have led to bias.

Conclusion:

From the findings of the study, it can be concluded that HIV infected individuals are predominantly male,

middle-aged, and young. The most common haematological abnormality is anaemia which significantly reduced in percentage after a mean treatment period of nine and a half month with ART. The red cell indices like Hct, MCV, MCH, and MCHC are found low at the initiation of therapy but changed to normality with ART. The duration and types of ART do not have a significant impact on differences in changes in haematological parameters.

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CASE REPORT

IN THE DEEP SEA OF HYPONATREMIA: A CASE SERIES

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Abstract:

Hyponatremia is a matter of concern in clinical practice. Hyponatremia can be associated both low or high tonicity and even with normal tonicity. Although severity and morbidity varies widely but sometimes serious hazard can occur from misdiagnosis or late diagnosis. In these 3 case we will discuss different pattern of presentations of hyponatremia. Megestrol acetate is a synthetic progestin used to treat the symptoms of loss of appetite and wasting syndrome in people with AIDS-related cachexia, breast cancer or endometrial cancer. Herein, we report a case of 32 years' female presented with clinical and biochemical features of central adrenal insufficiency who was taking megestrol acetate chronically. Pituitary function was otherwise essentially normal. Another case about a 46 year old male who was getting treatment for schizophrenia and later found to have hypopituitarism. Our last case about a male of 35 years old who was also diagnosed to have pituitary insufficiency

Key words: *Hyponatremia, Pituitary insufficiency, Megestrol acetate, Adrenal insufficiency, ACTH suppression.*

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Introduction:

Hyponatremia is most frequently found electrolyte imbalance among the hospitalized patient[1]. When Sodium Concentration in the blood came below 135 mmol/1 it is defined as hyponatremia[1]. Dilutional hyponatremia is more common among the different classes of hyponatremia which is caused by water retention and promotes life threatening complications[2]. Among other the nonhypotonic hyponatremias are hypertonic hyponatremia, isotonic hyponatremia, and pseudohyponatremia[3].

The common causes of hyponatremia are due to renal sodium loss by use diuretic agents, adrenal insufficiency and by excessive sodium loss due to diarrhea, vomiting, congestive cardiac failure, renal failure, burns, primary polydipsia, SIADH[4,5]. When Sodium level is low it is unwise to only give treatment without finding the underlying cause. Sometimes even after searching cause could not be found. An approach to the diagnosis of hyponatremia needs conscious and sincere history taking including drug history, meticulous clinical examination of cardiac, pulmonary,

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renal, neurological system[13]. Along with all routine clinical investigations urine osmolarity, plasma osmolarity and 24hour urinary Sodium measurements is pivotal for diagnosis[13]. For the complete evaluation of hyponatremia imaging of brain, hormonal and hypothalamo-pituitary-adrenal axis is sometimes necessary[14].

Case reports:

Case 1:

A 32 years old normotensive, non-diabetic female admitted in hospital with the complaints of persistent vomiting for three months. Vomiting was non projectile that occurred 5-7 times daily. Vomitus contained clear watery liquid, which was mild to moderate in amount. There was no undigested food particles, it was neither bile stained nor blood mixed. It was not associated with abdominal pain, headache but she complained about anorexia. She also gave a history of recent 15 kg weight loss which was unintentional.

She gave history of taking different antibiotics, antiemetic for her illness. On examination, The patient was afebrile, with a blood pressure of 100/70 mmHg on sitting position which was 80/60 mmHg in standing position. She appeared restless, toxic, her mucous membranes were dry and there was poor skin turgor. Inspection of abdomen revealed mildly distended abdomen with wide striae's which were purple colored, more on peripherally. She was fully oriented and cardiac, pulmonary & musculoskeletal examination were unremarkable and there were no gross neurologic deficits. Abnormalities on the blood chemistry panel included a low sodium of 122 mmol/L (normal range, 136–145), potassium of 4.96 mmol/L (normal range, 3.5–5.10), low bi-carbonate of 19 mmol/L (normal range, 22-28), hemoglobin of 15.4 g/dL (normal range, 12-14.5), HCT of 48.20% (normal range-34-45), RBS 6 mmol/l. Urine RME revealed mild albuminuria, plenty of pus cell with severe ketonuria.

On further questioning her drug history revealed that ,10 months back she had taken 1800 mg megestrol acetate daily for about 3 months to improve her anorexia which was developed after death of her first child. The patient's last menstrual period 1 month back which was regular. She denied galactorrhea, headaches or vision changes. There was no family history of pituitary or adrenal gland disease and there was no hyper-pigmentation of the palmar creases or buccal mucosa. As the diagnoses considered by the admitting team was adrenal insufficiency, and a serum cortisol & ACTH level was drawn at 8:00 am the next morning. When the result returned at 0.88 mcg/dL &<1.00 pg/mL respectively, short synacthen test was performed at 8.00 am of next morning, which concluded central

adrenal insufficiency. Results of Short Synacthen test came positive for adrenal insufficiency. Other pituitary hormones were normal.

Oral hydrocortisone was started at a dose of 20 mg at morning and 10 mg at afternoon.

Within 24 hours, the patients' symptoms had improved and she appeared much more energetic; hydrocortisone was continued. The endocrine laboratory results are shown inTable 1. A magnetic resonance imaging (MRI) scan of brain with and without gadolinium revealed normal pituitary gland.

Case 2:

Mr Y, 46years old, normotensive, non diabetic, non asthmatic, non smoker and non alcoholic man got admitted to PMCH with the complaints of vomiting for 5 days . Vomiting was non projectile that occurred 5-7 times daily. Vomitus contained clear watery liquid, which was mild to moderate in amount. There was no undigested food particles, it was neither bile stained nor blood mixed. It was not foul smelling and not preceded by nausea. It was not associated with abdominal pain, loose motion, headache, blurring of vision, dizziness, vertigo, chest pain, fever. The patient had a history of recurrent episode of similar pattern of vomiting for several times in the last 18 years. About 18 years back when he was at Middle East he had his first episode of vomiting. That time after few days he started to talk irrelevantly with gradual development of disorientation. For this problem he was admitted to the nearby local hospital, then he was sent to Bangladesh after recovery. He failed to recall this incident in exact manner. In around 2005 ,along with vomiting he developed low mood, started to remain home all the time and avoided social gathering. After some days, he developed incoherent talks with violent behavior. With these problems, he got admitted to a private hospital in Dhaka, where he had been diagnosed as a case of schizoaffective mood disorder and was under psychiatric evaluation. When conditions still did not improve, he was consulted by a neurologist for better evaluation. Here, he had been diagnosed as a case of paranoid schizophrenia with recurrent hyponatremia due to salt-losing nephropathy. Fludrocortisone was added on his treatment. After receiving infusions and injections, his condition improved slightly but then again, the situation of his recurrent vomiting and immediate hospital admission repeated again and again. In addition to all these, he had a lower sexual drive due to decreased libido and erectile dysfunction. For further evaluation and treatment, he got admitted to PMCH on 30th Octobor 2021. On general examination, he

was apathetic, mildly anemic, non-icteric, with body built below average. His decubitus was on choice. He had no visible pigmentation. He had loss of hair in axillary area. His pulse was 76 beats per minute, blood pressure was 110/70mmHg in sitting position and 90/60mmHg in standing position. Examination of other systems revealed no abnormalities.

His investigations revealed severe hyponatremia (116 mmol/l), 24 hour urinary electrolytes within normal limit. Urine osmolality 212 mosm/kg, Plasma Osmolality 227 mosm/kg.MRI revealed Partial empty sella. No other significant abnormality in MRI Brain. Baseline cortisol found to be 0.76 mcg/dl (Normal range: 4.458-22.689 mcg/dl), ACTH 11 (7.2-63.98 pg/ml) and short synacthen test cortisol was 42.51 nmol/l (Normal: >690 nmol/l). LH 1.12 mIU/ml (2.0-12.0 mIU/ml), Testesterone 9.08 (Normal: 10.40-35.71 nmol/l).

After investigations he was diagnosed to have hypopituitarism.

Case 3:
Mr. Abdul Wadud, 35 years old normotensive, non-diabetic, non-smoker, non-alcoholic man admitted to PMCH with the complaints of vomiting for 10 days. According to the patient's statement, while he was in Oman he developed fever 12 days back. It was high grade, intermittent in nature, persisted for 2 days, not associated with chills and rigors, subsided after taking paracetamol and highest recorded temperature was 103°F.After 2 days, he developed vomiting, 3-4 times daily, projectile in nature, not preceded by nausea, occurred mainly after eating, contained undigested food particle. It was neither bile nor blood stained & wasn't foul smelling. At 3rd day of vomiting patient suddenly became unconscious & he got admitted at hospital in Oman. Unconsciousness was not associated with any episode of seizure, no frothy discharge from mouth, no H/O fall or trauma or any weakness of any specific side of the body. Within 2-3 hour of admission; he regained consciousness after receiving infusions and some injections. There was no confusion after regaining his sense. He stayed in the hospital for 2 days. With treatment, the frequency of vomiting decreased and he was discharged from hospital in 3rd November. Then he came back to Bangladesh on 6th November, 2021. He again developed vomiting in similar manner. For further evaluation he got admitted in PMCH on 8th November. There was no H/O abdominal pain, yellow coloration of skin, sclera or urine, cough, hematemesis, malena, headache, vertigo, chest pain, skin rash, swelling, voice change, palpitation, blurring of vision.

On query he said he had history of 4 kg weight loss in last two months which was unintentional and associated with anorexia. It was not associated with palpitation. He also stated that he felt extremely lethargic and sleepy for the most of the time in day for last 2 months. He also stated about developing intolerance to cold. On query he mentioned that he had decrease frequency of shaving for last 6 months. He also complained about less sexual drive in last 7 years but now the problem is increasing.

On general examination he was irritated, mildly anemic, non-icteric, with average body build. He has pigmentation over the nose & cheek. He has loss of hair in axillary & pubic area. His Bp was 110/80 mm of hg in sitting position & 90/70 mmhg in standing position. Examination of other systems revealed no abnormality.

His investigations revealed Severe Hyponatremia (108 mmol/l), Blood count, RBS was normal. MRI of Pituitary was also normal. His baseline cortisol was low 0.84(Normal range: 4.45-22.68 mcg/dl), ACTH 13.38(Normal range: 7.2-63.38 pg/ml), LH <0.2 (2-12 MIU/ml), FSH 0.32 mIU/ml(Normal range: 1.0-8.0 mIU/ml), in Short synacthen after 1 hour cortisol level were still below normal level 2.97 microgram/dl.

He was diagnosed to have hypopituitarism although the cause could not be evaluated because of economical limitations.

Discussion:
Recognizing the presentation of hyponatremia is crucial for appropriate diagnosis and treatment. Laboratory tests, including blood sodium levels and a thorough clinical evaluation, help determine the underlying cause and severity of hyponatremia. Treatment focuses on addressing the underlying cause and correcting sodium levels, often through fluid restriction, adjusting medications, or using intravenous saline solutions in severe cases. At 1st case we have found that megestrol acetate causes adrenal insufficiency which in turns causes hyponatremia. Megestrol acetate agent often used in the treatment of certain conditions such as advanced breast cancer, endometrial cancer, and appetite stimulation in patients with cancer-associated anorexia and cachexia. While not a common side effect, there have been reports of megestrol acetate causing hyponatremia (low sodium levels) in some individuals[6]. This occurs due to the medication's potential to influence water and electrolyte balance in the body. Megestrol Acetate is a synthetic progesterone which use for treatment of anorexia in patients with AIDS and malignancy[6]. As it cross reacts with glucocorticoid receptor its increase appetite with a unknown

mechanism[7]. In case of sudden cessation of of MA it can cause AI[8]. Our patient presented with persistent vomiting and she used to take megestrol acetate without any proper indication and she was not on regular follow up of any physician. Hence she developed adrenal insufficiency which caused all her symptoms. There are few reported case of AI with megestrol acetate. A case was reported that a female came with nausea and generalized weakness later diagnosed to have adrenal insufficiency who was taking megestrol acetate hiddenly[10]. They have confirmed it by urinary glucocorticoid screening[10]. The admitting team in this didn't do glucocorticoid screening as the history of the patient and laboratory findings are consistent with the diagnosis.

The 2nd and 3rd we discussed presented with hyponatremia with underlying hypopituitarism. It is not uncommon to have hyponatremia in patients with hypopituitarism. Sometimes it could be the early presentation of the disease who has undiagnosed hypopituitarism[11]. Although it is not known that this hyponatremia is caused by hypersecretion of ADH[12]. The patient (2nd case) presented with repeated history of hyponatremia when he was also diagnosed to have schizophrenia and was under anti psychotic drug. The admitting team initially thought it was a case of SIADH. Later after biochemical investigations it revealed patient had hypopituitarism although the MRI was apparently normal except partially empty sella and other cause was yet to be evaluated due to limitations. According to a reported case, a 69 year old male presented with lethargy and hyponatremia who was initially thought to be having SIADH but even with correction hyponatremia was not corrected and later that patient found to be having hypopituitarism with underlying pituitary macroadenoma[13]. The discussing 3rd case also has underlying pituitary insufficiency who presented with hyponatremia. The admitting team follows the protocol and found to have hormonal deficiencies and treatment started accordingly.

Conclusion:
The cause of hyponatremia is like Pandora Box. The purpose of this case report is to let clinicians know to look for the cause vigorously when the cause is hidden under sea.

Conflict of Interest:
The authors stated that there is no conflict of interest in this study

Funding:

Ethical consideration:
The study was conducted after approval from the ethical review committee of Popular Medical College. The confidentiality and anonymity of the study participant was maintained.

Consent:
For the purpose of publishing this case report and any related photos, the parents are written informed consent was acquired.

Acknowledgments:

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CASE REPORT

DENGUE AND MALARIA CO-INFECTION IN A YOUNG ADULT WITH ATYPICAL FEATURE

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Abstract:

As an endemic zone, malaria and dengue coinfection can be expected in Bangladesh, although there have not been enough case reports of such coinfection. We describe apreviously healthy 22-year-old male from Dhaka, with a history of travelling to Coxs-Bazar3 weeks ago, presented with fever with chills and rigors, generalized weakness and cough for 2 weeks. Clinical examination showed tachycardia, hypotension, subconjunctival haemorrhage and positive tourniquet test. Lab reports showed NS1-Ag positive, thrombocytopenia, progressive anaemia, mild hyperbilirubinemia. He was treated initially for dengue haemorrhagic fever. His laboratory parameters started improving; however, he had persistent fever with chills and rigors daily and persistent coughing. Peripheral smear for Malaria showed schizonts and trophozoites of Plasmodium falciparum and ICT for malaria was positive. He recovered following treatment with IV fluids and oral artesunate. The presence of fever even in a critical phase of dengue, the typical rise of temperature daily, progressive anaemia, mild jaundice and specific travelling history gave a clue of coinfection with Malaria. On follow-up, after 2 weeks, he had no symptoms, and all the laboratory parameters were normal.challenge was the atypical features like dry cough and exertional dyspnoea. The timely diagnosis and appropriate treatment were crucial for prognosis of this patient.

Keywords: *Plasmodium falciparum, Dengue, Coinfection, Prognosis*

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Introduction

Mosquito borne infections like dengue and malaria are common in Southeast Asia, especially in Bangladesh. However, coinfections with these two diseases are rarely found because differences in the vector.Immunity also play a role in such endemic area [1]. Less diagnostic facilities in this part of the world lead to non-reporting of such cases. Delay in diagnosis and appropriate treatment in Dengue and malaria coinfection may increase morbidity and mortality [2]. Earlier there have been reports of concurrent infection of dengue virus with a flavivirus, Chikungunya [2] and with different bacteria including *Salmonella Typhi* [3] *ShingellaSonnei* [4] and *Leptospira* spp[5]. The first case report of dengue malaria coinfection was from France in July 2005. However, the cases about coinfection of those two pathogens were reported rarely since 2005 [3,4] Despite being the endemic zone, unfortunately, there have been very few case reports on dengue and malaria coinfection from the Southeast Asian countries [3] . *Falciparum* malaria has the highest incidence and

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mortality rate in malaria infection[7.] So, these confections especially with *Falciparum* malaria need early diagnosis and prompt management.

Case report:

We report a case of a 22-year-old male, student from Bangladesh, a resident of Dhaka, with a history of travelling to Coxs-Bazar, Bangladesh, 3 weeks ago. He did not receive any malaria prophylaxis before travelling to Coxs-Bazar. On admission, he presented with fever with chills and rigorsfor 5 days, with highest-recorded temperature was 105°F. He also complained of cough which was dry and was associated with exertional dyspnoea. He also mentioned of occasional gum bleeding within this period. On examination, He had tachycardia of 104 bpm and BP = 100/60 mm Hg. The tourniquet test was positive and subconjunctival haemorrhage was seen. His laboratory reports are shown in Table 1. Positive NS1-Ag, progressive thrombocytopenia, progressive anemia, reticulocytosis, mild hyperbilirubinemia, increased creatinine wasnoticeable. Ultrasonography abdomen showed spleen of size 12 cm and mild ascites. He was admitted with the diagnosis of dengue haemorrhagic

fever and was being treated accordingly. The patient became hemodynamically stable with 1 L of bolus normal saline. We continued adequate hydration, and repeated this daily. He was hemodynamically stable from 2nd day of admission; however, his Hemoglobin was gradually decreasing from 13.2 to 9.5 g/dl. Though other laboratory parameters were improving gradually, he was complaining dry cough which was associated with exertional dyspnoeaand a fever of 102–103°F with chills and rigors daily at around noon. His urine culture and blood culture reports were normal. Chest X-ray was normal.

We could not detect any other focus of infection. As we noticed the progressive reduction of Hb, then we did his peripheral smear for Malarial parasite during the peak of fever and sent immunochromatography test (ICT) for malaria. The peripheral smear for the malarial parasite report showed schizonts and trophozoites of *P. falciparum* as shown in Fig. 1. We started oral artemether-lumefantrine combination (Coartem) according to guideline. Fever started to subside on the 2nd day and fever did not rise after completion of 3 days course. On follow-up after 2 weeks of discharge, he had no symptoms and all the laboratory parameters were within normal range.

Table I

Laboratory parameters

| Lab parameters	Day 1	Day 2	Day 3	Day 4
Hb(g/dl)	13.2	11.2	10.0	9.5
Hct(%)	45	39	35.2	36.1
Total leukocyte counts(/il)	5500	5700	6800	7400
Differential leukocyte count	N45L46M08E01	N44L47M08E01	N74L21M04E01	
N76L17M04E03				
Platelets(/il)	90	000	29000	33
000	39	000		
Urea/creatinine(mg/dl)	1.2	1.6		
Bilirubin:	2.1		2.4	
ALT/AST/ALP(U/L)	42/47/160		53/123/28	
NS1 Ag/IgG, IgM for dengue	**Positive**/negative			
Blood C/S	Negative			
Urine C/S	Negative			
Chest X-ray P/A view	Normal			
ICT for malaria	Positive			
ICT for Kala-azar	Negative			
USG of whole abdomen	Mild Ascites, Splenomegaly (12 cm)			
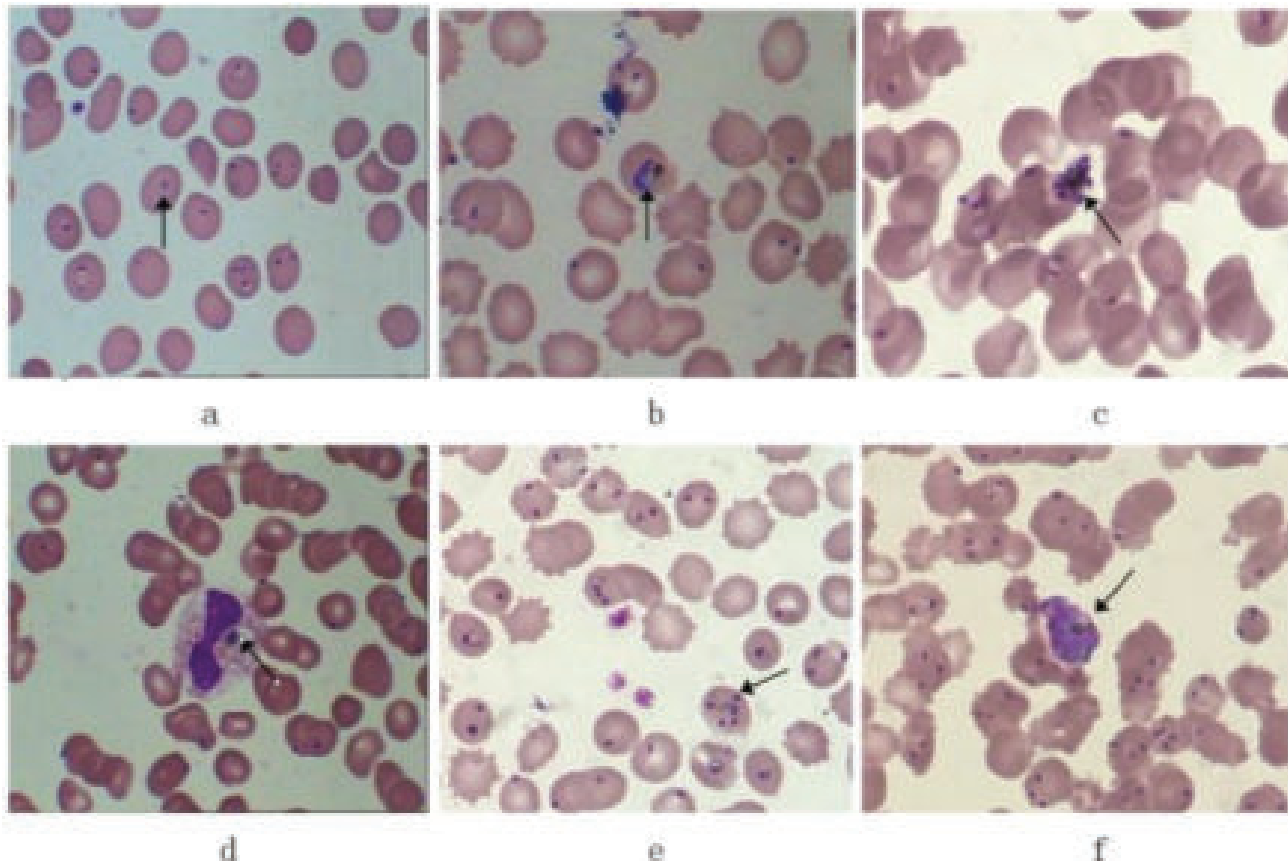
Figure 1: *The microscopic examinations of peripheral blood smear of Plasmodium falciparum infection (Wright's staining, ×1000)*

Notes: a. Early trophozoites; b. Big trophozoite; c. Schizonts; d. Malaria pigment; e. Early trophozoites ; f. Mixed metabolites

Discussion:

Overlapping of clinical features in concurrent infection with two different infective agents leads to a diagnostic challenge to the physician. In addition, a coinfection may be more severe [8].Usually in critical phase, dengue patients remain afebrile [9]. Persistence of fever in this period, guided us to consider associated other infection. The pattern of rise of temperature, specially peaking at night daily at a similar time along with progressive reduction of Hb and mild jaundice, all these features were suggestive of coinfection with malaria. Sometimes, these infections mimic features whichoften leadto missing of the coinfections [6]. Along with the fever, he was complaining of pulmonary symptoms like dry cough and exertional dyspnoea which led us to consider RTI or pneumonia initially. But chest examination and chest X-ray was insignificant [11] .Cough is associated with malaria sometimes but not common.Usually, the cough is dry and irritating. Most of the times, in acute febrile illness, we often draw conclusion to a single diagnosis even if we find atypical features and forget to look after the coinfections [10].

The study of cases with coinfection may help us to avoid the diagnostic dilemmas. In patients residing or travelling in the endemic area of dengue and malaria, we should think of dengue malaria coinfection. If the clinical picture is not fitting well to the single diagnosis, early diagnostic and therapeutic interventionmay reduce the morbidity and mortality[12].

Conclusion:

Malaria and dengue are difficult to differentiate clinically as is emphasized by this case, yet the treatment of the illnesses is different and delay in appropriate therapy can be devastating, especially in malaria. It would be expected therefore that since both infections are endemic in our area, coexisting malaria and dengue infection could be common. We suggest that such concurrent infections should always be kept in mind by the physician while encountering such clinical situations as such mixed infections are likely to occur more frequently than reported in the available literature.

Consent:
For the purpose of publishing this case report and any related photos, the parents are written informed consent was acquired.

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CASE REPORT

PRIMARY HYPERALDOSTERONISM IS AN UNUSUAL CAUSE OF PERIODIC PARALYSIS: A CASE REPORT

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Abstract:
Primary hyperaldosteronism a synonym for Conn's syndrome is characterized by hypernatremia, arterial hypertension, and, in certain situations, potentially fatal hypokalemia. A rare class of neuromuscular disorders known as periodic paralysis (PP) is brought on by an affection of the skeletal muscle's ion channels. In patients with hypokalaemic PP, potassium levels are normal in between attacks, but they remain low in those with secondary hypokalaemic PP. Although secondary causes of PP have been documented in the literature, the majority of cases are hereditary. We report the case of a 46-year-old man who had a history of hypertension and was admitted to the neurology ward after experiencing sudden onset weakness in all four limbs, primarily affecting the lower limbs, two days earlier. This present case demonstrates a peculiar and severe primary hyperaldosteronism manifested by PP.

Keywords: *Primary hyperaldosteronism, Conn's syndrome, Periodic Paralysis. Hypokalemic periodic paralysis*

Introduction:

Primary hyperaldosteronism or Conn's syndrome is characterized by an independent and excessive production of aldosterone in the adrenal cortex[1]. It accounts for approximately 2% of cases of systemic arterial hypertension in unselected patients. Moreover, elevated renal potassium excretion can result in potentially severe and refractory hypokalaemia, which should always be ruled out in hypokalaemic hypertensive patients[3]. The clinical presentations of primary aldosteronism are headaches, paresthesia, muscle weakness, arterial hypertension, polyuria, and polydipsia, [2,3]

Hypokalemic periodic paralysis is a rare disorder characterized by transient attacks of flaccid paralysis of varying intensity and duration [4]. The condition has

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the potential to be life-threatening. Early detection and rapid diagnosis are crucial, as some of the underlying causes are correctable. Although mostly familial in etiology, several sporadic cases of different etiologies have been reported, including rare cause like primary hyperaldosteronism (PA)[5]. This article reports the case of a middle aged man presented as quadriparesis due to hypokalaemia as a result of PA.

Case report:

A 46-year-old male was admitted to the neurology department with the chief complaint of sudden weakness of all four limbs for the last 2 days. He had hypertension since last 5 years and irregularly on treatment. Weakness first appeared in bilateral lower limbs, symmetrical in onset and in next 6 - 8 h progressively involved upper limbs. There is also mild weakness of neck causing drooping of neck. He had no respiratory or swallowing difficulty no weakness facial muscles. On query, he had history of three episodes of limb weakness for last 3 years. Every time his weakness recovered completely with taking rest within a period of 2-3 days. His weakness was not provoked by rest following intense exercise or by a high-carbohydrate meal. He denied any history of upper respiratory tract infection and diarrhea. Patient denies any history of fever, joint pain, trauma, weight loss, heat intolerance, excessive sweating and polyuria. He denied any bowel, bladder involvement.

On physical exam, the patient's pulse rate was P: 70 b/min, regular, and his blood pressure was 220/110 mm of hg, with no postural drop. No thyromegaly or lymphadenopathy were appreciated. Cardiac examination revealed tachycardia with a regular rhythm and no murmurs. Examinations of the chest and abdomen were unremarkable. There were no deformities or edema of the extremities, and distal pulses were present and equal bilaterally. Neurologic examination revealed the cranial nerve intact. There was grossly flaccid paralysis of all extremities, which involved the proximal and distal muscles and included the hips and shoulders. Muscle powers in the lower and upper limbs were 2/5 and 3/5, respectively. Sensation was intact, but deep tendon reflexes were diminished.

Investigations revealed low potassium levels (1.34 mmol/L) and normal renal function, liver function, and thyroid function tests (Table 1). ECG findings revealed flattening of the T wave with prolongation of the PR interval and QRS duration, suggesting hypokalaemia (Fig. 1). Serum electrolytes suggested severe hypokalemia with metabolic alkalosis. Urinary chloride level was 36 mmol/L, urinary potassium 33 mmol/L, and urinary potassium 40 mmol/L, and serum PTH was 74.3 pg/mL. USG for abdomen shows bilaterally raised renal cortical echogenicity but no adrenal mass, and eGFR 53.. The patient was managed on the line of hypokalemic periodic paralysis with potassium supplementation. To rule out any possibility of Cushing's syndrome, the serum cortisol (Morning sample) level was found to be7.5 µg/dl (7.26 – 32.28 µg/dl)Case report:

Table - I

Laboratory test of Serum potassium , renal n, liver n and thyroid function

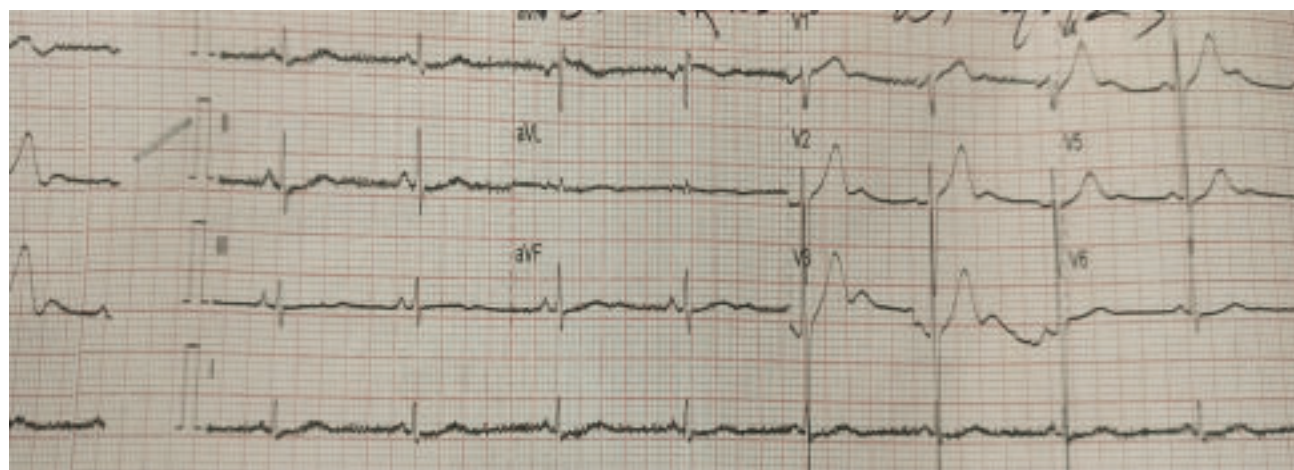| Sodium(Na+)	143.00 mmol/L	138.0 mmol/L	139.0 mmol/L	143.0 mmol/L	139
Potassium(K+)	1.34 mmol/L	2.0 mmol/L	2.2 mmol/L	2.6 mmol/L	3.6
Chloride(Cl-)	100.00 mmol/L	105.0 mmol/L	105.0 mmol/L	107.0 mmol/L	111
Carbondioxide(TCO2)	29.00 mmol/L	26.0 mmol/L			

Fig:1 *ECG finding revealed flattening of T wave with prolongation of PR interval and QRS duration suggestive of hypokalemia*

In view of hypertension, hypokalemia, metabolic alkalosis, and normal serum cortisol, serum aldosterone and plasma renin activity were measured after normalizing plasma potassium levels. Further laboratory studies revealed an elevated plasma aldosterone level, with renin activity levels being inappropriately reduced (Table 2).

Plasma aldosterone concentration (PAC) upright was 446.20 pg/ml (normal 30–400 pg/ml), plasma renin activity (PRA) was 1.02 pg/ml (normal 4.0–37.52 pg/ml), and the Aldosterone–Direct Renin concentration ratio (ARR) was 437.45:1 (primary aldosterism >91 pmol/L/μIU/ml). ARR are considered sensitive test and lack specificity. Upto 50% of elevated APR may be "false-positives". So we go for confirmatory testing; an aldosterone suppression test with a saline infusion test was done. Plasma aldosterone was found to be non-suppressible with a level of 495.40 pg/ml (normal 30.0–400.0 pg/ml, 5 ng/dL) after the saline infusion test (Table III).

To find out its cause, a CECT of the abdomen was performed. CECT of abdomen showed no adrenal adenoma or hyperplasia (Fig:2) . So the final diagnosis is Conn's syndrome with a rare presentation of quadriparesis and recurrent hypokalaemic paralysis. The patient was managed with spironolactone 100 mg and amlodipine 20 mg. The patient responded very well to treatment, and the patient's BP and serum K+ levels were well controlled with the drugs.

Table II
Laboratory test for plasma aldosterone level with renin activity levels

Test	Result	Reference value
Aldosteron	446.20 pg/ml	Early Morning :20.0 – 180.0 pg/mlUpright 2 hours :30.0 – 400pg/ml
Renin	1.02 pg/ml	4.0 – 37.52 pg/ml
Cortisol (Morning sample)	7.5 μg/dl	7.26 – 32.28 μg/dl
Serum Aldosterone(Upright)	446.20 pg/ml	Early morning: 20-180 pg/mlUpright 2 hours: 30-400 pg/ml
Plasma Direct Renin Concentration(fasing)	1.02 pg/ml	4.0 – 37.52 pg/ml
Aldosteron –Direct Renin concentration Ratio(ARR)	437.45 : 1	>91 pmol/L /μIU/ml : PrimaryAldosterinism probable

Table III
Results of saline suppression test.

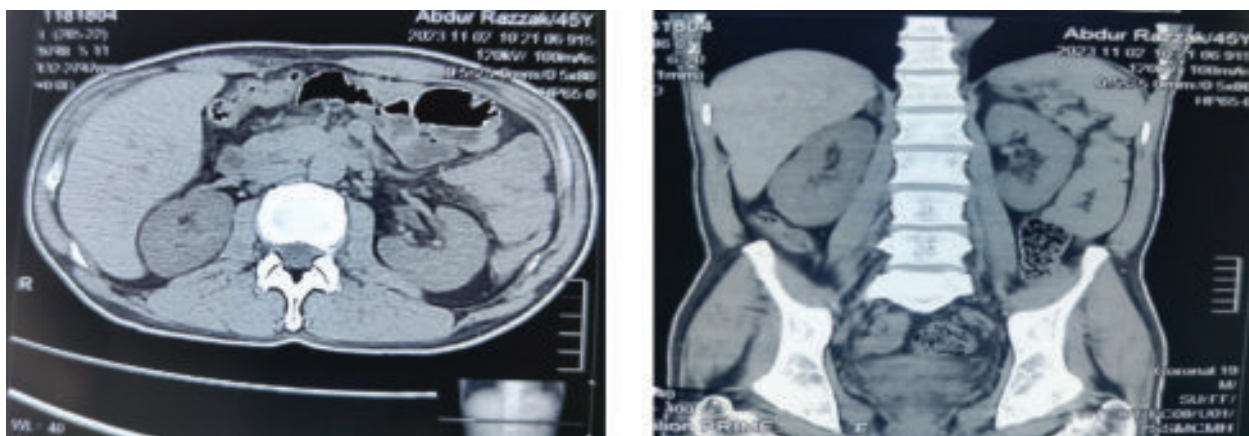| Test	Result	Normal rang Reference value es
Serum. Aldosterone(First sample-Before saline infusion)	633.90 pg/ml	Early Morning : 20.0 – 180.0 pg/mlUpright 2 hours : 30.0 – 400.0 pg/ml
Fasting plasma Renin	1.10 pg/ml	4.0 – 37.52 pg/ml
Serum Aldosterone(Last sample-After saline infusion)	495.40 pg/ml	Early Morning : 20.0 – 180.0 pg/ml Upright 2 hours : 30.0 – 400.0 pg/ml

Fig.-2: *CT features consistent with mild hepatomegaly tiny right renal calculi but no adreanal adenoma/ hyperplasia*

Discussion:

Periodic paralysis (PP) is a rare group of neuromuscular diseases that occur due to the affection of the ion channels of the skeletal muscle. Typically, blood potassium levels are used to distinguish between hypokalemic and hyperkalemic PP [6]It is estimated that 1 in 100,000 people have hypokalemic PP, however the precise prevalence is unknown [7]. Although secondary causes of PP have been documented in the literature, the majority of cases are hereditary. . THyrotoxic hypokalemic poisoning (PP) is the most commonly acquired form of secondary PP and a rare but potentially fatal complication of a thyrotoxic state[8]

This case illustrates the uncommon case of a middle aged man with poorly controlled HTN and PA diagnosis after three episodes of severe hypokalemia. Once described as a rare disease, PA diagnosis has increased prevalence mainly due to wide screening in hypertensive patients [6].

PA diagnosis was formerly thought to be an uncommon disease, but it has become more common as a result of widespread screening for hypertensive patients 8.PP episodes can last anywhere from a few minutes to several days. While the majority recover on their own, severe potassium deficiency can result in tetraplegia, respiratory muscle failure, and/or fatal arrhythmias [6,7].

As demonstrated in this case report, early causal investigation for hypokalemia while treating the electrolyte disturbances is fundamental. The most common causes include excessive thiazide diuretics use, laxatives, diarrhea, and vomiting episodes . Renal loss of potassium also may occur with Type I and Type II renal tubular acidosis. Other rarer etiologies like thyrotoxic periodic paralysis, Andersen-Tawil, Batters, Gilteman syndromes, and familial hypokalemic periodic paralysis should be evaluated if the initial diagnostic workup is unclear [9]. In the presented case, they were ruled out based on physical examination and laboratory results. Primary hyperaldosteronism, also known as Conn's syndrome, is the second most frequent endocrinopathy causing PP [8], when severe hypokalemia occurs, as in our case. This presentation is reported more frequently in East Asians and is very rare in Western countries [9]

The aldosterone-producing adrenal adenoma is the main cause of primary aldosteronism. Clinical manifestations include arterial hypertension, muscle weakness, headache, paresthesia, polydipsia, and polyuria [9]. The aldosterone to renin ratio is used to support the diagnosis (raised aldosterone levels with renin levels being normally low). Several confirmatory tests such as oral sodium loading test, saline infusion test, and furosemide upright test are used. CT imaging is helpful in detecting adrenal lesions but it carries significant false results: idiopathic adrenal hyperplasia or small adenomas (< 1 cm) can be falsely interpreted as normal in CT, and non-functioning adrenal macroadenomas can be misinterpreted as functioning tumors [10]. Adrenal Vein Sampling (AVS) may be required to confirm lateralization before surgery11. Additionally, surgical removal of the unilateral tumor has been shown to cure HTN in 50-60% of patients [11].

Patients with PA have higher cardiovascular and renal risks compared to patients with essential HTN, so early diagnosis is important to prevent comorbidities and mortality [7,8]. In our case CT scan is normal and there is no adenoma or adrenal hyperplasia, so did not go for AVS (Fig:2) and planned for medical treatment . Due to the higher cardiovascular/renal risk in patients with PA compared to those with essential HTN, early diagnosis is vital to prevent comorbidity and mortality[9].

Conclusion:

A high clinical index of suspicion of Conn's syndrome should be kept in every hypertensive and hypokalemic patients to make its early diagnosis. More importantly, the detrimental effect brought about by aldosterone in multiple tissues may go far beyond a pure complication from hypertension, and early treatment, surgically (adrenalectomy) or medically (spironolactone) will effectively relieve these adverse events and potentially prevent permanent end organ damage.

Ethical consideration:

The study was conducted after approval from the ethical review committee of Sir Salimullah Medical College. The confidentiality and anonymity of the study participant was maintained.

Consent:

For the purpose of publishing this case report and any related photos, the parents are written informed consent was acquired.

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PHYSICIAN ON PRACTICE

A PERSONAL JOURNEY IN PATIENT CARE

HAM NAZMUL AHASAN

To get the opportunity to wear the white coat with dignity and pride is an honor and privilege to get to serve the public as a physician. This separates this profession from others. A physician has qualities like well behaved, sincere, devoted, knowledgeable, skillful, honest, sympathy and empathy towards his patients. This is not easy. To become a good physician, he has to pass a long life with lots of sacrifices

In the realm of medicine, the essence of being a great physician extends beyond the clinical expertise to encompass a profound understanding of the patient as a whole. This realization became profoundly apparent to me during a winter morning round at Dhaka Medical College, an experience that left an indelible mark on my journey as a physician.

As I embarked on my rounds, accompanied by a freshly placed intern, the scene that unfolded before me was emblematic of the harsh realities faced by patients in resource-strapped environments. The hospital floor was flooded with a sea of patients, each vying for attention and care. Among them, I noticed a wife sitting stoically next to her unconscious husband, engaged in a silent battle with the biting winter cold.

Upon closer examination, it became evident that the patient's condition was dire, marked by the ominous signs of hepatic encephalopathy. What struck me further was the grim backdrop of their financial struggles – having already spent a significant portion of the meager 10,000 taka they possessed, a sum derived from renting their only property. The weight of their poverty hung heavy in the air, accentuating the urgency of the situation.

In this critical moment, I found myself at a crossroads, faced with the responsibility of making decisions that could profoundly impact the lives of both the patient and their family. I made a conscious choice to advocate for judicious resource allocation, advising my team against unnecessary investigations that could deplete the remaining funds. The following morning, I returned with the intention of offering some financial relief from our medical team to the grieving wife. However, fate had dealt a harsh hand, and the patient had succumbed to their ailment the previous night. The opportunity to provide immediate assistance had vanished, leaving behind a profound sense of responsibility and reflection.

This poignant experience underscores a fundamental truth in the practice of medicine – a great physician is one who transcends the boundaries of clinical diagnosis and treatment. It is an understanding that extends beyond the laboratory results to encompass the broader context of the patient's life. In the intricate tapestry of healing, financial, social, and emotional threads are woven together, each requiring the physician's attention and consideration.

As physicians, we are entrusted not only with the task of diagnosing and treating ailments but also with the responsibility of advocating for our patients' overall well-being. The importance of a holistic approach becomes apparent in situations where financial constraints dictate the course of medical care. In such instances, our decisions can profoundly impact not only the patient's health but also the trajectory of their family's future.

Sir William Osler said " The good physician treats the disease; the Great Physician Treats the Patient who has the disease". It is a testament to the transformative power of empathy, reminding us that the art of healing extends far beyond the prescription pad and stethoscope. In the heart of the physician-patient relationship lies the potential to create profound impact, fostering not only physical recovery but also contributing to the preservation of dignity and hope in the face of adversity.

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CLINICAL IMAGE

MEDICAL QUIZ: IMAGE-1

AKM MONWARUL ISLAM[1], HUMAYRA JESMIN[2]

A 55-year-old lady hypertensive, non-diabetic lady presented to a district hospital with central chest pain for 4 hours. Electrocardiography (ECG)was abnormal (Figure 1), and troponin I was raised. He was treated with streptokinase, and was referred to a cardiac hospital. There, she underwent transthoracic echocardiography (TTE) (Figure 2A), and cardiac magnetic resonance (CMR) (Figure 2B) during the index hospitalization. Her coronary angiography (CAG) revealed normal epicardial coronary arteries. She was treated with antiplatelets, statin, beta blocker, angiotensin converting enzyme inhibitor, spironolactone and anticoagulant. Her condition improved. Besides clinical parameters, she was followed up by repeat TTE after 3 months (Figure 2C).

Figure 1
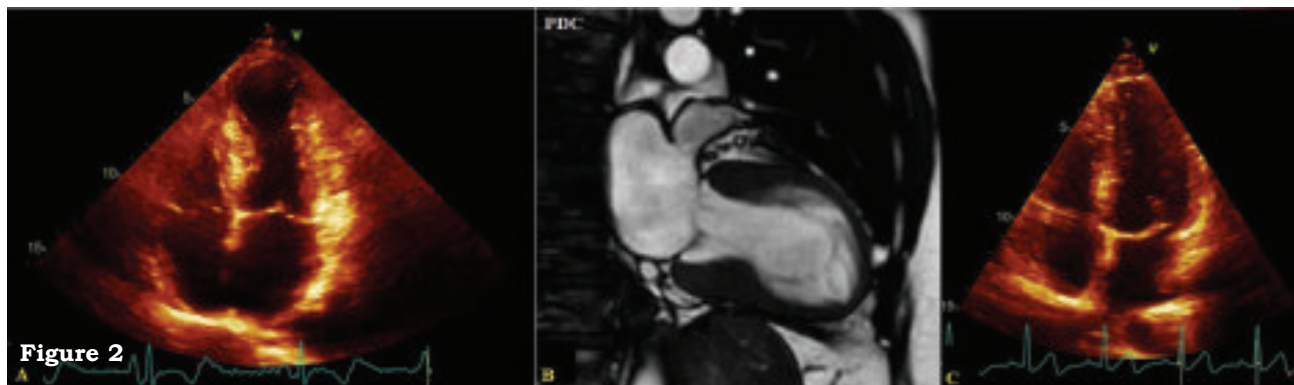
Figure 2

Questions:
1. What are the findings in resting ECG?
2. What is the single-most important observation in echocardiography during index hospitalization?
3. Mention the relevant finding(s) in CMR.
4. What is the clinical diagnosis?
5. Outline the pathophysiology of the condition.

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CLINICAL IMAGE

MEDICAL QUIZ: IMAGE-2

REFAYA TASNIM[1], QUAZI TARIKUL ISLAM[2]

A 57-year-old hypertensive, non-diabetic ex-smoker male presented with a history of productive cough and left sided upper back pain with radiation of the pain to the front of the chest and left shoulder and arm for last 3 months. The pain was gradual on onset and now persistent, moderate in intensity and unremitting in nature. He also lost a significant amount of weight over this period.

On examination, he was generally emaciated, mildly anemic and his vitals were within normal limit. He had left sided incomplete ptosis of recent onset; pupils were equally reactive to light and normal in diameter in both eyes. He also had left sided non-pulsatile engorged neck vein, there were no palpable peripheral lymphadenopathy. There was coarse crepitations involving whole lung field but most prominent over left apex with rhonchi. Neurological examination of upper limbs revealed intact sensory and motor functions.
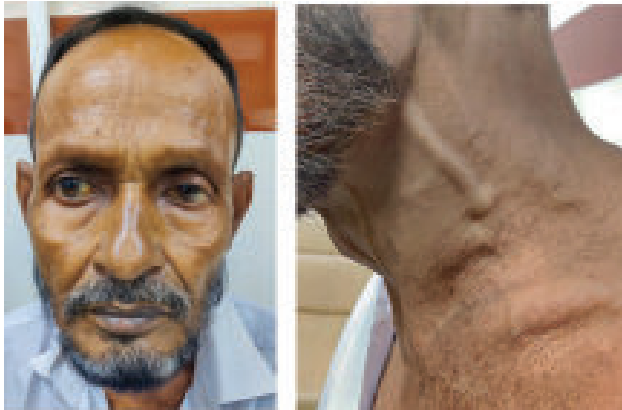
His full blood count showed, neutrophilic leucocytosis with markedly elevated ESR (100 mm in 1st hour), severe hyponatremia (117 mmol/L).
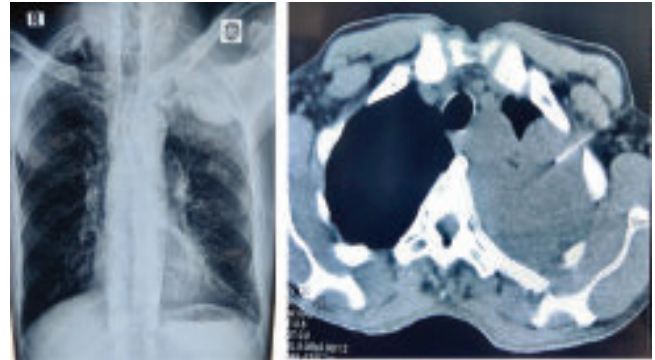
Question 01: Write the radiological abnormalities in the chest x-ray and the CT chest.

Question 02: Mention 4 clinico-radiological differentials for this case.

Question 03: What are the best diagnostic modalities?

Question 04: Mention 3 possibilities if this patient presents with seizure.

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Answer to Medical Quiz - 1

AKM MONWARUL ISLAM[1], HUMAYRA JESMIN[2]

Answers:

Q1. What are the findings in resting ECG?

ECG shows ST segment elevation and T wave inversion in precordial leads consistent with the diagnosis of acute ST-elevation myocardial infarction (STEMI).

Q2. What is the single-most important observation in echocardiography during index hospitalization?

Two-dimensional echocardiography apical 4-chmber view shows apical ballooning affecting the left ventricle.

Q3. Mention the relevant finding(s) in CMR.

CMR shows apical ballooningaffecting the left ventricle.

Q4. What is the clinical diagnosis?

Apical ballooning syndrome, takotsubo cardiomyopathy,stress cardiomyopathy,or the broken heart syndrome.

Q5. Outline the pathophysiology of the condition.

The exact pathophysiology of apical ballooning syndrome is still unknown, however, the catecholaminemediated myocardial stunning is thought to underlie the condition.

Overview of apical ballooning syndrome.

Apical ballooning syndrome, also known astakotsubo cardiomyopathy, stress cardiomyopathy, or the broken heart syndrome, is a reversible cardiomyopathy often precipitated by a stressful event. The word 'takotsubo' comes from the name of a pot used by Japanese fishermen to trap octopuses. When the left ventricle changes shape, it develops a narrow neck and a round bottom resembling the octopus' trap. The catecholamine mediated myocardial stunning is thought to underlie the pathophysiology. Chest pain and dyspnoea often lead to the initial diagnosis of acute coronary syndrome. ECG may show transient ST elevation, and cardiac biomarkers including troponin I may be raised as well. Cardiac imaging, e.g., echocardiography and CMR reveal hypokinesia or akinesia of the mid and apical segments with sparing of the basal segments of the left ventricle. The epicardial coronary arteries do not have obstructive lesions in CAG. Supportive treatment, including prophylaxis for thromboembolism, leads to spontaneous recovery usually within months. Apical ballooning syndrome should be included in the differential diagnosis of an apparent acute coronary syndrome, especially when there is a stressful trigger.

Answer to Medical Quiz - 2

REFAYA TASNIM[1], QUAZI TARIKUL ISLAM[2]

Answers

Answer 01:

Chest x-ray PA view showing-

1. A well circumscribed homogenous radio-opaque shadow involving the whole of the left upper zone including apex.

2. Left costo-phrenic angle is mildly obliterated indicating mild effusion

CT scan of the chest axial view: showing dense homogenous consolidation with a biopsy needle in.

Answer 02:

Pancoast syndrome with SIADH due to-

• Bronchogenic carcinoma of left apical lung

• Tuberculosis

• Chronic lung abscess

• Carcinoid tumor

Answer 03:

1. CT/ USG guided core biopsy of the lesion and histopathological examination

2. MRI of the neck, chest and upper abdomen after the diagnosis to identify the extent of vascular and brachial plexus involvement.

Answer 04:

1. Severe hyponatremia

2. Hypercalcemia

3. Metastasis to the brain

Review:

Superior sulcus tumors (SSTs), also known as Pancoast tumors, are a clinically distinctive and difficult subtype of non-small cell lung cancer (NSCLC), accounting for fewer than 5% of all lung cancers[1].

Pancoast tumors, located peripherally, often lead to delayed diagnosis due to their minimization of typical lung cancer symptoms like cough, hemoptysis, and dyspnea[1]. Pancoast-Tobias syndrome is a clinical condition characterized by severe and unremitting shoulder and arm pain along with the distribution of the C8, T1, and T2 dermatome, Horner's syndrome, and atrophy of the intrinsic hand muscles[1,2].

Diagnosis involves mass biopsy, often through CT or ultrasound-guided fine-needle aspiration due to the peripheral tumor location. Fiberoptic bronchoscopy is effective in less than 30% of cases unless there is nodal involvement. Video-assisted thoracoscopy (VATS) or axillary minithoracotomy may be considered for tissue diagnosis when other methods yield negative results or to rule out pleural metastatic disease[1].

Pancoast tumors are typically classified as T3 or T4, with most being T3 due to chest wall or sympathetic chain invasion. T4 tumors extend to brachial plexus, vertebral bodies, and vascular structures. Prognosis is generally poor, especially with metastases to mediastinal nodes (N2 disease), resulting in less than 10% 5-year survival. 2013 ACCP guidelines recommend pre-surgery evaluation for N2/N3 disease via endobronchial ultrasound or cervical mediastinoscopy, even in the absence of involved nodes in CT or PET scans[1]. Despite surgery, quality of life is low, and the pain from the surgery can be crippling. Radiation therapy shows no significant improvement in locoregional recurrence or long-term survival[2].

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