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EDITORIAL

RECENT TREND IN DENGUE IN BANGLADESH

MD ROBED AMIN

Bangladesh is facing the onslaught of Dengue infection in 2023 with an impact of huge mortality and morbidity. Although dengue is an endemic disease in Bangladesh since 2020 with few thousand of admitted reported case and low case fatality rate (CFR), there has been few epidemics in between these long endemicity. The 2000, 2002, 2019, 2022 are the years where we observed epidemic situation with large number of cases and increased CFR.(Health emergency and operation control room report, DGHS)[1]This year seems to be heading towards breaking all the previous records in this respect. In 2023, we are observing hundreds of cases since January with occasional death but from June, the scenario changes abruptly due to unusual hot and humid condition of climate changes and followed by premature rainfall leading to stagnant water source on the background of unplanned urbanization and huge infrastructure development around Bangladesh.

The fig 1 showed the current reporting of dengue syndrome from DGHS (10th August 2023) where it is seen the admitted patients in June, July and upto 10th august is 5956, 43854 and 26196 with increasing

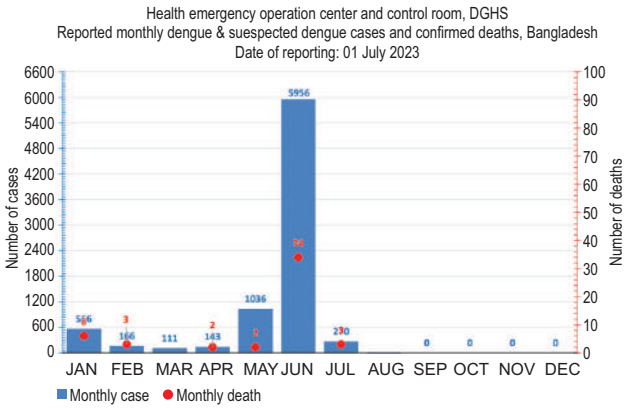

Fig 1: *The 2023 dengue report from MIS, DGHS showing month wise cases and death*

mortality. This year already 78028 patients were admitted in different health facility in Bangladesh with total mortality of 364. Although initially it was observed as Dhaka Metropolitan city is having highest case loads but later it was seen that spread of disease outside Dhaka become a predominant challenge. Currently there is almost half cases in Dhaka city and half outside of this city. Among the admitted case, 87% patients get discharged from hospital while CFR is 0.5% which is high above the national average death of 0.1% for last 20 years with an average 10000 patients admitted in a day around Bangladesh. Among the admitted cases, 67% is male, around 49% are within age group of 16-40 years and 44% of death is also observed in the age group of 16-40 years indicating the onslaught of this deadly virus among the active young generation[2].(Dengue 2023 Report — HEOC & CR, MIS, DGHS). The Fig 2 shows the month wise distribution is having raising trends and year wise there is variability of epidemic potentials due to covid 19 intervene and post covid consistent rising trends.

Although there are far more cases who are not captured within the report system, this trend is observed only in admitted cases (who are reporting) in public and private hospitals. Although dengue is a notifiable disease, the reports are not deriving from cent percent hospitals or facilities. The Dhaka city is providing report from 20 public facilities and 57 private facilities where 23350 cases with 208 death (CFR 0.89%)were observed in public facility while the privates have 16561 cases with 75 death(CFR 0.45%).This indicates the extreme burden in public facility with bizzare emergency system and hence raised mortality while the private system is also running very busy exhausting schedule of dengue patients with raised mortality. The outside of Dhakametropolitan city is even frustrating as few private facility is reporting while the capture from public facility is almost cent percent. The 38117 cases

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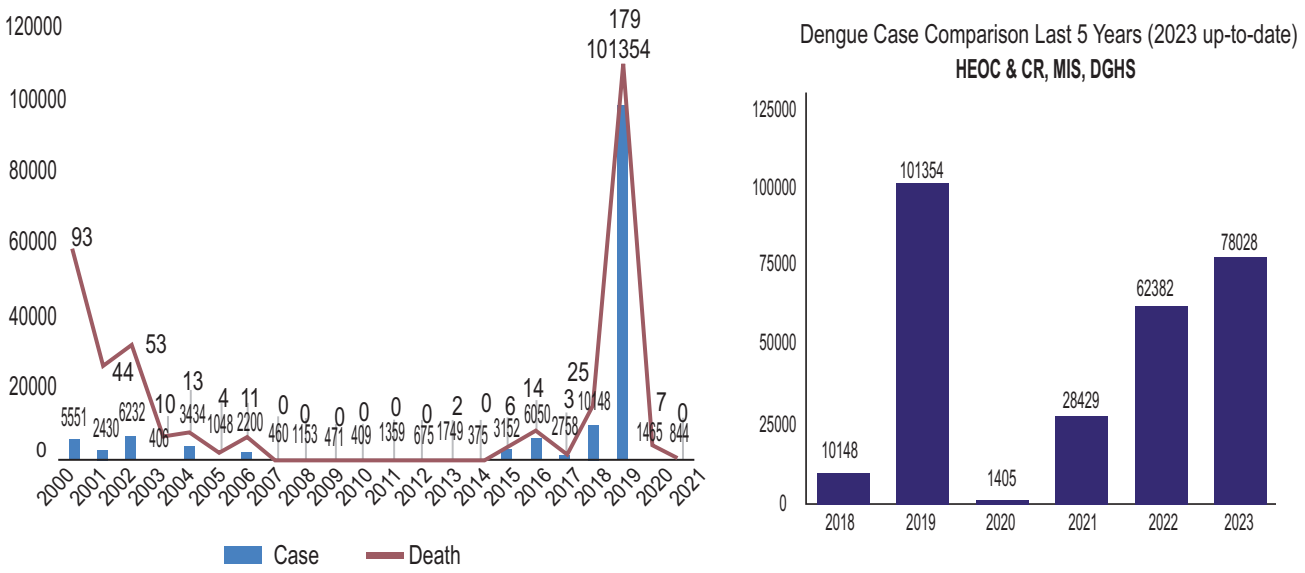

Fig.-2: *The dengue trends of morbidity and mortality from 200-2021 and comparison of last 5 years*

from outside Dhaka metropolitan city is having 81 death(CFR 0.21%) which is far low than Dhaka metropolitan city.

The raising trends of mortality and morbidity may have many reasons. There is also changing pattern of dengue syndrome that has been observed for last few years (2018 is the year where paradism was starting to shift).In 2018, the dengue outbreak was characterized by predominant

gastrointestinal symptoms (more than 60%) and 17.6% with hypotensionin adult cases[3]. Since then every year typical as well as atypical presentation in dengue was observed frequently in outbreak conditions. In 2019, Gastrointestinal(GI) features, including anorexia and/or vomiting (69.4%), abdominal pain (39.8%) and diarrhoea (25.6%), were more prevalent than typical rash and pain symptoms. Hypotension was present in approximately one-quarterof patients (25.4%)[4]. A decade analysis of dengue in Bangladesh revealed the changing trends of clinical features in dengue syndrome. Thrombo-cytopeniawas present in 66.1% of cases. Fever (100%) was common for all. Gastrointestinal (GIT) features, includingabdominal pain (86.5%), anorexia and/or vomiting (69.6%), and Diarrhea (>3 motions/day) (26.2%) were morefrequent than typical rash and other pain symptoms. Hypotension was present in approximately a quarter of patients(25%).[5] GIT features (anorexia, nausea, and/or vomiting) and hypotension were more common among adult participantswhile bleeding manifestation (melena and vaginal bleeding, p = 0.009 & 0.032) was more frequent in pediatricpatients. Compared to outbreaks of 2008, 2016, and 2018, increasing trends in GIT symptoms e.g. anorexia, abdominalpain, and diarrhea were observed. While a negative trend in hemorrhagic manifestations (skin rash, melena, and conjunctival hemorrhage/hemorrhagic sclera) and arthralgia/joint pain were found[5]. There was variation in mortality within this time frame also. Since 1998 to 2002, the CFR was 1.38% while the intervention by CDC, DGHS leads to decline mortality to 0.66% in 2000-2017 but since then, there is again raising of mortality observed (2018-2023). In last 20 years the mortality was more in male while in 2023 upto august, female fatality was observed more[1,2,5]. It was observed that 70% death happens within 24hours of hospital admission which is alarming and perhaps indicating the delay of admission by patients perspective and lack of quality emergency management system in Bangladesh especially in public hospitals.[2,5] It has been observed that there is a tendency in the private facilities to avoid the occurrence of any deaths to maintain their reputation and hence they refer more complicated cases to the public facilities to minimize the impact on their reputation. The Expanded dengue syndrome is also taking its role to show the atypical presentation of dengue since the transition of clinical entity observed since 2017.A 32 patients case series in one private hospital revealed 13 hepatitis n others, 9 myocarditis and others, 5 pancreatitis and others and 3 AKI.[6] In 2023, there is more description of encephalitis than previous years (Personal communication)

The epidemiology of DF/DHF is complex and remains poorly understood. It involves host, viral and vector status that are further influenced by demographic, economic, behavioural and varied societal factors. Epidemiologic transition was observed in 2014 when the seasonal variation was started to shift from purely monsoon based illness to endemic status. From 2000-2014, the seasonal rainfall and post rain season was responsible for 98% cases but since 2014, the intermittent rainfall at pre- monsoon pick up the trends at pre-seasonal cases which is augmented by poor urbanization and developmental work.[7] Climate changes starts to show its effect since 2014 as well as a strong and significant correlation with humidity and positive dengue cases ($p < 0.001$) and also showed a significant correlation with low and medium rainfall ($p<0.039$)[7].The climate information showed that the average rainfall, humidity, and temperature were comparatively higher in 2015–2017 than that of the previous years and this year 2023 the highest temperature and humidity was observed. These changes are an important niche to develop mutation in dengue virus and hence the burden of morbidity and mortality. Every year the CDC, DGHS perform the entomological survey at premonsoon. Monsson and post mosoon period and which clearly shows trends of shifting the season from July to October to all season. While the plastic drums (15%), buckets (15%), flower

tubs and trays (2%), and water tanks (0.77%) were commonly seen as outdoor or indoor reservoir of larva,[7] there is now new places like roof garden, the garage water lane where the density is even found more for *Aedes aygeptii.* The new area involves including the periurban and rural territory for dengue cases is marking fingers to *Aedes Albopictus* which may remain abundant in rural areas. The entomological survey at different region with exploration on *Aedes albopictus* is time demanding issue now.

The serotype of DEN 1 to DEN 4 were observed at different time in Bangladesh and also mixed or more than 2 serotype in same season was also seen. In 2019, when Largest dengue outbreak of the decade in Bangladesh history (more than 100000 admitted case) was seenwith high fatality may be due to reemergence of DEN-3 serotype in Dhaka, Bangladesh, necessitating immediate public health attention[8]. The presence of multi serotype and switch over to one predominant serotype to other may be an important reason to change the paradismshift to rural spread, seasonality and climate variability. Besides, Socio cultural and socio economic factors affecting vector longevity and survival is also an important reason. Studies in Thailand have revealed the following quantum of DHF risk with different sequences of dengue viruses with DENV 1/ DENV 2: 500 fold,DENV 3/DENV 2: 150 fold , DENV 4/DENV 2 equals to 50 fold risk. We need to explore similar viral genotype affecting time interval between sequential infections in Bangladesh.

Integrated vector management and important public health measurement is crucial to contain and control the dengue infection in a country. There is gross need of whole society and whole governement approach in multisectoral pathway to alleviate this serious public health issue in Bangladesh. The lack of coordination, inter- ministerial conflicts, peoples non-engagement, lack of community participation etc all are creating a non viable environment to control dengue in Bangladesh. A year through continued sustainable integrated vector and environmental management is the key to success for preventing the onslaught of dengue. Research contextualizing Bangladesh situation of dengue viruses with genotype and phenotype exploration, vector bionomics, the clinical situation, the epidemiology, the critical case management, death audit, the environmental niche, the vector containment innovation strategy (BTI, Woolbachiaetc), the vaccine and medicine trials etc are needed to develop evidence based policy for dengue control in Bangladesh. We must all realize that "Dengue is one disease entity with different clinical presentation and often with unpredictable clinical evolution and outcome."

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REVIEW ARTICLE

RENAL DISEASE IN BANGLADESH PERSPECTIVE

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Abstract:

Bangladesh is one of the most densely populated areas in the world. Renal diseases are increasingly recognized and encompasses a large share of the health sector. About 20 million people are suffering from chronic kidney disease, and of them, approximately 35,000–40,000 develop end-stage renal disease each year. Chronic glomerulonephritis, diabetes mellitus and hypertension are the principal causes of chronic kidney disease. Hypovolemia, sepsis, obstetric complications and drugs (including herbal and homeopathic remedies) are common causes of acute kidney injury. All three renal replacement therapy modalities (hemodialysis, peritoneal dialysis and renal transplantation) are performed in Bangladesh, yet only 25% of end-stage renal disease patients have access to treatment due to inadequate facilities and high healthcare costs. Nephrology as a specialty started its journey in 1973 in Bangladesh and now about 300 Nephrologists are managing the subject. Still there is huge need for more Nephrologists, as only one nephrologist is available for about every 0.8 million people. The country has improved financially from low- to low-middle-income country. Health sector is also more improving gradually. The government is now setting up renal care at rural level, introducing screening programs for early detection and prevention of kidney and other noncommunicable diseases. At the same time steps are under way to improve the advanced renal services at secondary and tertiary health institutes. Kidney transplantation started in 1982 and only live related transplantation are being done in several government and private organization. ABO-incompatible kidney transplantation has already been performed. Recently decease renal transplantation has also been performed. Research and training opportunities are expanding in collaboration with international organizations. Renal services appears up to date in this country but needs more and more enhancement to cope up the ever increasing burden.

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Introduction:

Nephrology, as a medical specialty, has evolved significantly in Bangladesh over the years. This review article aims to consolidate the wealth of knowledge provided by published literature on nephrology aspects in the country. It seeks to highlight the historical progression of nephrology and provide a comprehensive understanding of the challenges and advancements in this critical field of healthcare

History of Nephrology in Bangladesh:

In the vibrant journey of Bangladesh since its independence in 1971, the field of nephrology has undergone a remarkable transformation. Back in 1973, the pioneering presence of Professor Dr. Matiur Rahman, the country's lone nephrologist, marked the beginning of a medical revolution into Institute of Postgraduate Medicine and Research (IPGMR), now known as Bangabandhu Sheikh Mujib Medical University (BSMMU). The initiation of nine-bed

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nephrology ward in 1973 marked the beginning of a big growth in nephrology care. Joining the endeavor in 1981, Dr. Harun Ur Rashid, a postgraduate doctor in internal medicine, returned from the University of Newcastle Upon Tyne with a Ph.D. in nephrology. Together, these two dedicated specialists worked tirelessly to elevate nephrology from primary clinical care to kidney transplantation, touching lives across the nation.

1974 marked a defining moment when Intermittent Peritoneal Dialysis (IPD) emerged as a distinct treatment for End Stage Renal Disease (ESRD), catapulting nephrology into the realm of specialized medicine. The possibilities of hemodialysis (HD) had been attempted before, but it was only in 1986 that this therapeutic technique blossomed into a regular form of treatment, bringing hope to countless patients. The year 1982 witnessed a milestone event - the first successful live related kidney transplantation (KT), ushering in a new era of cutting-edge nephrological practice in Bangladesh. Noteworthy progress was further accentuated with the establishment of the Bangladesh Renal Association in 1977, a monumental stride towards the advancement of nephrology in the country. Scientific seminars in nephrology have since become an annual affair, attracting esteemed nephrologists from across the globe, making it a melting pot of knowledge and innovation.

The dawn of the '80s welcomed the birth of the country's sole nephrology journal, the esteemed 'Bangladesh Renal Journal (BRJ),' lending a platform for groundbreaking research and profound discoveries. The subsequent launch of postgraduate courses started in nephrology in 1986. Additionally, the Kidney Foundation, Bangladesh's Renal Registry, and data sharing with the United States Renal Data System (USRDS) contributed to global advancements.[1]

The tale of nephrology in Bangladesh is one of resilience, innovation, and compassion - a tale that continues to unfold, enriching lives, and reaching new heights of excellence with each passing year.

Acute kidney injury- Bangladesh scenario:

Incidence of AKI is poorly known because we do not have a national registry, there is no system of reporting, regional disparities and there is never a national or regional survey. There is difference in definition and case management protocols in the treating institutes. There is practically no referral culture and most of the cases come with delayed referral leading to poor outcome.

In one study 8.1% of the total hospitalized patients had AKI, and the death rate was 18.5%. In the same study out of 3764 patients in the ICU, 14% had AKI out of which 17.2% of the patients died.[2]

The causes of acute kidney injury are mostly medical, surgical and obstetrical causes are responsible in less than 25% cases. Pre-renal cause accounted for 63%, renal 19% and post-renal 18%. The most common etiology of pre-renal AKI was post-diarrheal hypovolemia, renal cause of AKI includes glomerulonephritis.[2] Recently AKI related to sepsis is an important issue in managing critically ill patients.[3]

Prevalence of CKD in Bangladesh:

Bangladesh, a densely populated developing nation in Southeast Asia, is witnessing a notable increase in the annual prevalence of chronic kidney disease (CKD). According to the latest WHO data published in 2020 Kidney Disease Deaths in Bangladesh reached 10,841 or 1.51% of total deaths. The age adjusted Death Rate is 9.14 per 100,000 of population ranks Bangladesh 143 in the world.[2] A global assessment encompassing multiple regions, including Bangladesh, approximated the overall CKD prevalence at 18%.[4,5] As part of the world warming Bangladesh is becoming the one of the worst countries to suffer the devastation. This country currently ranks 10th among the most vulnerable countries for a population with kidney ailments because of climate change. Research conducted in Dhaka city revealed a CKD prevalence of 26% among adults aged over 30,[6,7,8] while a study among urban Dhaka residents aged over 15 found a 13% prevalence.[9] A 2013 analysis of community-based prevalence data unveiled that one-third of rural individuals in Bangladesh were at risk of undiagnosed CKD [10]. It's highlighted that CKD prevalence varies among age groups, genders, socioeconomic conditions, and geographical locations. Those with CKD face a heightened risk of progressing to End-Stage Renal Disease (ESRD), which necessitates resource-intensive management like dialysis and kidney transplantation.

The prevalence of chronic kidney disease (CKD) in Bangladesh surpasses the global and even South Asian averages. This revelation raises an alarm, urging us to take notice. It becomes imperative for policymakers in public health and government officials to step in, addressing this critical issue head-on. The focus must shift towards controlling and mitigating the high risk of CKD-related disabilities, thus safeguarding the health and well-being of our population.

CAPD in Bangladesh:

Continuous Ambulatory Peritoneal Dialysis (CAPD) holds a significant yet underexplored status in the context of Bangladesh's healthcare landscape. Although the initial implementation of Continuous Ambulatory Peritoneal Dialysis (CAPD) in Bangladesh took place in 1982, there was a temporary pause due to shortages of peritoneal dialysis (PD) fluids. However, since 1992, nephrologists have consistently carried out CAPD procedures on a regular basis.

CAPD presents itself as a viable and patient-friendly option for renal replacement therapy, its utilization remains limited within the country. Challenges related to patient awareness, healthcare infrastructure, and trained personnel pose hurdles to its wider adoption.

Barriers of increasing use of CAPD in Bangladesh:[11]

- *Cost of Supplies*: The foremost concern in low- and middle-income countries (LMICs) is the substantial cost associated with peritoneal dialysis (PD) supplies. Importing dialysate fluid, a critical component of PD, often incurs high expenses. Bangladesh, levies an advanced income tax of 5% and handling charge 2% on these imports contributing to the overall expense. Trade value added tax is exempted.
- *Import Tax*: The high import taxes placed on PD supplies act as a significant barrier. In contrast, countries like Thailand, Malaysia, and Nepal have adopted a different approach, charging minimal or no import taxes on these materials.
- *National PD-First Program*: Implementing a national PD-first program has shown promise. This approach involves prescribing PD as the default treatment, with hemodialysis (HD) recommended only if PD is not suitable for the patient. This strategy, adopted in Thailand and Hong Kong, has resulted in a surge in PD utilization rates. The economies of scale generated by promoting PD adoption can significantly reduce the costs associated with PD supplies and equipment.
- *Lack of Trained Personnel*: A critical hurdle is the shortage of well-trained personnel capable of administering PD therapy. Both nephrologists and non-specialists can be trained to offer PD. However, efforts are being made to address this gap.
- *Nursing Shortage*: Nurses play a vital role in the success of PD therapy. However, their scarcity is evident in Bangladesh, where only around 15,000 are actively practicing [12]. Various organizations, including non-governmental entities, are attempting to bridge this gap through scholarship support. However, ensuring the long-term sustainability of such programs remains a challenge.

Despite these obstacles, a growing awareness of CAPD's advantages, such as increased autonomy and decreased dependency on healthcare facilities, is fostering interest among healthcare providers and patients alike. Initiatives aimed at raising awareness, building specialized centers, and training healthcare personnel could potentially contribute to a more robust presence of CAPD in Bangladesh, offering patients an alternative and flexible approach to managing their kidney health.

Renal transplantation in Bangladesh:

In 1982, a significant milestone was achieved in Bangladesh with the country's first successful donor kidney transplantation. Since then, more than 2,300 kidney transplants have been performed, marking a considerable advancement in renal care. In 2018, the introduction of ABO-incompatible kidney transplantation further expanded the possibilities in this field, with seven cases successfully executed.[13]

Despite these achievements, challenges persist in both living and deceased donor transplantation. Scarcity of living donors remains a primary obstacle due to a lack of awareness and fear of donation among potential donors. Moreover, the high cost of investigations, surgery, and immunosuppressive drugs, coupled with limited government subsidies, renders transplantation unaffordable for many patients. Additionally, the shortage of trained transplant physicians, surgeons, and nurses, as well as inadequate laboratory facilities, poses significant hurdles in the smooth execution of transplant procedures. These issues need to be addressed to enhance transplant services and provide better care to patients with end-stage renal disease (ESRD).

In the context of deceased donor transplantation, several challenges hinder its implementation. The lack of intensive care unit (ICU) infrastructure for identifying, declaring, and managing brain-dead donors is a crucial concern. Furthermore, insufficient awareness among the general population and healthcare professionals about deceased donation, combined with certain socio-cultural and religious beliefs, contributes to the scarcity of deceased donors.

To address these challenges, efforts are underway to raise awareness about organ donation in Bangladesh. Various programs and conferences have been

organized, involving healthcare professionals, the general public, Islamic scholars, and international advisors. Informational leaflets, posters, and donor cards have been developed to disseminate knowledge about the importance of organ donation.

To facilitate deceased donor transplantation, dedicated committees such as the Brain Death Committee and Organ Procurement Committee have been established. Moreover, training programs for transplant coordinators and grief counselors have been initiated to ensure appropriate support and care for both donors and recipients.

While living donor transplants have been the primary focus thus far, the collective efforts aim to pave the way for deceased donor transplantation in Bangladesh. By increasing awareness, enhancing infrastructure, and training healthcare professionals, it is hoped that deceased donor transplantation will become more feasible and accessible in the future.

Country's 1st Deceased donor transplantation took place in January 2023. Whenever the topic of organ transplantation arises, one name instantly comes toto the forefront: Sarah Islam. In a touching gesture, 20-year-old Sarah expressed her desire to donate her organs while on her deathbed, leaving a lasting impact. Sarah's kidneys and corneas were transplanted in four individuals. The collaboration between Bangabandhu Sheikh Mujib Medical University (BSMMU) and the Kidney Foundation made this accomplishment possible.

Human OrganTransplant Act of Bangladesh:

Under the *Human Organ Transplantation Act of 1999*, only close relatives are authorized to donate organs with the sole purpose of saving the lives of other close relatives. This category includes first and second-degree blood relatives, as well as spouses. First-degree blood relatives encompass parents, adult siblings, adult children, while second-degree blood relatives consist of paternal and maternal uncles and aunts. Spouses, encompassing both husbands and wives, are also recognized. Apart from these closely related individuals, no one was legally permitted to donate organs.

In January 2018, the government endorsed a series of amendments to several provisions of the existing law. The updated Act from 2018 broadens the definition of "close relatives" to now encompass third-degree blood relatives, expanding upon the existing donor criteria. In this expanded scope, third-degree blood relatives encompass individuals such as grandparents, grandchildren, and first cousins.[14]

In December 2019, the High Court of Bangladesh enacted a revision to the 2018 legislation, permitting individuals with established relationships beyond relatives to contribute kidneys as donors. This amendment was accompanied by a comprehensive nine-point policy. The revised regulations mandated thorough physical and mental evaluations, alongside an assessment of the "genuine emotional intention" behind known or connected donors' contributions. Additionally, prerequisites such as historical photographs, a three-year financial record to identify significant inconsistencies in income, and other protocols were introduced.[15,16]

Arguments for donation restriction:

Limitations on organ donation are often supported by several key points.

Corruption and Commercialization: Permitting organ sales might lead to a rise in human trafficking, a concern seen particularly in countries like Bangladesh. Even when people know each other, money might still be involved. Stopping secret deals is very hard.

Exploitation: If organs are bought and sold freely, weaker people might be taken advantage of. It's not just about money – imbalances in relationships can also lead to exploitation.

Government projects on Nephrology in Bangladesh:

- *Kidney Disease Prevention and Awareness Programs*: The government of Bangladesh has taken steps to raise awareness about kidney diseases, their prevention, and early detection. These programs aim to educate the public about risk factors, healthy lifestyle choices, and the importance of regular health check-ups.
- *Establishment of Dialysis Centers:*Government has decided to set up 10-bed dialysis centers at each 44 Sodor district hospitals across the country to provide essential dialysis services to patients with kidney diseasesalso to upgrade every medical college hospital with 50-bed dialysis centre. These centers will help to address the growing demand for dialysis and improve access to treatment.
- National Health Programs: Kidney health is integrated into the broader framework of national health programs in Bangladesh. These programs focus on providing accessible and affordable healthcare services to the population, including those with kidney-related issues.

- Increasing Manpower: Government has created for 3 dialysis technicians in every Sodor hospital dialysis center and 3 dialysis technicians for every medical college dialysis center.
- Capacity Building and Training: The government collaborates with medical institutions and universities to provide training and capacity-building programs for healthcare professionals, including doctors, nurses, and technicians. These programs enhance the expertise of medical professionals in diagnosing and managing kidney diseases.
- *Research and Data Collection:* The government supports research initiatives to gather data on the prevalence, causes, and outcomes of kidney diseases in the country. This information is crucial for developing effective strategies to address kidney health issues.

Nephrology trainings in Bangladesh:

In Bangladesh, postgraduate training in nephrology offers two types of courses: MD (Nephrology) and FCPS (Nephrology).

MD (Nephrology): Since 2009, MD residency courses began, focusing on practical training. Before that, only non-residency MD courses were available. Currently, only MD residency courses are available in many institutions like BSMMU, Dhaka medical college, National institute of kidney disease and Urology (NIKDU) and more. These courses last for 5 years, with 2 years in different medicine branches (Phase A) and 3 years in advanced nephrology training (Phase B). Renal transplant training and thesis work are included.

FCPS (Nephrology): After passing FCPS Nephrology Part 1, students undergo 2 years of medicine training before taking FCPS mid-term. Then, 3 years of advanced nephrology training with research work follows, accredited by BCPS in various hospitals. Dialysis and CAPD procedures are available in several institutions, while renal transplant is performed in select ones.

Presently, there are over 300 Nephrologists spread across the entire country, providing their expertise in each district of Bangladesh. Their services encompass the treatment of diverse kidney diseases, as well as the execution of critical procedures including kidney biopsy, vascular catheterization, intermittent peritoneal dialysis (IPD), and Continuous Ambulatory Peritoneal Dialysis (CAPD).

Renal care in private organization:

Bangladesh government through the public hospitals and institutes are gradually improving the Nephrology care countrywide but the bulk of the kidney care including dialysis and transplantation are now being provided by the private nongovernment organizations (NGO) and corporate hospitals. All types renal care is available in these corporate hospitals but beyond the reach of bulk population of the country. Different NGOs are serving the underprivileged citizens with affordable cost.

- *Gonoshasthaya Kendra*, a prominent non-profit organization in Bangladesh provides renal care with affordable cost. The center is the largest dialysis country, was founded with a clear objective: to make dialysis treatment easily accessible to individuals who require it. Operating under a non-profit model, they prioritize dialysis services at the lowest possible cost in Bangladesh according to financial ability of the patients. The treatment cost is according to a health insurance: poor will pay less and rich will pay more with same quality care for all. With highest number of hemodialysis machines, the center serves a substantial volume of patients, providing hemodialysis treatment to around 400 individuals daily. But it's not just about numbers — it's about the transformative impact on each person's life, on their families, and on the community as a whole. This initiative reflects their commitment to addressing the healthcare challenges faced by the underprivileged population in Bangladesh, particularly those suffering from kidney-related ailments.
- *Kidney Foundation:* The Kidney Foundation of Bangladesh is a nonprofit organization providing renal care at low cost and dedicated to quality services in kidney-related issues across the nation. Their efforts encompass a wide spectrum of activities, including offering comprehensive medical care such as dialysis and transplantation services, conducting awareness campaigns to educate the public, advancing research in kidney health, training healthcare professionals, advocating for policy changes, engaging with communities through outreach programs, and collaborating with international partners. Through these multifaceted initiatives, the foundation strives to prevent kidney diseases, improve treatment outcomes, and enhance the overall quality of life for individuals affected by kidney-related health challenges in Bangladesh.
- There are other small NGOs which are active in providing renal care especially dialysis services to the underprivileged population of the country.

Conclusion:

Nephrology burden of Bangladesh is huge and present resources are not sufficient. Every day there is upgradation of all modalities of renal care. As a developing nation Bangladesh is not lagging behind but needs more trained staff and resources to cope up.

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ORIGINAL ARTICLE

CLINICAL RELEVANCE, ETIOLOGY AND IMAGING CHARACTERISTICS OF CEREBRAL VENOUS SINUS THROMBOSIS AT A TERTIARY CARE HOSPITAL IN BANGLADESH

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Abstract

Background: *Cerebral sinus thrombus (CVST) is a rare form of stroke often affects young people with diverse clinical, etiological and radiological presentation. The aim of the study was to evaluate clinical relevance, etiologies, and imaging characteristics of CVST in Bangladesh.* ***Methods:*** *A prospective, observational study was done at a tertiary care hospital with patients recruited in the period of January 2021 to January 2023. 38 patients with clinical and radiological features suggestive of cerebral venous sinus thrombosis (CVST) were studied with thorough clinical evaluation and comprehensive work up.* ***Results:*** *The mean age of presentation was 28.42 years with female predominance (n = 24). Headache was the most common presenting symptoms (92%, n = 35) followed by vomiting (52%, n = 20). Hemi paresis (38%; n = 14) was the most common clinical sign followed by cranial nerve palsy (26%, n = 10). 31% of the patients (n=12) had provoked CVST among those the most common cause was found to be pregnancy/puerperium in 58% (n = 7 patients) followed by OCP which were 25% (n = 3). 69 % of the patients (n=26) had unprovoked CVST among those the most common cause was found to be prothrombotic conditions in 85% (n = 22 patients) followed by idiopathic which were 15% (n = 4). In magnetic resonance imaging venography (MRV), 74% of patients (n = 28) had thrombosis of transverse sinus, 53% of patients (n = 20) had thrombosis of the sigmoid sinus and 42% patients (n = 16) of patients had saggital sinus thrombosis.*

Conclusion: *Clinical presentation is variable, etiology must be determined, and diagnostic method of choice is MRV. Headache was most the common clinical presentation and the most common etiological factor is puerperium. Provoked CVST is more common than unprovoked CVST and transverse sinus thrombosis frequently involved.*

Key words: *Clinical relevance, Cerebral venous sinus thrombosis, Hemorrhagic infarct, imaging characteristics*

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Introduction:

Cerebral sinus thrombus (CVST) is a rare form of stroke that accounts for 0.5-1% of all strokes and often affects young people[1]. Overall CVST has an incidence of 0.22– 1.32/100,000/year.[4] It occurs more frequently in young adults in contrast to arterial stroke and three times more common in females than in males.[2, 3] The basic pathology of CVST is thrombosis of cerebral veins and the commonest site of origin is thought to be the junction of cerebral veins and larger sinuses.[4] Once a thrombus is formed in the cerebral or cortical veins, it can propagate and occlude large draining venous sinuses. This causes physiological back pressure in the venous system, leading to cerebral oedema and occasionally cerebral infarction and haemorrhage.[5, 6]

The variability of clinical pictures complicates the clinical diagnosis of CVST and sometimes leads to a high rate of suspicion in the diagnosis. In addition, there may be regional differences in the incidence of risk factors and clinical manifestations.[7] The clinical presentation of CVST is variable and categorized like this: symptoms and signs of raised intracranial pressure (ICP), a focal brain lesion, or both a focal lesion and raised ICP. Onset is also variable and up to 40% of patients can present acutely with a stroke-like syndrome within 48 h of symptom onset. [5] Headache is the most common symptom and is present in <"90% of cases; in 25% of patients, it is reported as the only symptom .[7] Given a lower incidence of headache in arterial stroke (25–30%), [8] the presence of severe headache in the context of stroke-like symptoms can raise suspicion of CVST. Seizures are also a presentation in CVST compared with arterial stroke (40% vs 6%). Focal neurological symptoms and signs are common, such as motor weakness (present in up to 40% of patients). [5] Cerebral venous sinus thrombosis can be provoked or unprovoked and numerous risk factors are reported in individual patients. Up to 90% of patients with CVST have at least one risk factor for venous thromboembolism (VTE), and thrombophilias (genetic or acquired) are detected in more than 30% of patients.[5] Female-specific risk factors are more important in younger age groups (ie oestrogen containing contraceptives, pregnancy and puerperium). [6]

Neuroimaging is important to the diagnosis of CVST and working with radiologists to identify the most appropriate imaging techniques is important. There are certain characteristics of parenchymal lesions that are suggestive of CVST, including bilateral or parasagittal lesions, lesions crossing arterial territories, and juxtacortical lesions.[9] Magnetic Resonance Imaging (MRI) brain with Magnetic Resonance Venography (MRV) is the current diagnostic modality of choice with very high sensitivity and specificity.[110] Management of CVST is focused on timely diagnosis and treatment. The current therapeutic options for CVST includes antithrombotic treatment with heparin overlapping with oral anticoagulants, thrombolysis (intravenous/local thrombolysis by selective sinus catheterization) and a combination of thrombolysis and anticoagulation.[11] Evaluation for an underlying pro-coagulant state may be rewarding for further prevention with long term anti coagulation. Outcome of CVST is a bit unpredictable, it is not unusual to see dramatic recovery in deeply comatose patient and, sudden worsening in conscious patients due to extension of thrombosis. [12] Early diagnosis and appropriate treatment of CVST is essential, as it may prevent morbidity and can be life saving.

On the contrary to the disease burden, there is a scarcity of data on CVST in Bangladesh. We therefore attempted to fill the gap to understand CVST in a Bangladeshi setting, by conducting this study at our referral center. Our aim was to see the clinical profile, etiological factors and imaging charecteristics CVST patients who were admitted at a tertiary care hospital.

Methods:

We conducted a single-center, prospective, descriptive study was carried out in the neurology department of BIRDEM General Hospital, Dhaka, Bangladesh. Study protocol was approved by the institutional ethics committee and only patients/next of kin who gave a written informed consent were included in the study. The study design was a prospective, observational study with patients recruited in the period of January 2021 to January 2023. A successive of 38 admitted patients in neurology department were included in the study initially based on the clinical profile of raised intracranial pressure and seizures with or without neurological deficits.

The diagnosis of CVST was made using established diagnostic criteria [13], which include (i) a clinical hypothesis of CVST (headache, focal neurological deficit and cranial hypertension) (ii) supported by neuroimaging showing a "delta sign" on cranial computed tomography (CT) scan and magnetic resonance imaging (MRI) or MR venography showing cerebral sinus or venous occlusion. Cranial hypertension was clinically diagnosed by neuroimaging. After diagnosis, all consecutive patients (aged 20–60 years) with confirmed CVST were

included in the study after obtaining written informed consent. Patients with clinical symptoms suggestive of arterial stroke or primary cerebral hemorrhage, aged 18 to 60 years, with sinusitis, intracranial space occupying lesions, metabolic encephalopathy, visual impairment due to optic nerve papilledema diagnosed by fundoscopy, or unenhanced CT showing the arterial region, infarction or hemorrhage were excluded from the study.

Neuroimaging was performed by experienced radiologists who were unaware of the patients' clinical signs and symptoms to avoid influencing the diagnosis. Magnetic resonance imaging (MRI) was performed on a 1.5 T machine (Philips). The MR scan protocol included an axial Fluid Attenuated Inversion Recovery (FLAIR), axial and coronal T2W, T1 3D sagittal. The location, extent and nature of abnormalities were recorded. Magnetic resonance venography (MRV) was used in both coronal and axial planes in the lower saturation band to eliminate signals from arterial structures.

All patients underwent complete blood count, routine blood biochemistry and coagulation profile, and routine laboratory tests for hypercoagulable conditions including protein C, protein S, antithrombin III, factor V Leiden, homocysteine, phospholipid bodies (APLA). Other studies were performed when necessary. Genetic tests were not performed due to financial constraints.

The data thus collected was entered into Microsoft Excel work sheets. Frequencies for the clinical features, etiology and radiological findings were analyzed. Statistical analysis was done via SPSS version 25 (SPSS Inc. Chicago, IL USA). Discrete variables were listed as counts or percentages.

Results:

A total of 38 patients were included in this study, 24 (63%) were females and 14 (37%) were males. The mean age of presentation was 28.42 years with female predominance (n = 24). Headache was most the common presenting symptoms (92%, n = 35) followed by vomiting (52%, n = 20). Most common pattern of headache was diffuse throbbing type (51%) followed by dull aching headache (22%). Hemi paresis (38%; n = 14) was the most common clinical sign followed by cranial nerve palsy (26%, n = 10). Among the cranial nerve palsy cases, upper Motor Neuron (UMN) seventh nerve palsy was present in 6 cases and bilateral sixth nerve paresis in 4 patients.

Table-I

Clinical profile of cerebral venous sinus thrombosis in study group.

Symptoms and signs	No. of patients	Percentage
Headache	35	92
Vomiting	20	52
Seizure	8	21
Altered Sensorium	12	32
Hemiparesis	14	38
Fever	4	11
Papilledema	7	18
Cranial nerve involvement	10	26
Dysarthria/aphasia	3	8

In Table II an etiological point of view, 12/38 (31%) had clear clinical triggers and were considered provoked CVT in this study. In this subset, pregnancy/ puerperium 7/12(58%), OCP use 3/12 (25%) and para infectious 2/12 (17%), were identified as risk factors for provoking CVT. The breakdown of para infectious CVST included mastoiditis (1 patient), bacterial meningitis (1 patient). In the other subset of unprovoked CVST 26/38 (69%) where no clinical triggers were evident, a standard procoagulant workup was done. In 22 (85%) of these cases a prothrombotic state could be identified.

Table-II

Etiologic profile of cerebral venous thrombosis in the study

Risk factors	No. of patients	Percentage
Provoked (12/38)		
Parainfectious	2	17
Pregnanacy/puerperium	7	58
OCP use	3	25
Unprovoked (26/38)		
Procoagulant conditions	22	8515
Idiopathic	4	

In Table: III This included Protein C deficiency in 9/ 22 (41%), Protein S deficiency in 7/22 (32%), APLA in 2/22 (9%) and Anti thrombin III deficiency 1/22 (5%). Some patients had combined pro-thrombotic states like combined Protein C & S deficiency in 3 cases. In the remaining 4/26 (15%) no clear clinical or lab abnormality could be identified and these were considered Idiopathic subset in this study. They may

have factor VIII elevation or genetic prothrombotic states like FVL (Factor V Leiden) or MTHFR (methylenetetrahydrofolate reductase) which was not tested for in this study.

Table III

Pro-coagulant conditions identified in unprovoked CVST

Procoagulant conditions (n = 22)	No. of patients	Percentage
Protein C deficiency	9	41
Protein S deficiency	7	32
APLA panel	2	9
At III deficiency	1	5
Combined Prot C & S Def	3	14

There were various MRI findings of CVST patients in which hemorrhagic infracts were 53%, and 18(47%) cases had dural and cortical CVST without parenchymal lesions as shown in Fig.-1.

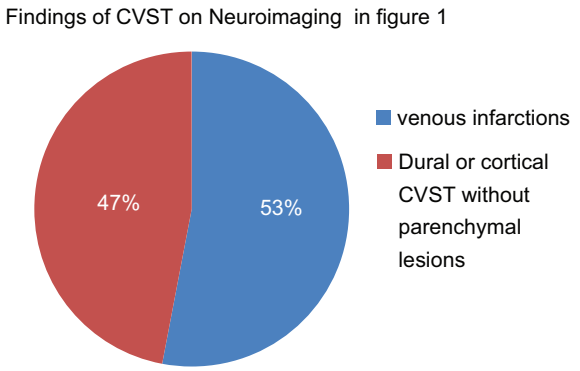

Fig.-1: *Findings of CVST on MRI of Brain.*

In Table IV 74% of patients (n = 28) had thrombosis of transverse sinus, 53% of patients (n = 20) had thrombosis of the saggital sinus thrombosis and 42% patients (n = 16) of patients had sigmoid sinus. 40% of patients (n = 15) had multiple sinus involvement.

Table IV

Sinuses involved on MRV in the study group.

Sinus involved	No. of patients	Percentage
Transverse sinus (TS)	28	74
Superior sagittal sinus (SSS)	20	53
Sigmoid sinus (SS)	16	42
Straight sinus	2	5
Cortical veins	1	3
Deep veins	1	3
Multiple sinus involvement	15	40

Discussion:

Cerebral venous sinus thrombosis, unlike arterial stroke, often occurs in young individuals.[14] Due to diverse clinical presentation, it is often a diagnostic challenge for the clinicians. Modern neuro-imaging techniques and diagnostic laboratory investigations are providing precious information about risk factors and clinical profile of CVST. In this study, we tried to highlight and compare its variable clinical presentations, etiological factors and neuro-imaging findings with other studies.

Comparing the age group involved, 20–40 years was the commonest age group involved in various studies with mean age of onset being 35 years. The present study also showed similar finding with mean age of onset being 28.42 years. Our study showed female preponderance (F: M – 1.7:1), in contrast to some other studies.[15,16] Headache was the most common symptom in the present study accounting for 92% of patients. Most common pattern of headache was diffuse throbbing type (56%) followed by dull aching headache (26%). Seizures are far more frequently seen in CVST than in arterial stroke. At times seizures are heralding symptoms in CVST and should arouse the suspicion of the diagnosis. In our study, 21% of cases had seizures which are comparable with another study.[12] The types of the seizures observed in the patients were generalized tonic-clonic (68%), focal with or without dyscognitive features (22%) and focal with secondary generalization (10%). 32% patients had altered level of consciousness at presentation, which is comparable with Vidyasagar S et al.[17] and Dhadke VN et al.[18] In this study, 11% patients had fever at the onset which is similar to findings of another study.[18]

Prothrombotic conditions are the most common risk factor identified for unprovoked CVST in published literature throughout the world. In the International study on Cerebral Venous Thrombosis (ISCVT) cohort[5], 34% patients had prothrombotic conditions, and 22% had underlying genetic prothrombotic states. However, we didn't find earlier published studies from Bangladesh that have information regarding these prothrombotic conditions due to paucity of laboratory data. Recently Pai et al.,[12] and Zhou L.-X et al.,[14] reported thrombophilia as a risk factor for CVST in 18% and 12.3% patients respectively. In our study 22/26 (85%) of the unprovoked CVST patients had predisposing thrombophilic conditions. Another study stated that, 29/36 (81%) of the unprovoked CVST of their patients had underlying thrombophilic condition.[19] This included Protein C deficiency in 9/22 (41%), Protein S deficiency in 7/22 (32%), APLA in

2/22 (9%) and Anti thrombin III deficiency 1/22 (5%). Majority of cases of CVST as recorded in published literature, have multifactorial etiology, which suggests that pro-thrombotic workup should be extensive. However, this is not always possible to do due to financial issues. In the present study, 12/38 (31%) had clear clinical triggers and were considered provoked CVST. In this subset, pregnancy/ puerperium 7/12(58%) were identified as risk factors for provoking CVST. Another study stated that, puerperal group consists of 4/15 (26%).[18] Among the cases of unprovoked CVT In 15% (4/26) of cases we were unable to find any cause even after procoagulant workup, this constituted Idiopathic cases in our study. They may be harboring some form of genetic thrombophillia like FVL or MTHFR mutation or Factor VIII elevation, but we could not test due to financial constraints.

In the present study transverse sinus was most frequently involved (28/38) 74% followed by superior sagittal sinus in (20/38) 53%, sigmoid sinus in (16/ 38) 42%, Straight sinus in (2/38) 5%, cortical veins alone in (1/38) 3% and deep veins in (1/38) 3% which is comparable with another study.[1] Another study done in India showed that, transverse sinus was most frequently involved (40/54) 74% followed by superior sagittal sinus in (29/54) 52%, sigmoid sinus in (27/ 54) 50%, Straight sinus in (4/54) 7%, cortical veins alone in (2/54) 4% and deep veins in (1/50) 2% in their study. [19] In the present study, 20 cases (53%) had venous infarctions on MRI brain, out of which 12 cases (60%) were hemorrhagic infarctions and 8 cases (40%) were non-hemorrhagic infarctions in a venous distribution. The remaining 18 (47%) cases had only dural or cortical CVST without parenchymal lesions. Similar observations were noted in other studies.[20]

Conclusion:

CVST is an under recognized cause of headache and stroke in young patients. Our study suggested that an essential clinical feature of CVST is the new onset of headache. The most common etiological factor is puerperium . Provoked CVST is more common than unprovoked CVST. It was also observed that the most common sinus involved in transverse sinus. So early diagnosis of CVST will help in planning for the appropriate management of the patients.

Limitations of the study:

This study was conducted in a single center. A complete thrombophilia evaluation could not be performed in every patient due to financial constraints and genetic study was not done.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

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

Funding:

This research received no external funding.

Ethical consideration:

The study was approved by the Ethical Review Committee of of BIRDEM General Hospital, Dhaka, Bangladesh. Informed consent was obtained from each participant or caregivers of the patients.

Author Contributions:

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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ORIGINAL ARTICLE

PATTERN OF ANAEMIA AMONG NON-HAEMATOLOGICAL MALIGNANT PATIENTS IN A TERTIARY CARE HOSPITAL: A CROSS-SECTIONAL STUDY

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Abstract:

Background: *Anaemia is a frequent complication in cancer patients and has been linked to a reduction in quality of life as well as a poor prognosis. Considering the paucity of dataregarding anaemia in non-haematological carcinoma in developing countries, this studyaimed to evaluate the pattern of anaemia in non-haematological carcinoma patients admitted in a tertiary care hospital of Bangladesh.* ***Methods:*** *This cross-sectional study was conducted over 56 adult anaemic patients of non-haematological carcinoma inDhaka Medical College Hospital, from 1st of September 2017 to 1stdecember 2017.After getting written informed consent, a detailed history, clinical examination and thorough investigation were carried out in each patient. All the methods in the present study were carried out following the ethical guidelines of the 1975 Declaration of Helsinki.Data were recorded in separated case record form and analyzed by IBM SPSS version 26.* ***Results:*** *The majority of the study participants were male (62.5%), aged >50 years (64.3%), and from rural areas (60.7%). Metastasis affected 50% of the research participants, and colorectal carcinoma (17.9%) was the most common type of non-haematological carcinoma. The majority of patients had moderate to severe (73.2%), hypochromic (62.5%), and microcytic (62.5%) anemia. In contrast to patients without colorectal cancer, those who had it were more likely to get severe anemia (p=0.001). In patients with metastasis, the likelihood of having hemoglobin below 10 g/dL was 11.27 times higher than in patients without metastasis (COR = 11.27; 95% CI 2.23-56.86).* ***Conclusion:*** *Maximum anaemic non-haematogical patients had haemoglobin <10 g/dL with microcytosis and hypochromia.*

Keywords: *Non-haematological carcinoma, Solid malignancy, Anaemia*

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Introduction:

Anemia is a clinical status indicated by a reduced red blood cell (RBC) mass together with low hemoglobin (HGB) and hematocrit levels.[1] Anemia is a critical issue for cancer patients since it has been linked to worse medical outcomes[2] and may worsen their already compromised health.[3] Anemia is expected to affect 30% to 90% of cancer patients at some point during their treatment.[4–6]The occurrence of cancer-related anemia varies according to the nature, stage, duration and spread of the malignancy, as well as the type and timing of therapy.[7] In a meta-analysis, anemic patients with lung cancer, cervico-uterine carcinoma, head and neck cancer, prostate cancer had shorter survival times than those without anaemia.[8] It is an indicator of poor prognosis in T1-T2 squamous cell carcinoma of the glottic larynx.[9]

As Malignancy results by uncontrolled division of cells and the ability of these cells to invade other tissues, either directly or by metastasis, therefore, different types of cancers present differently and in diversified manner.[10] An abnormal hematological picture may be the first manifestation of many non-hematological malignancies.[11] In addition, anaemia is a recognized complication of myelosuppressive chemotherapy, and it has been estimated that around 1.3 million cancer patients who are not anemic at the time of diagnosis may acquire anaemia during the course of their disease in the United States.[12] Most studies have found that pre-treatment anaemia is an important predictor of prognosis, survival, and disease free period.[13]Grigieneet al. and Zhang et al., in their study found that the hemoglobin (Hb) level before treatment had a significant influence on overall survival, disease-free survival and local relapse-free survival in uterine cervical carcinoma treated with irradiation[14] and Breast Cancer[13], respectively.

The cause of anaemia in cancer patients is diverse and frequently complicated. It may be the result of malignancy itself, acute or chronic blood loss, hemolysis, marrow suppression from medication, or chronic illness anaemia.[15] Besides, iron metabolism disorders, bone marrow insufficiency or infiltration, malnutrition, tumor catabolism, and erythropoietin deficiency also play key role in anemic pathogenesis.[11] In addition, interaction of immune system with iron metabolism and erythropoiesis is known to be an important factor in the development of anaemia in cancer patients.[16]

On the whole, cancer-associated anemia confers general adverse consequence mainly in anemic patients with lung, prostate, or head and neck cancers or lymphoma, which have a substantial decrease in survival time compared to their nonanemic counterparts.[7] Therefore, It is essential to recognize the incidence and severity of anemia among cancer patients to support the most appropriate treatment plans. Several studies have undergone to examine the relation of anaemia with hematological malignancies. However, study regarding anaemia or hematological presentation of non-haematological malignancies are scarce, and hence, this study was designed to evaluate the pattern of anaemia in non-haematological malignancy patients admitted in a tertiary care hospital of Bangladesh.

Methodology:

Study design, settings and sample:

This descriptive cross-sectional study was conducted in the departments of medicine, surgery and oncology in Dhaka Medical College Hospital, a tertiary care center of Bangladesh. The study data were collected between 1st Sept 2017 to 1st December 2017.Based on the number of patients admitted per month, an estimated participation rate of 50%, and the time allocated for data collection, we finally recruited a convenience sample of 56 adult anaemic patients from aforementioned departments of the study site, who were admitted due to any type of non-haematological carcinoma. Patients who were severely ill and having other associated diseases responsible for anaemia, were excluded from this study.

Data collection procedure:

After admission of an anaemic patient with non-haematological carcinoma in the hospital ward, the case was immediately assessed by the indoor medical officer and the principal investigator (PI) was informed. The PI then immediately examined the patient thoroughly. After fulfilling the inclusion and exclusion criteria, each patient was enrolled with unique ID. Patient's guardians were briefed about the objectives of the study, benefits, freedom for participating in the study and confidentiality. Informed written consent was obtained from each patient and/or their guardian. Face to face interview was conducted by using a semi-structured questionnaire. Data were collected at enrollment including age, gender, residence, family history of carcinoma, history of tobacco and alcohol consumption. Venous blood samples were obtained

from the patients on admission and measurements of blood counts (red blood cell, haemoglobin, haematocrit, and red blood cell indices) were performed immediately after sampling. All the collected data were recorded in a separate case record form.

Operational definition:

Anaemia was defined as an Hb level <12 g/dL, in accordance with the toxicity grading criteria from the National Cancer Institute and the European Organization for Research and Treatment of Cancer. For statistical analyses, anaemia was further categorized as: Mild anaemia: Hb 10 - 12.9 g/dl for men & Hb 10 - 11.9 g/dl for women; Moderate anaemia: Hb 7 - 9.9 g/dl for both genders and severe anaemia: Hb < 7 g/dl for both genders.

Data acquisition and statistical Analysis:

Following data collection, entered into a password-protected Microsoft Access data entry platform. The entered data were assessed for completeness, accuracy and consistency before analysis was commenced. Data analysis was carried out by using SPSS version 26 (IBM Corp., Armonk, NY). Continuous data were expressed as mean and standard deviation. Categorical data were expressed as frequency and percentage. To determine the association between categorical variables, chi square test was done. Mean comparisons were assessed by student t-test. Univariate logistic regression to detect factors associated with moderate to severe (haemoglobin<10 g/dL) anaemia. Statistical significance was set at p <0.05, with a 95% confidence interval.

Results:

Maximum study patients were male (62.5%), aged >50 years (64.3%), and hailed from rural residence (60.7%). History of tobacco and alcohol consumption were given by 44.6% and 10.7% patients, accordingly. Family history of any type of carcinoma was present in 21.4% patients. In this study, colorectal carcinoma (17.9%) was the most common type of non-haematological carcinoma followed in decreasing order lung carcinoma (16.1%), upper GI carcinoma (12.5%), gynaecological carcinoma (12.5%), hepatobiliary carcinoma (8.9%) and miscellaneous type of carcinoma (21.4%). Half of the study patients had metastasis (50%). [Table I].

In this study, maximum patients had microcytic (62.5%), hypochromic (62.5%) and moderate to severe (73.2%) anaemia. [Figure 1]

Table-I

Socio-demographic profile of study participants (N=56)

Variables	n (%)
Gender	
Male	35 (62.5)
Female	21 (37.5)
Age (in years)	
21-30	8 (14.3)
31-40	4 (7.1)
41-50	8 (14.3)
51-60	12 (21.4)
61-70	16 (28.6)
>70	8 (14.3)
Residence	
Rural	34 (60.7)
Urban	22 (39.3)
Occupation	
Government employee	4 (7.1)
Non-government employee	13 (23.2)
Business	8 (14.3)
House wife	12 (21.4)
Unemployed	7 (12.5)
Others	12 (21.4)
History of tobacco consumption	25 (44.6)
History of alcohol consumption	6 (10.7)
Family history of cancer	12 (21.4)
Tumourlocation	
Breast	6 (10.7)
Lung	9 (16.1)
Colorectal	10 (17.9)
Upper GI	7 (12.5)
Gynaecological	7 (12.5)
Hepato-billiary	5 (8.9)
Others	12 (21.4)
Presence of metastasis	28 (50)

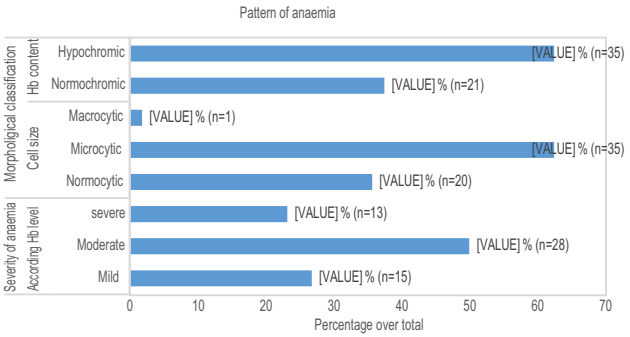

Fig.-1: *Pattern of anaemia in non-haematological malignant patients (N=56)*

Patients with colorectal carcinoma suffered more severe anemia as compared to a patient without colorectal carcinoma (p=0.001). Besides, patients with metastasis had significant association with severity of anaemia (p=0.003). Nevertheless, there was no statistically significant difference found in gender, age group, residence, family history of carcinoma, tobacco and alcohol consumption among the severity of anemia. [Table II]

Univariate logistic regression analysis showed that patients with metastasis were 11.27 times more likely to have haemoglobin <10 g/dL than those without metastasis (COR = 11.27; 95% CI 2.23–56.86). [Table III]

Table II

Haemoglobin level and severity of anaemia according to different socio-demographic factors. (N=56)

	Haemoglobin level			Severity of anaemia			
	Minimum to maximum	Mean±SD	P_1	Mild n (%)	n (%) Moderate	n (%) Severe	P_2
All (n=56)	3.90-12.30	8.59±1.92		15 (26.8)	28 (50.0)	13 (23.2)	
Gender			0.239				0.464
Male	3.90-12.30	8.34±2.10		9 (25.7)	16 (45.7)	10 (28.6)	
Female	5.50-10.90	8.99±1.53		6 (28.6)	12 (57.1)	3 (14.3)	
Age (in years)			0.402				0.184
21-50	3.90-11.20	8.19±2.18		6 (30.0)	7 (35.0)	7 (35.0)	
>50	4.50-12.30	8.81±1.75		9 (25.0)	21 (58.3)	6 (16.7)	
Residence			0.987				0.241
Rural	4.50-12.30	8.67±1.77		8 (23.5)	20 (58.8)	6 (17.6)	
Urban	3.90—11.20	8.47±2.16		7 (31.8)	8 (36.4)	7 (31.8)	
History of tobacco consumption	3.90-12.30	8.33±2.16	0.448	7 (28.0)	10 (40.0)	8 (32.0)	0.297
History of alcohol consumption	7.28-10.30	9.26±1.16	0.414	3 (50.0)	3 (50.0)	0 (0.0)	0.233
Family history of cancer	5.42-10.90	7.94±1.74	0.165	2 (16.7)	6 (50.0)	4 (33.3)	0.584
Tumour location							
Breast	8.90-10.90	9.65±0.72	0.245	1 (16.7)	5 (83.3)	0 (0.0)	0.191
Lung	6.90-11.00	9.21±1.24	0.396	3 (33.3)	5 (55.6)	1 (11.1)	0.633
Colorectal	3.90-11.20	6.78±2.25	0.006	1 (10.0)	2 (20.0)	7 (70.0)	0.001
Upper GI	6.10-12.30	8.21±2.12	0.329	1 (14.3)	4 (57.1)	2 (28.6)	0.724
Gynaeological	5.00-10.30	8.45±1.76	0.734	1 (14.3)	5 (71.4)	1 (14.3)	0.478
Hepato-billiary	5.50-10.10	8.42±1.99	0.933	2 (40.0)	2 (40.0)	1 (20.0)	0.782
Others	5.00-10.90	9.48±1.56	0.058	6 (50.0)	5 (41.7)	1 (8.3)	0.093
Presence of metastasis	4.50-10.90	8.13±1.71	0.016	2 (7.1)	19 (67.9)	7 (25.0)	0.003

SD=standard deviation, GI= Gastro-intestinal.$P_1$was determined by independent sample T test and $P_2$was determined by Chi-square test.

Table III

Univariate logistic regression to detect factors associated with moderate to severe (haemoglobin<10 g/dL) anaemia (N=56)

Factors	95%CI (lower-upper)	p-value
Male gender	1.16 (0.344-3.89)	0.815
Age >50 years	1.29 (0.38-4.35)	0.686
Rural residence	1.517 (0.458-5.02)	0.495
Having history of tobacco consumption	0.894 (0.273-2.93)	0.854
Having history of alcohol consumption	0.316 (0.056-1.78)	0.191
Having family history of cancer	1.74 (0.312-9.69)	0.528
Tumour location		
Breast	1.94 (0.208-18.16)	0.560
Lung	0.686 (0.148-3.18)	0.630
Colorectal	3.94 (0.454-34.12)	0.213
Upper GI	2.40 (0.264-21.79)	0.437
Gynaeological	2.40 (0.264-21.79)	0.437
Hepato-billiary	0.513 (0.077-3.42)	0.491
Others	0.257 (0.067-1.01)	0.058
Presence of metastasis	11.27 (2.23-56.86)	0.003

OR=odds ratio, CI= confidence interval, GI=Gastro-intestinal

Discussion:

Anemia in cancer patients is a consequence ofmalignancy itself, anti-cancer treatment, blood losses, nutritional deficiencies, hemolysis, endocrine disorders, or inflammatory cytokines associated with chronic diseases. In the present study, 56 anaemic non-haematological carcinoma patients at Dhaka Medical College Hospital of Bangladesh, were assessed for pattern of anemia. This study found thatmajority study patients had moderate to severe anaemia (Hb <10 g/dL). This might be because of bone marrow suppression from chemotherapy, radiation therapy and bone metastases due to the breast, lung, kidney, bladder and prostate cancer. About half of the patients had metastasis in this study, and metastasis was found to be the significant risk factor for developing moderate to severe anaemia in non-haematological carcinoma (unadjusted odds ratio = 11.27; 95% CI 2.23–56.86). Similarly, several previous studies also observed the association between metastasis and anaemia in different non-haematological cancers.[17–19] Moreover, some studies also reported that microangiopathic hemolytic anemia (MAHA) is a presenting feature of an occult malignancywith documented metastases.[20,21] Hence, prompt diagnosis is essential because conditions that mimic the symptoms of MAHA, including thrombotic thrombocytopenic purpura, have different prognoses and therapeutic options.[18]

In present study, maximum non-haematological carcinoma patients had microcytic and hypochromic anaemia.Our findings corresponds to the study done by various other authors on different non-haematological carcinoma.[22,23] In addition,a cohort study of patients aged e□40 years using UK primary care electronic patient records found that microcytosis is a predictor of underlying cancer, especially in colorectal, lung, breast, kidney and stomach carcinoma. However, in contrast to our study findings, several studies found normocytic normochromic anaemia is the most prevalent type in non-haematogical carcinoma patients,[11,23] which might be due to the variation in cancer types, disease stage, and treatment modalities.

In current study, colorectal carcinoma (17.9%) was the most frequent non-haematological carcinoma followed in decreasing order lung carcinoma (16.1%), upper GI carcinoma (12.5%), gynaecological carcinoma (12.5%), hepatobiliary carcinoma (8.9%) and miscellaneous type of carcinoma (21.4%). Previous studies also found lung carcinoma and colorectal

carcinoma as the commonest non-haematological carcinoma.[7,24] Moreover, this study observed that patients with colorectal carcinoma hadhigher frequency of severe anemia as compared to a patient without colorectal carcinoma (p=0.001). This confirms the results of several previous studies.[25,26] One of the main causes of anemia in colorectal carcinoma patients is blood loss to the bowel leading to iron deficiency.[27,28] Indeed, anemia in CRC has been reported to frequently show microcytic phenotype[25], which also support our study findings.

In this study, maximum study patients were older aged, male and hailed from rural residence. This is probably because of the fact that the elderly people often present in hospitals in very late stages of their disease conditions in our country. Besides, rural people often have a bad habit of heavy smoking of low-grade nicotine cigarettes and hookahs, and they also have to use non-electric makeshift ovens that let out a lot of smoke while cooking causing COPD changes in them. As they age, they often present with lung disease conditions.Our study found no significant association of age and gender with severity of anaemia. This finding is similar to a study done in Ethiopia showing that gender and age category did not show any evidence of association with severity of anemia among patients with solid malignancy.[24]

Our results may not be generalizable due to a number of limitations. First off, the sample size was small, thus there weren't enough cases of each form of tumor. Secondly, both new and old cases were considered that might have an impact on the overall anaemia pattern. Thirdly, we did not specially track treatment effect in study subject that might affect the study result. Fourth, shortage of accompanying iron studies and evaluation of other factors that can affect iron indices could not be evaluated.

Conclusion:

The majority of the anemic non-haematological patients in this study showed microcytosis and hypochromia in addition to hemoglobin levels below 10 g/dL. Patients with colorectal cancer and metastatic disease were more likely to experience moderate to severe anemia. However, we advise conducting more, larger studies to examine the effect of anemia on non-haematological cancer and treatment outcomes.

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Conflict of Interests: None

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 review committee of Dhaka Medical College Hospital.

Consent for Publication: The authors agreed to publish the article by written consent.

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ORIGINAL ARTICLE

ACCURACY OF TRANSIENT ELASTOGRAPHY IN IDENTIFYING FIBROSIS AMONG PATIENTS WITH CHRONIC HEPATITIS B: A CROSS-SECTIONAL OBSERVATIONAL STUDY

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Abstract:

Background: *Hepatitis B virus (HBV) infection is a significant global public health problem, affecting millions of people worldwide. Liver biopsy is the gold standard for assessing fibrosis but is invasive and carries post-procedural risks. Noninvasive tests to evaluate liver fibrosis are needed, and transient elastography is one such method. This cross-sectional observational study aimed to assess the accuracy of transient elastography in identifying fibrosis among patients with chronic hepatitis B.* ***Methods:*** *The study was conducted at the Department of Medicine and Hepatology, Sir Salimullah Medical College Mitford Hospital, Dhaka. The study subjects were patients diagnosed with chronic hepatitis B infection, both outpatient and inpatient cases. Data were collected from 25 patients using convenient and purposive sampling techniques. Demographic data, clinical examination, and relevant investigations were recorded in a structured case report form. Data were processed, registered, edited, computerized, and analyzed.* ***Results:*** *The study included 25 patients with a mean age of 26.8±6.5 years, predominantly male (80%). All patients were HBsAg positive, 12.0% were HBeAg positive, and 56.0% were antiHBe positive. The mean HBV DNA PCR was 1516293.4±7475976.3 IU/ml. The mean ALT level was 45.4±13.8 U/L. The mean liver stiffness measurement (LSM) was 7.5±2.3 kPa, with 64.0% of patients showing fibrosis stage F0-F1. The mean periportal +/- bridging necrosis was 2.92±1.58, intralobular degeneration and focal were 1.16±0.55, portal inflammation was 2.52±0.87, histological activity index was 6.6±2.2, and fibrosis score was 1.44±1.04. Positive correlations were observed between LSM and histological activity index (r=0.239; p=0.251) and between LSM and fibrosis score (r=0.107; p=0.612).Conclusion: Our study demonstrates that transient elastography provides a non-invasive, easy, and cost-effective method for identifying fibrosis in chronic hepatitis B patients, serving as a potential alternative to liver biopsy.*

Key words: *Transient Elastography Liver Fibrosis, Chronic Hepatitis B*

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Introduction:

Viral hepatitis, including Hepatitis B virus (HBV) infection, is a significant global public health concern affecting millions of people worldwide.[1] In Bangladesh, HBV is of intermediate prevalence, with an estimated 5.4% prevalence in the general population.[2] HBV infection can lead to chronic disease, and its complications, such as cirrhosis and hepatocellular carcinoma, are of grave concern. The progression of liver fibrosis is a key factor in determining the severity of HBV-related liver disease.[3]

Liver fibrosis results from the accumulation of extracellular matrix proteins and activation of hepatic stellate cells. The host immune response plays a crucial role in the natural history of HBV infection, with chronic infection leading to liver injury primarily caused by the host's immune cells.4 Additionally, viral genomic factors, such as genotype D of HBV, have been associated with more severe diseases and increased hepatocellular carcinoma risk, especially in young patients.[4,5]

Liver biopsy is the gold standard for evaluating liver fibrosis, but its invasiveness and post-procedural risks make noninvasive alternatives highly desirable.[6] Transient elastography, also known as FibroScan, is a promising noninvasive test that assesses liver fibrosis by measuring liver stiffness.[7,8] It uses shear waves to determine tissue stiffness, providing immediate, operator-independent results.

This study aims to assess the accuracy of transient elastography in identifying fibrosis among patients with chronic hepatitis B(9).By comparing its effectiveness against liver biopsy, we can determine if transient elastography could be a reliable alternative for identifying liver fibrosis in these patients, reducing the need for invasive procedures and improving patient care.

Methods:

Study Design, Population, and Settings:

This cross-sectional observational study was conducted at the Department of Medicine and Hepatology, Sir Salimullah Medical College & Mitford Hospital, Dhaka, Bangladesh, from August 2019 to February 2020. The study included 25 patients with chronic hepatitis B infection who met the inclusion and exclusion criteria. Written approval was obtained from all participating patients. Inclusion criteria comprised age ≥18 years, compensated liver disease with chronic hepatitis B infection, chronic hepatitis B-infected individuals not meeting treatment criteria, transient elastography value ≥7 kPa with other normal parameters, and coarse liver on ultrasound with other normal parameters. Patients with co-infection with hepatitis C or human immunodeficiency virus, history of anti-viral drug use for more than six months or current treatment, hepatic encephalopathy, prolonged prothrombin time (>4 seconds), platelet count < 80,000/cumm, ascites, severe anemia, advanced chronic obstructive pulmonary disease (COPD), heart failure, or chronic kidney disease were excluded from the study.

Data Collection and Laboratory Procedures:Data were collected through face-to-face interviews using a semi-structured questionnaire to obtain socio-demographic information and clinical presentations. Physical examinations were performed, and reports of ultrasound, blood tests, and transient elastography were recorded during hospital admission. Liver biopsy and relevant laboratory test results were also recorded.

Data Management and Analysis:

Data on socio-demographic and clinical variables were collected using a pre-designed questionnaire, ensuring clarity and accuracy in respondents' answers. Data were checked, verified for consistency, and edited for final analysis. Statistical analysis was performed using the Statistical Program for Social Science (SPSS), version 25, IBM Corp., Chicago, USA, 2017. P values of 0.05 or higher were considered significant, and p values below 0.01 were considered highly significant.

Results :

Table I

Demographic characteristics of the study patients (n=25)

Demographic characteristics	Number of patients	Percentage
Age (years)		
≤20	4	16.0
21-25	10	40.0
26-30	6	24.0
31-35	2	8.0
36-40	2	8.0
>40	1	4.0
Mean±SD	26.8	±6.5
Range (min-max)	16.0	-41.0
Sex		
Male	20	80.0
Female	5	20.0

Table I shows that 10(40.0%) patients belonged to age 21-25 years. The mean age was found 26.8±6.5 years with range from 16 to 41 years. Majority (80.0%) patients were male and 5(20.0%) were female. Male female ratio was 4:1.

Table II

Distribution of the study patients according to HBV serology(n=25)

HBV serology	Number of patients	Percentage
HBsAg		
Positive	25	100.0
Negative	0	0.0
HBeAg		
Positive	3	12.0
Negative	22	88.0
AntiHBe		
Positive	14	56.0
Negative	11	44.0
HBV DNA PCR (IU/ml)	1516293.4	±7475976.3
Range (min-max)	200.0	-37400000.0

Table II shows that all (100.0%) patients were found in HBsAg positive, 3(12.0%) in HBeAgpositive and 14(56.0%) in antiHBe positive. Mean HBV DNA PCR was found 1516293.4±7475976.3 IU/ml with range from 200 to 37400000IU/ml.

Table III

Distribution of the study patients according to ALT (n=25)

ALT (U/L)	Number of patients	Percentage
≤40 9	36.0	
>40 16	64.0	
Mean±SD	45.4	±13.8
Range (min-max)	19.0	-64.0

Table III shows that 16(64.0%) patients were found ALT level >40 U/L. The mean ALT was found 45.4±13.8 U/L with range from 19 to 64 U/L.

Table IV

Distribution of the study patients according to fibroscan of liver (n=25)

Fibroscan of liver	Number of patients	Percentage
LSM (kPa)		
≤10	22	88.0
>10	3	12.0
Mean±SD	7.5	±2.3
Range (min-max)	5.1	-14.2
Fibrosis stage		
F0 -F1	16	64.0
F2	3	12.0
F2 -F3	4	16.0
F3 - F4	2	8.0

Table-IV shows that mean LSM was found 7.5±2.3 kPa with range from 5.1 to 14.2 kPa.Majority (64.0%) patients was found fibrosis stage F0-F1.

Table V

Distribution of the study patients according to histological activity index (n=25)

Histological activity index (HAI)	Mean	±SD
Periportal +/- bridging necrosis	2.92	±1.58
Range (min-max)	1.0	-5.0
Intralobular degeneration and focal necrosis	1.16	±0.55
Range (min-max)	1.0	-3.0
Portal inflammation	2.52	±0.87
Range (min-max)	1.0	-3.0
Histological activity index	6.6	±2.2
Range (min-max)	3.0	-11.0

Table V shows that mean periportal +/- bridging necrosis was found 2.92±1.58 with range from 1.0 to 5.0. The mean intralobular degeneration and focal was found 1.16±0.55 with range from 1.0 to 3.0. The mean portal inflammation was found 2.52±0.87 with range from 1.0 to 3.0. The mean histological activity index was found 6.6±2.2 with range from 3.0 to 11.0.

Table VI

istribution of the study patients according to fibrosis score (n=25)

	Mean	±SD
Fibrosis score	1.44	±1.04
Range (min-max)	0.0	-3.0

Table VI shows that mean fibrosis score was found 1.44±1.04 with range from 0.0 to3.0.

Table VII

Distribution of the study patients according to knodell score (n=25)

	Mean	±SD
Knodell score	8.04	±3.13
Range (min-max)	3.0	-14.0

Table VII shows that mean knodell score was found 8.04±3.13 with range from 3.0 to 14.0.

Correlation between LSM and periportal necrosis

Spearman's rank correlation, ρ(rho) = 0.207 (p=0.320)

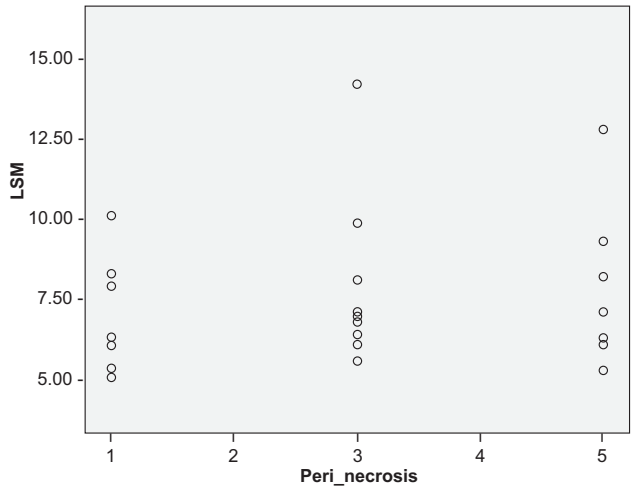

Fig.-1: *Correlation between LSM and periportal necrosis*

This figure 1 shows Correlation between LSM and periportal necrosis.

According to Spearman's rank correlation, it is ñ (rho) = 0.207 (p=0.320)

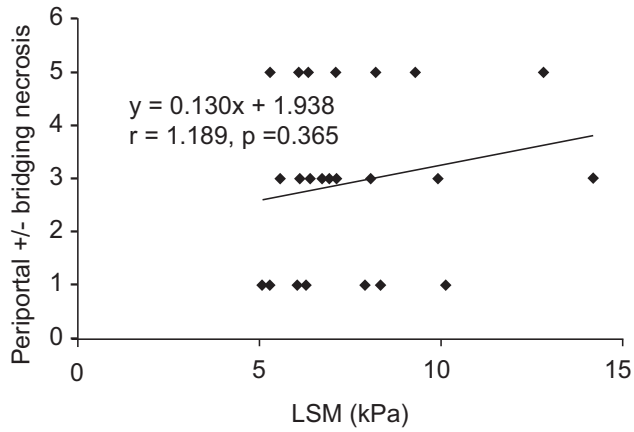

Fig.-2: *Scatter diagram showing positive correlation (r=0.189; p=0.365) between LSM and periportal +/- bridging necrosis*

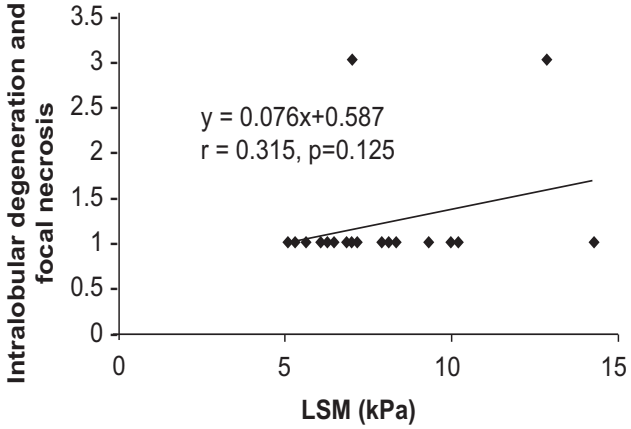

Fig.-3: *Scatter diagram showing positive correlation (r=0.315; p=0.125) between LSM and intralobular degeneration and focal necrosis.*

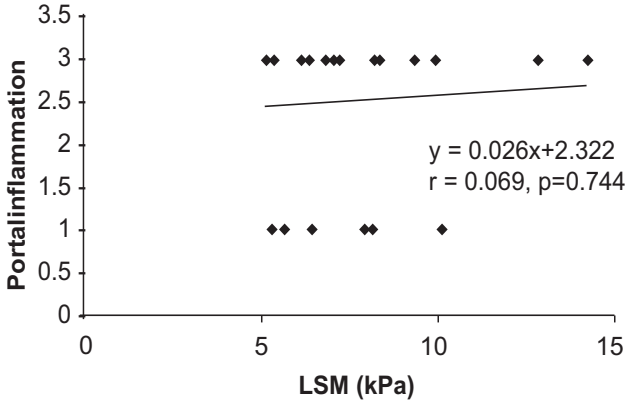

Fig.-4: *Scatter diagram showing positive correlation (r=0.069; p=0.744) between LSM and portal inflammation.*

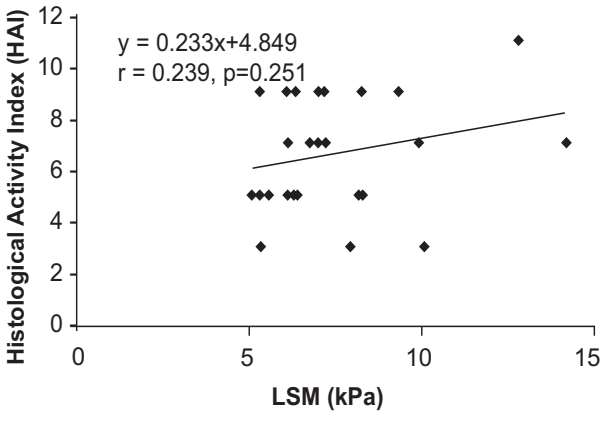

Fig.-5: *Scatter diagram showing positive correlation (r=0.239; p=0.251) between LSM and histological activity index.*

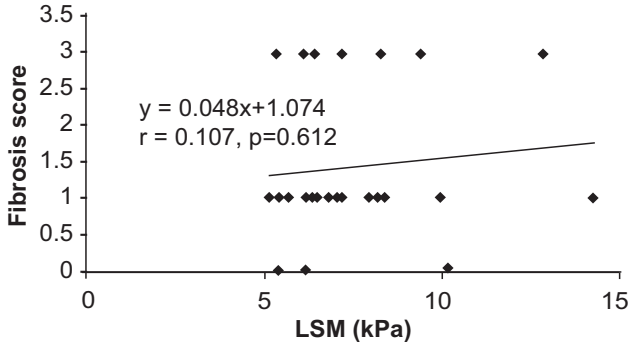

Fig.-6: *Scatter diagram showing positive correlation (r=0.107; p=0.612) between LSM and fibrosis score.*

Correlation between LSM and Knodel score

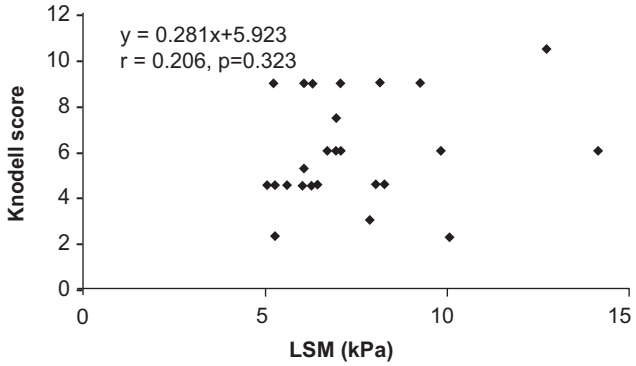

Fig.-7: *Scatter diagram showing positive correlation (r=0.206; p=0.323) between LSM and knodell score.*

Discussion:

In this study observed that 10(40.0%) patients belonged to age 21-25 years. The mean age was found 26.8±6.5 years with range from 18 to 41 years. Majority (80.0%) patients were male and 5(20.0%) were female. Male female ratio was 4:1. Li et al. reported that the mean age was found 36±10 years and 66.4% were male. Xu et al. reported the mean age was 33.5±10.4 years. Male sex was predominant in both patients with CHB with and without NAFLD (84.0% and 78.6%, respectively. Paul et al. also observed these patients were 176 males and 64 females, of mean age 32.6±11.6 years (range 15-75 years). Mansour et al. observed 62 females (68.9%) and 28 males (31.1 %), aging 18–72 years (mean age 45.53 ± 11.5 years).

In this study showed that all (100.0%) patients were found in HBsAg positive, 3(12.0%) in HBeAg positive and 14(56.0%) in antiHBe positive. Mean HBV DNA PCR was found 1516293.4±7475976.3 IU/ml with range from 200 to 37400000 IU/ml. Han et al. reported that the one-way ANOVA of the correlations between serological indexes and liver hardness in the 36 patients showed statistically significant (P < 0.05) differences in HA, type III procollagen (PCIII), LN, and type IV collagen (CIV) levels among patients with different liver hardness. The early screening of hepatitis B and timely administration of antiviral therapy are important measures to reduce the risk of liver failure and death.[7] Li et al. observed HBeAg positive cases were found 92(79.3%) and median HBV DNA was found 7.5 log10 copies/mL.[10]

In this study itis observed that 16(64.0%) patients were found ALT level >35 U/L. The mean ALT was found 45.4±13.8 U/L with range from 19 to 64 U/L.Han et al. In addition, patients with HBV DNA levels of >2,000 IU/mL regardless of ALT level should receive antiviral therapy. When the ALT level is <2 ULN, the pathological changes of the liver are taken into account to determine whether antiviral treatment is required.[8,9] Parikh et al.reported the AAR, has been widely utilized as a predictor of cirrhosis in different aetiologies of liver disease.[11] In a study published by Williams et al.[12] among 100 patients with HBV, the mean AST/ALT ratio was 0.59 in those without and 1.02 in those with cirrhosis respectively. However, Eminler and colleagues[12] found that the AAR performed inferiorly to other blood-based non-invasive algorithms in estimating the fibrosis stage in 237 HBV patients. Xu et al. reported that the median ALT was 84.0 U/L. Li et al. observed among the 116 enrolled patients, 37 (31.9%) had normal ALT levels, 52 (44.8%) had mildly elevated ALT levels (1–2 upper limit of normal [ULN]) and 27 (23.3%) had significantly elevated ALT levels (>2 ULN).

In current study showed that mean LSM was found 7.5±2.3 kPa with range from 5.1 to 14.2 kPa. The majority (64.0%) patients were found fibrosis stage F0-F1.Han et al. reported among 36 patients, 15 patients were at F1–F2 stage, 17 patients were at F2–F3 stage, and 4 patients were at F3 or above stage(13). Parikh et al. also observed the stiffer the liver, the higher is the velocity, indicated by a numeric value between 4.0 to 75 kPa. The cut-off values for significant fibrosis (e”F2) ranged from 5.8 to 8.8 kPa, for fibrosis ≥F3 from 7.0 to 13.5 kPa, and for cirrhosis (F4) from 9.0 to 16.9 kPa (97-103)(11). Qi et al. observed that the presence of an IQR/M > 30% and liver stiffness median ≥7.1 kPa lead to a lower accuracy determined by the area under receiver operating curve (AUROC) and these cases were considered “poorly reliable”.[14] Zhang et al. reported liver stiffness measured with TE ranged from 3.2 to 38.5 kPa (IQR, 5.1-9.5 kPa)(12). Xu et al. reported that the mean LSM was 11.0±5.5 kPa.[9]

In this study showed that mean periportal +/- bridging necrosis was found 2.92±1.58 with range from 1.0 to 5.0. The mean intralobular degeneration and focal was found 1.16±0.55 with range from 1.0 to 3.0. The mean portal inflammation was found 2.52±0.87 with range from 1.0 to 3.0. The mean histological activity index was found 6.6±2.2 with range from 3.0 to 11.0.Some authors have suggested that TE cut-offs should incorporate ALT levels which fluctuate with inflammation in HBV, and TE may be particularly useful forHbeAg-negative patients with normal LFTs to guide the need for biopsy of treatment.[6,9,12,13]

In this study observed that mean fibrosis score was found 1.44±1.04 with range from 0.0 to 3.0. Han et al. reported hepatic fibrosis refers to the condition when excessive extracellular matrix (ECM) deposition occurs in the liver, and the abnormal hyperplasia of a large number of fibrous tissues occurs in the portal area. This is a reversible pathological condition during the process where various chronic liver diseases develop to cirrhosis.[10–12]

In current study observed that the positive correlation (r=0.239; p=0.251) between LSM and histological activity index. A Han et al. reported that hepatic stiffness was measured to monitor the outcomes of hepatic fibrosis in antiviral therapy, and the result confirmed that long-term viral inhibition was correlated with the outcomes of hepatic fibrosis.[13]. Therefore, monitoring the degree of hepatic fibrosis is useful during antiviral treatment. In China, the Guidelines for the Prevention, Management, and Treatment of Chronic HBV Infection (2015 Edition) also emphasize that FibroScan can be used to monitor hepatic hardness in chronic HBV infection, to improve the success rate and speed of detection.[1]

In present study positive correlation (r=0.107; p=0.612) between LSM and fibrosis score. Han et al. reported serum fibrosis indexes are associated with liver stiffness values ($P < 0.05$). Zhang et al. also observed that the correlation coefficients of TE and US scores with fibrosis stage were 0.69 (95% CI: 0.55, 0.78; P<0.001) and 0.47 (95% CI: 0.30, 0.61; P<0.001), respectively.[15] The correlation coefficients of TE were significantly higher than that of the US scores (P=0.022). However, the degree of hepatic steatosis did not correlate with fibrosis stage (r=0.041, P=0.69), TE scores (r=0.037, P=0.72), or US scores (r=0.091, P=0.38). Li et al. observed FibroScan (r=0.67, P<.001), GPR (r=0.44, P<.001) and APRI (r=0.34, P<.001) demonstrated a correlation with liver histological fibrosis stages.[10]

Conclusion:

Our study highlights the value of transient elastography as a viable, noninvasive, and cost-effective tool for identifying fibrosis. This technique provides a valuable alternative to liver biopsy, offering physicians and patients a more accessible and less intimidating option for monitoring disease progression. As we continue to address the complexities of Chronic Hepatitis B, integrating such noninvasive methods into clinical practice can significantly enhance patient care and outcomes.

Limitations:

Small sample size and this single hospital based study did not reflect exact scenario of the whole community. Patients from all socioeconomic status and all parts of the country did not come to seek medical attention in the study place.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

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

Funding:

Funding from Bangabandhu Fellowship under the Ministry of Science and Technology, Bangladesh was received for this study.

Ethical consideration:

The study was conducted after approval from the ethical review committee. The confidentiality and anonymity of the study participants were maintained.

Authors' Contributions:

RSR was responsible for conception and design, obtaining funds, data interpretation, manuscript drafting and manuscript editing, and final approval data acquisition, data interpretation and critical revision for important intellectual content conception and design, obtaining funds, data interpretation, manuscript editing, and final approval. MDI was responsible for data analysis and statistical analysis. AR and MDI were responsible manuscript writing and editing RSR and SSJ were responsible for data collection. All authors have read and approved the final version of the manuscript.

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ORIGINAL ARTICLE

SERUM ADIPONECTIN IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Abstract:

Background: *An imbalance of different adipocytokines may play a role in the pathogenesis of PCOS. This study aimed to observe the association and diagnostic utility of adiponectinin PCOS and its manifestations.* **Methods:** *This cross-sectional study included 40 newly diagnosed females of reproductive age (18-40 years) with PCOS on the basis of international evidence-based guidelines and an equal number of matched healthy control. Along with clinical information, blood was drawn for biochemical and hormonal analysis. Glucose was measured by glucose oxidase, lipid by glycerol phosphate dehydrogenase peroxidase, all hormones by CMIA, and adiponectin by ELISA method. Insulin resistance was measured by homeostasis model assessment (HOMA-IR) and defined with a cut-off of 2.6.* **Results:***Patients with PCOS had lower serum adiponectin than controls without significant differences even irrespective of body mass index status(ns for all). Adiponectin levels had no significant associations or correlations with any manifestations among patients with PCOS (ns for all). ROC curve analysis showed that serum adiponectin could not be used as a marker of PCOS. It was a poor marker of both metabolic syndrome [AUC (95% CI): 0.64 (0.46-0.81] and insulin resistance [AUC (95% CI): 0.61 (0.44-0.79)] in patients with PCOS.***Conclusion:** *Our study failed to find any significant association between adiponectin and PCOS and its characteristics. Serum adiponectin could not be used as a marker of PCOS. It was a poor marker of insulin resistance and metabolic syndrome among patients with PCOS.*

Keywords: *Polycystic ovary syndrome, Adiponectin, Insulin resistance, Metabolic syndrome.*

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Introduction:

Polycystic ovary syndrome (PCOS) is one of the most common reproductive endocrinopathies in females with unknown pathophysiology. Recently it is thought that the condition originates during fetal life (developmental origin) in genetically susceptible persons and several maladaptive postnatal adaptations occur in response to exposure to the modern environment (evolutionary hypothesis).[1] These maladaptations include the cardinal features of PCOS (hyperandrogenism and insulin resistance) as a result of escape from the accumulation of excess hepato-visceral fat.[2] This proinflammatory central fat mediates its effects by producing an imbalance in several adipocytokines production with modulation in ovarian and adrenal tissue steroidogenesis.[3]On the other hand, these adipocytokines also contribute to insulin resistance and compensatory hyperinsulinemia, and stimulation of androgen production. Thus a vicious cycle is produced by the

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visceral fat and androgen-producing glands that maintain the condition.[4]So, the role of adipocytokines in the pathogenesis of PCOS is very important.

Adiponectin is the most abundant adipokineand is also produced from other tissues. It hasseveral circulating molecular weight forms with different tissue-specific efficacy. It directly acts in different metabolic tissues including the liver, skeletal muscles, vasculature, etc. mediated by its receptors.[5] It has a protective role against insulin resistance, inflammation, atherogenesis, etc. This 'guardian angel' cytokine is thus reduced in these conditions.[6] Hence, the replacement of this adipokine in diseases with these conditions such as obesity, diabetes mellitus, and cardiovascular (CV) diseases is a potential therapeutic target.[7] PCOS is also a metabolic disorder and transplantation of brown adipose tissue as well as replacement of adiponectin ameliorate PCOS too.[8]

PCOS is a heterogeneous disorder with higher metabolic as well as androgenic features in patients from South-Asian backgrounds.[9]However, the association between PCOS and adiponectin is not well documented in this region. Besides, the association between adiponectin with different manifestations of PCOS along with its diagnostic role is not adequately reported in the literature. We aimed to assess the association and diagnostic role of adiponectin with PCOS as well as its manifestations.

Methods:

This cross-sectional study was done in the Endocrinology department of a University hospital during the period from March 2019 to September 2020. The study protocol was approved by the institutional review board of the University. Informed consent was taken from each participant. The sample size was calculated from the following formula: $n= \{(Z_\alpha+ Z_\beta)^2 \times (\sigma_1^2 + \sigma_2^2)\} \div (\mu_1 - \mu_2)^2$. At a 95% confidence interval (Z_α=1.96), 95% power (Z_β=1.64), and taking the mean±SD from a previous study the minimum sample size was 37.[10] We included 40 females with PCOS and an equal number of matched healthy control.

Newly diagnosed adult females of reproductive age (18-40 years) with PCOS on the basis of international evidence-based guidelines were enrolled consecutively by purposive sampling.[11] Participants having a regular menstrual cycle and insignificant hirsutism were enrolled as control. Participants having similar endocrine disorders, systemic disorders, or a history of taking hormonal contraceptives, antiandrogens, insulin sensitizers, ovulation-inducing drugs, anti-lipid, or antiobesitywithin 3 months of enrollment were excluded. Each participant was asked about their reproductive history (menstrual cycle, subfertility, menstrual regulation/ abortion). Height (cm), weight (kg), waist circumference (WC, cm), hip circumference (HC, cm), blood pressure (BP, mm-Hg), hirsutism by modified Ferriman-Gallwey (mFG) score were measured, and the presence of acne and acanthosis nigricans were noted. Body mass index (BMI, kg/m^2), waist/hip ratio (WHR), and waist/height ratio (WHtR) were calculated. A BMI ≥25 kg/m^2 was taken as obesity.[12] A mFG score ≥6 was considered significant hirsutism.[11]Venous blood was collected in a fasting state and during the follicular phase of the menstrual cycle (days: 2 – 5) to measure glucose (fasting plasma glucose, FPG), lipid profile (total cholesterol, TC; HDL-cholesterol; triglyceride, and LDL-cholesterol from Friedwald formula), insulin, total testosterone (TT), sex hormone binding globulin (SHBG), dehydroepiandrosterone sulfate (DHEAS), luteinizing hormone (LH), follicle-stimulating hormone (FSH), and adiponectin levels. An oral glucose tolerance test (OGTT) was done to measure glucose (2H-OGTT). Free androgen index was calculated [FAI= (TT in nmol/L÷SHBG in nmol/L)×100%] and a FAI e"5% was considered hyperandrogenemia.[13] Insulin resistance was measured by homeostasis model assessment [HOMA-IR=(fasting insulin in μIU/mL × FPG in mmol/L)÷22.5, and a HOMA-IR ≥2.6 was considered insulin resistance (IR).[14]A LH/FSH ratio (LFR) >2 was taken as an altered ratio.[15] Abnormal glycemic status was defined by the presence of at least impaired fasting glucose (IFG ≥5.6 mmol/L) &/or impaired glucose tolerance (IGT ≥7.8 mmol/L).[16] Metabolic syndrome (MS) was diagnosed by the presence of at least any 3 out of 5 components.[17]Ultrasonography of the ovaries was done during the follicular phase of the menstrual cycle for the presence of polycystic ovarian morphology (PCOM).

Glucose was measured by glucose oxidase, lipid by glycerol phosphate dehydrogenase peroxidase, and all hormones including SHBG by chemiluminescence microparticle immunoassay method. The adiponectin samples were measured using ACRP30 ELISA kit, a nonradioactive quantification of Human Adiponectin (DRG International Inc., USA) with the analytical sensitivity of 0.493 ng/mL, intra-assay coefficient of variation (CV) of 2.8% – 3.9%, and inter-assay CV of 5.9% – 6.4%.

Data were analyzed using SPSS software version 25.0. Qualitative data were expressed in frequency (%), and quantitative data were expressed in mean±SD or median (IQR) depending on their distribution. A comparison between the two groups was done by independent samples t-test or Mann-Whitney U test

for medians and distribution. A comparison among more than two groups was analyzed by Kruskal-Wallis one-way ANOVA for medians and distribution. The correlations between adiponectin with clinical and laboratory variables were done by Spearman's correlation test. A receiver operating characteristics (ROC) curve analysis was done to see adiponectin as a marker of PCOS, and a marker of MS and IR in patients with PCOS. Statistical significance was set with a two-tailed p-value below 0.05.

Results:

The characteristics of the study population showed that patients with PCOS had significantly poor metabolic features (higher BMI, WC, WHR, WHtR, SBP, DBP, 2H-OGTT, TC, LDL-C, fasting insulin, but lower HDL-C), higher androgenic features (higher TT, DHEA-S, but lower SHBG), and higher LFR than controls. Age, FPG, and triglyceride were statistically similar among the study groups (Table-1).

Table-I

Characteristics of the study population (n=80)

Variables	PCOS (n=40)	Control (n=40)	p
Age, years	23.0	24.5	0.654*
	(20.0-29.8)	(21.0-29.0)	0.455†
Body mass index, kg/m^2	29.0±5.7	22.8±3.1	<0.001‡
Waist circumference, cm	92.1±13.1	77.9±8.9	<0.001‡
Waist/hip ratio	0.91	0.87	0.014*
	(0.85-0.93)	(0.82-0.89)	0.001†
Waist/height ratio	0.6±0.1	0.5±0.1	<0.001‡
Systolic blood pressure, mm-Hg	120.0	110.0	0.002*
	(100.0-120.0)	(100.0-110.0)	0.005†
Diastolic blood pressure, mm-Hg	80.0	67.5	<0.001*
	(70.0-85.0)	(60.0-70.0)	<0.001†
Serum luteinizing hormone/ follicle-stimulating hormone ratio	2.0	1.1	0.001*
	(1.1-2.6)	(0.7-1.5)	<0.001†
Serum total testosterone, ng/ml	4.6	2.0	<0.001*
	(3.1-9.8)	(1.7-2.6)	<0.001†
Serum sex hormone binding globulin, nmol/L	10.4	37.1	<0.001*
	(8.1-20.7)	(24.4-66.1)	<0.001†
Serum dehydroepiandrosterone sulfate, µgm/dL	233.1±121.3	157.0±76.3	<0.001‡
Fasting plasma glucose, mmol/L	5.0	5.2	0.370*
	(4.8-5.5)	(4.8-5.5)	0.582†
2 hours after OGTT glucose, mmol/L	7.5	6.9	0.014*
	(6.2-8.7)	(6.1-7.2)	0.016†
Serum total cholesterol, mg/dL	188.5	165.5	0.074*
	(172.5-210.8)	(149.5-187.5)	0.002†
Serum HDL-cholesterol, mg/dL	46.0	42.0	0.074*
	(40.3-52.5)	(35.8-47.8)	0.019†
Serum LDL-cholesterol, mg/dL	119.5	99.0	0.044*
	(102.3-135.5)	(89.8-121.3)	0.003†
Serum triglyceride, mg/dL	131.3±53.4	117.0±59.7	0.264‡
Fasting plasma insulin, µIU/mL	11.4	8.4	<0.001*
	(10.0-22.7)	(6.3-10.1)	<0.001†

Mann-Whitney U test for medians* and distribution†, and independent samples t-test were done

Patients with PCOS had lower serum adiponectin than controls without significant differences [PCOS vs. control: 6.8 (4.9-10.2) vs. 7.0 (5.1-8.6), µgm/mL, median (IQR), p=0.823 (medians), p-0.969 (distributions)]. Similarly, they had also higher percentages of low adiponectin levels (<4 µgm/mL), again without significant differences (17.5% vs. 5.0%, p=0.154) with control participants (Figure-1). There were no significant differences in serum adiponectin levels (µgm/mL) when the study groups were compared considering BMI subgroups also [PCOS vs. control- nonobese (<25 kg/m^2): 6.7 (5.0-9.5) vs. 7.2 (5.7-8.7), p=0.785; obese (25 kg/m^2): 6.8 (4.4-10.4) vs. 4.7 (4.4-8.7), p=0.541, median (IQR)].

Serum adiponectin levels were compared between groups of different characteristic features of PCOS. None of the variables had any significant associations with adiponectin in patients with PCOS (Table-II).

Table-II

Serum adiponectin levels with different characteristics in patients with PCOS (n=40)

Variables	Groups	No.	S. adiponectin, µg/mL	p
Menstrual cycle	Irregular	35	7.4 (5.0-10.3)	0.4680.092
	Regular	5	4.0 (3.1-11.5)	
Subfertility	Present	10	4.6 (3.5-9.5)	0.7150.109
	Absent	30	7.3 (5.4-10.4)	
Menstrual regulation/ abortion	Present	7	5.9 (3.8-7.7)	0.4050.293
	Absent	33	7.4 (4.9-10.7)	
Hirsutism	Significant (≥8)	39	7.2 (4.9-10.3)	1.0000.473
(Modified Ferriman-Gallwey score)	Insignificant (<8)	1	5.0	
Acne	Present	23	7.7 (5.0-11.5)	0.5220.107
	Absent	17	5.9 (3.9-8.9)	
Acanthosis nigricans	Present	28	8.0 (5.1-10.5)	0.3010.122
	Absent	12	5.3 (3.3-7.9)	
Body mass index(Kg/m^2)	Obese (≥25)	30	6.8 (4.4-10.4)	0.7151.000
	Nonobese (<25)	10	6.7 (5.0-9.5)	
Androgenemia	Hyperandrogenemia (≥5.0)	30	6.8 (4.8-10.5)	0.7151.000
(Free androgen index, %)	Normoandrogenemia (<5.0)	10	6.8 (4.5-10.2)	
Polycystic ovarian morphology	Present	32	6.8 (4.9-10.5)	0.6930.561
	Absent	8	7.1 (1.9-9.7)	
LH/FSH ratio	Altered (>2.0)	21	6.4 (4.5-9.5)	0.4270.569
	Normal (≤2.0)	19	7.9 (5.0-10.6)	
Glycemic status	Abnormal	24	7.6 (5.0-10.9)	0.3330.331
(FPG ≥5.6 &/or 2H-OGTT≥7.8 mmol/L)	Normal	16	6.0 (4.6-8.9)	
Insulin resistance (HOMA-IR)	Present (≥2.6)		10	6.0 (4.6-8.8)
0.3430.221				
	Absent (<2.6)	20	8.2 (4.9-11.2)	
Metabolic syndrome	Present (≥3/5)	18	5.9 (4.3-8.9)	0.3400.147
(No. of component)	Absent (<3/5)	22	7.8 (5.0-11.1)	
Phenotypes	A	27	7.4 (5.5-10.6)	0.3500.137
	B	8	7.1 (1.9-9.7)	
	C	5	4.0 (3.1-11.5)	

LH (Luteinizing hormone); FSH (follicle-stimulating hormone); FPG (fasting plasma glucose); OGTT (oral glucose tolerance test)

Mann-Whitney U test or Kruskal Wallis test for medians and distributions were done

The correlations between serum adiponectin with different clinical and laboratory variables are shown in Table-III. There were no significant correlations between serum adiponectin with any of the studied variables (ns for all).

ROC curve analysis showed that serum adiponectin could not be used as a marker of PCOS [area under the curve, AUC (95% confidence interval, CI): 0.50 (0.37-0.63); standard error, SE: 0.07; p=0.969). It was a poor marker of both metabolic syndrome [AUC (95% CI): 0.64 (0.46-0.81; SE: 0.09, p=0.142] and insulin resistance [AUC (95% CI): 0.61 (0.44-0.79); SE: 0.09; p=0.218] in patients with PCOS (Figure-2 and Figure-III).

Table-III

Correlation of Serum adiponectin with clinical and laboratory variables in patients with PCOS (n=40)

Determinants of 'ρ'	ρ	p
Age, years	-0.3	0.079
Body mass index, kg/m^2	-0.1	0.850
Waist circumference, cm	-0.3	0.120
Waist/hip ratio	-0.1	0.904
Waist/height ratio	-0.2	0.144
Systolic blood pressure, mm-Hg	-0.1	0.434
Diastolic blood pressure, mm-Hg	-0.1	0.629
Modified Ferriman-Gallwey score	0.1	0.505
LH/FSH ratio	0.1	0.435
S. total testosterone, ng/mL	-0.1	0.382
S. sex hormone binding globulin, nmol/L	-0.1	0.382
S. dehydroepiandrosterone, µgm/dL	-0.1	0.786
Fasting P. glucose, mmol/L	-0.2	0.294
2-hours after OGTT glucose, mmo/L	-0.1	0.440
S. total cholesterol, mg/dL	-0.1	0.623
S. HDL-cholesterol, mg/dL	0.1	0.702
S. LDL-cholesterol, mg/dL	0.1	0.779
S. triglyceride, mg/dL	-0.2	0.345
S. fasting insulin, µIU/mL	-0.3	0.084

Spearman's correlation test was done

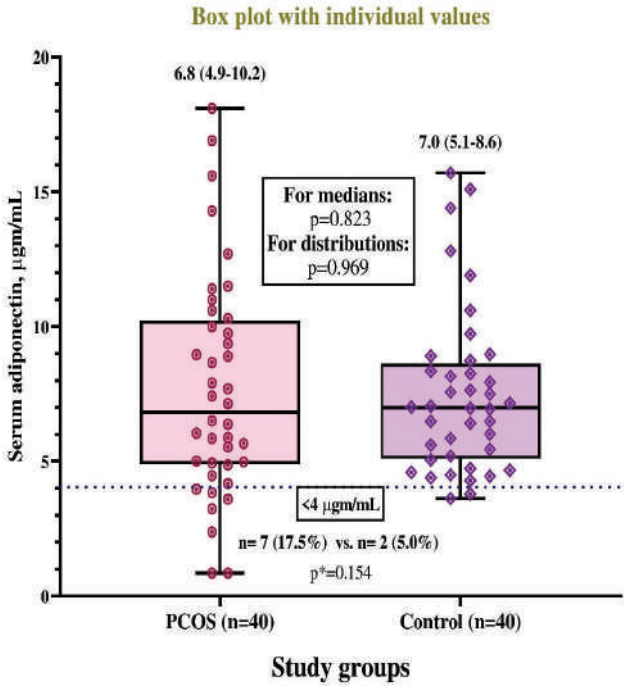

Fig.--1: *Serum adiponectin levels and category in the study population (n=80)*

Mann-Whitney U test (medians and distributions) and *Fisher's exact test were done

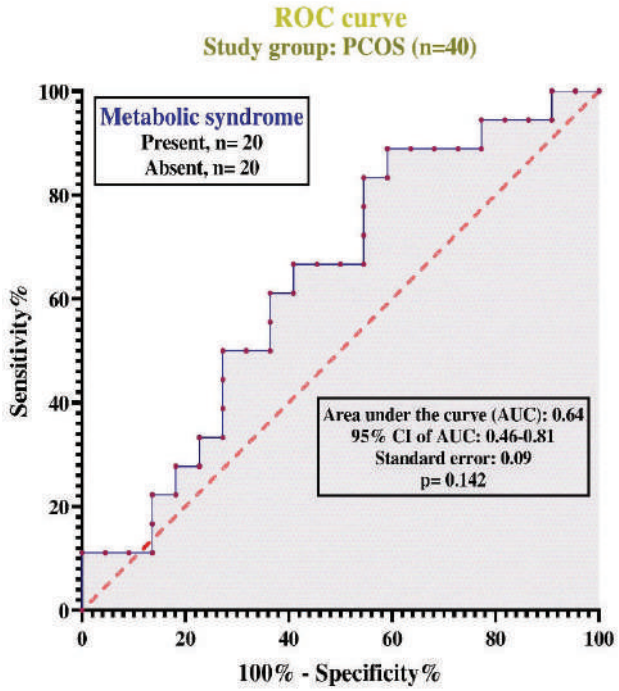

Fig.-2: *Serum adiponectin as a marker of metabolic syndrome in patients with PCOS (n=40)*

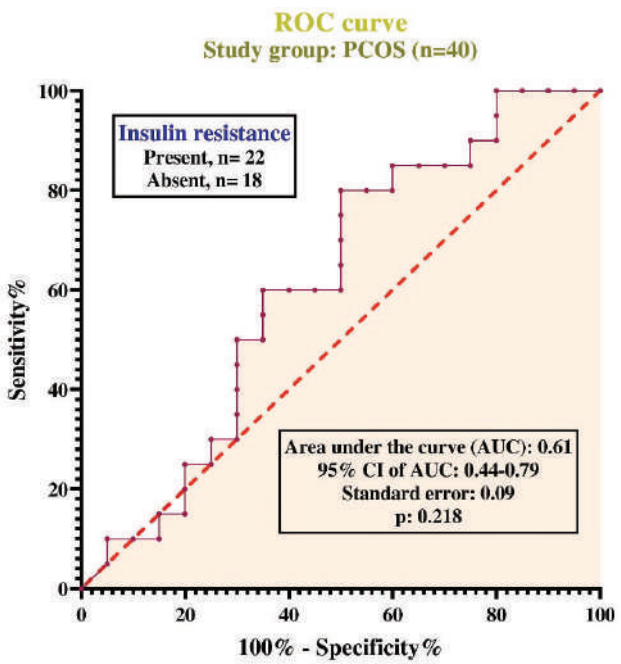

Fig.-3: *Serum adiponectin as a marker of insulin resistance in patients with PCOS (n=40)*

Discussion:

This study failed to show any significant association of serum adiponectin in patients with PCOS or any significant association or correlation with any studied features in patients with PCOS. Furthermore, serum adiponectin could not be used as a marker of PCOS. However, it was a poor marker for metabolic syndrome and insulin resistance in patients with PCOS.

We found a little bit lower but statistically similar levels of adiponectin despite poorer metabolic status in patients with PCOS than in the control group. Our finding is similar to some studies' observations.[18-20]However, systematic reviews and meta-analyses showed lower adiponectin levels irrespective of obesity status in women with PCOS.[21,22] We also found a higher percentage of hypoadiponectinemia(17.5%) in the PCOS group than in the control group but again with an insignificant association. A study conducted among 49 Indian women found 22.0% of patients with PCOS with hypoadiponectinemia. However, this study did not include a control population.[23]

We did not find any significant association between adiponectin and any diagnostic features and phenotypes in patients with PCOS. Several studies and a meta-analysis also found an insignificant association between adiponectin and different androgens including TT.[21,24,25]In contrast, several studies found a significant association between them.[25,26]Karkanaki et al. (2009) found lower adiponectin levels in phenotype A and B than in phenotype D. They hypothesized a negative association of irregular cycle and hyperandrogenism with adiponectin, and no association with PCOM.[26] However, in our study, there were no patients with phenotype D and other phenotypes had similar levels of adiponectin.

We did not find any significant association between adiponectin and any metabolic features including insulin resistance in patients with PCOS. Several studies also found an insignificant association between serum adiponectin and different metabolic features.[18,19,24,28] However, contradictory findings were observed by others.[21,25] Several studies showed that high molecular adiponectin rather than total adiponectin is associated with PCOS and its features.[29,30] Again, an insignificant association was also observed.[31]

Serum adiponectin could not be used as a marker of PCOS in our study.A similar finding was also observed in several studies.[10,32,33] We found adiponectin as a poor marker for IR and MS in women with PCOS. However, the role of adiponectin as a marker of IR and MS remains controversial.[34]

Conclusion:

Our study did not find any significant association between adiponectin and PCOS and its characteristics indicating an insignificant/minor role of adiponectin in the pathogenesis of PCOS. Serum adiponectin could not be used as a marker of PCOS. It was a poor marker of insulin resistance and metabolic syndrome among patients with PCOS.

Limitations:

Small sample size and this single hospital based study did not reflect exact scenario of the whole community. Patients from all socioeconomic status and all parts of the country did not come to seek medical attention in the study place.

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Authors' Contributions:

IAJ, HB, MAH were responsible for conception and design, obtaining funds, data interpretation, manuscript drafting and manuscript editing, and final approval data acquisition, data interpretation and critical revision for important intellectual content conception and design, obtaining funds, data

interpretation, manuscript editing, and final approval. IAJ, MSM, EURC were responsible for data analysis and statistical analysis. IAJ and MAH were responsible manuscript writing and editing. IAJ and MAH were responsible for data collection. All authors have read and approved the final version of the manuscript.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

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

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Ethical consideration:

The study was conducted after approval from the ethical review committee. IRB clearance from BSMMU (No. BSMMU/2019/3865, Date: 11/04/2019). The confidentiality and anonymity of the study participants were maintained

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ORIGINAL ARTICLE

THE ASSESSMENT OF POST-COVID-19 MANIFESTATIONS IN RECOVERED PATIENTS AND THE FACTORS ASSOCIATED WITH HIGH SYMPTOMS BURDEN

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Abstract:

Background: *Persistent COVID-19 symptoms and post-COVID chronic diseases have received more attention rather than the infection itself. This study's goal was to evaluate the health status of recovered COVID-19 patients and analyze the factors associated with a high burden of symptoms.* ***Methods:*** *This was acohort study among hospital-released and recovered COVID-19 patients after three to six months of infection. Data was collected through a structured interview and analyzed by IBM SPSS (version25).* ***Results:*** *Fatigue (74.2%) followed by anxiety (38.9%) and joints paint (34.7%) were the most common symptoms of post-COVID period. Among participants, 21.34% had low dietary adherence and 17.2% had high adherence. A statistically significant correlation of high symptoms burden with dietary adherence and age was observed. People with low dietary adherence are at risk of high symptom burden and chronic diseases (AOR: 3.56, 95%CI:1.46-8.69). Habit of smoking, Asthma, Hypothyroidism, Ischemic heart disease are significant predictor (P<0.05). Patients those did not required ICU also had a lower risk of burden.* ***Conclusion:*** *Effective control of post-COVID symptoms is important to confirm a healthy life. Therefore, it is important to maintain good dietary practice, avoid bad habits and control of chronic diseases for a good quality of life.*

Keywords: *COVID-19; Long COVID; Symptoms; Dietary adherence; Chronic disease.*

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Introduction:

The SARS-CoV-2 usually cause an acute multisystem disease which can have symptoms that last for up to two weeks.[1-3] According to the WHO, some symptoms may persist for a long period, some may start to show up three months after the onset of COVID-19 and may linger for at least two months.[4] Patients with serious infections are more likely to require hospitalization and hence are more likely to experience persistent symptoms.[5] The post COVID-19 symptoms are recent public health concern that has drawn a lot of attention. The duration of these symptoms is not well understood.[3]

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As of December 2022, almost 6.7 million people had died from COVID-19 infection worldwide. In Bangladesh, there have been over two million confirmed illnesses and about 30000 recorded fatalities (6). While most afflicted individuals recovered and resumed their regular lives, many patients reported health issues after beating the sickness.[2,7] Genetic variations, viral load exposure, and immune system reactions to the virus are just a few examples of the elements that might cause an individual to display a wide range of clinical symptoms.[5] Numerous known and improbable reasons can be used to account for individual clinical discrepancies. Age, coexisting disorders (such diabetes, cardiovascular disease, chronic lung diseases, etc.), genetic variances, and others can all contribute to disease severity.[8,9]

After the recovery of COVID-19, the presence of any remaining symptoms is regarded as Long COVID.[10,11] Persistent symptoms might be associated with variety of factors (disease related, demographic, immune system, cardiovascular system, brain, lungs, and other organs). The frequent Long COVID symptoms include fatigue, dyspnea, chest pain, muscle/joint pain, heart palpitations, hair loss, loss of taste and smell, digestive issues, cognitive symptoms, and psychosocial issues. High burden of post-COVID-19symptomsis more common in people with coexisting medical conditions and increases with age. But it's important to keep in mind that it can also affects young patients and those with comorbidities most.[12,13]

The rates of COVID-19 symptomatic persistence were found to be 13.3% at 1 month and 4.5% at 2 months in a prior study involving 4118 participants.[14] Another study in the UK found that, after 12 weeks, 13.7% of 20000 participants still had a symptom.[15] More recently, research using commercial electronic health record data found that 1 in 5 people (aged 18 to 64) and as many as 1 in 4 people (aged 65 or older) had an illness that was newly diagnosed using a diagnosis code.[16]

A plant-based diet known as the Mediterranean diet (MD) is linked to a lower risk of COVID-19 comorbidities and manifestations, which lessens the burden of symptoms in the post-COVID-19 period.[17] In earlier research, it was discovered that the MD score was negatively correlated with the severity of COVID-19 symptoms such as dyspnea, cough, fever, chills, weakness, myalgia, nausea and vomiting, and sore throat. Higher adherence to the MD was also associated with a shorter period of hospitalization and convalescence, and inflammatory biomarkers.[18] According to previously conducted studies the MD adherence has been reported an increase in various countries due to the raised awareness.[19] There is a scarcity of studies that clearly reveal the impact of high MD adherence on reducing the burden of post-COVID-19 symptoms. The recommendation of a complete Mediterranean dietary pattern is more effective than that of its individual food groups in preventing the infection and symptoms of COVID-19.[20]

The patients' quality of life is negatively impacted by the COVID-19 disease and post COVID symptoms. The factors those contribute to Long COVID have also been discussed in various studies. However, studies those evaluated the symptoms those arises after recovery of COVID-19 and discussed the association with dietary adherence is not available. A deeper comprehension of the risk factors that contribute to the development of new symptoms or diseases after recovery from infection is also required. We set out to evaluate the symptoms that manifested and persisted in people who had been hospitalized after three to six months of COVID-19 infection.

Methods:

Study design:

This was a cross-sectional study among recovered adult COVID-19 patients in Dhaka city. The study population were people who were infected by COVID-19 during January to March 2022, admitted to the hospital, survived and released from hospital after recovery. The hospital registrar was the source of the sample population, which was used to select study participants. The patient list was collected from the targeted hospital with contact details. The Data collection period was May to June, 2022. The article is developed following the strengthening the reporting of observational studies in epidemiology (STROBE) checklist for cross sectional studies. All the patients were confirmed COVID-19 positive by reverse transcription polymerase chain reaction (RT-PCR) assay and had available health records for the study.

Study setting and site:

The study site was Dhaka City and the sampling frame was the patient registrar of Ad-din Medical College Hospital, which is one of the largest privately facilitated tertiary level hospitals in Dhaka City. Data was collected through phone call interview and face

to face interview between May to June 2022 by experienced physicians.

Study participants, sampling and data collection

The participants were confirmed COVID-19 patients admitted to the Ad-din Medical College Hospital between January and March 2022 and who recovered. During the study period, around 30 or more COVID-19 patients were admitted each day in the targeted facility. To control the selection bias, systematically one of every five patients from the register was selected for the interview. If we were unable to connect the targeted study sample, the immediate sample was interviewed. Participants who were aged less than 20 years, did not have any symptoms or complexity, infected with COVID-19 during later days, and those who were not interested were excluded from the study. Data with incomplete information were also excluded from the analysis. Finally, 314complete interviews of surviving patients were included in the analysis.

Tools and variables:

During the hospitalization period, the clinical records were documented and checked by experienced medical doctors. We had asked the participants about their current health condition and the status of symptoms and co-morbidies those have taken place after the recovery from COVID-19. Dietary adherence was measured by the Mediterranean Diet Adherence Screener (MEDAS) tool for MD adherence assessment. The 14-item MEDAS tool categorized the adherence level into three categories(low adherence: d”5 points, moderate adherence: 6–9 points, andhigh adherence: e”10 points).[21] MEDAS was validated in various countries, includingItaly, Macedonia, Spain, Greece, Portugal, Bulgaria, etc.[22]

Statistical analysis:

Based on the burden of symptoms and chronic conditions, study participants were categorized as (i) d”4 manifestations and (ii) >4 manifestations. The collected data were entered in Microsoft Excel-2013 and statistical analysis was performed by IBM Statistical Package for the Social Sciences (SPSS) version-25 software. The descriptive analysis of categorical variables was performed by frequency, percentage and continuous variables were reported as means with standard deviation. Association between dependent and independent variables were analyzed by Pearson’s Chi-square test or Fisher’s exact test when appropriate. Statistically significant variables were subjected to multiple logistic regression analysis to identify the predictors high manifestation burden.

Results:

The mean age of the study participants was 55.4 (±13.6) years, ranged between 24 to 90 years. Majority of our study participants (51.3%) were between 41-60 years old as a smaller number of young people usually admitted to hospital for COVID-19 and male were predominant (66.2%). More than 32% of our study participants had smoking habit. During the time of infection, a large proportion had comorbidities including, hypertension (37.7%), Asthma (17.5%), Hypothyroidism (14%), Cardiovascular problem (23.6%), Anemia (23.6%), Acute kidney infection (14.3%). ICU was required for 20.7% of our study participants and 88.5% said they are already vaccinated (Table I).

The mean Dietary adherence score 7.36(±2.1) ranged between 3 to 12 out of 14. We have categorized the adherence level into three categories following (low adherence, moderate adherence, and high adherence). Among study participants, 21.34% showed low adherence to MD and only 17.2% showed high adherence (Figure 1).

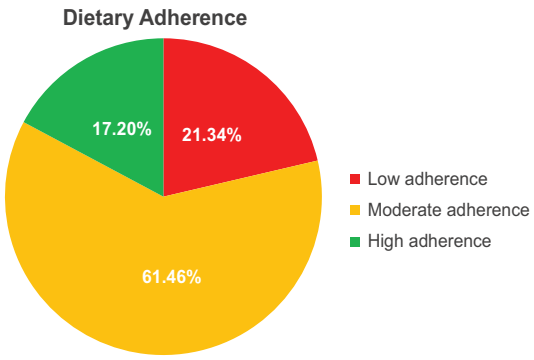

Fig.-1. *Dietary adherence of recovered COVID-19 patients*

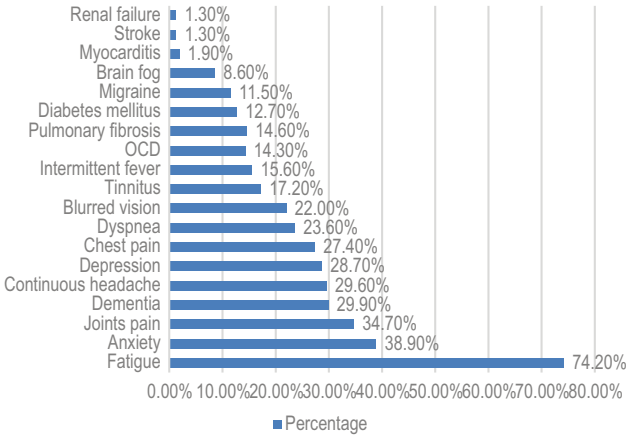

Fig.-2. *Symptoms of COVID-19 recovered patients in post-COVID period*

The median number of manifestations arises after infected with COVID-19 is 4 and maximum 10 manifestation. The frequency of various manifestations is shown in figure 2. Fatigue (74.2%) followed by the anxiety (38.9%) and joints paint (34.7%) are the most common manifestations faced during the after COVID-19 period.

We have analyzed the association between dietary adherence and manifestations appeared after recovered from COVID-19 by Spearman co-relation. According to test statistic, number of manifestations increases with the decrease of MD adherence level ($r=-0.34$, $p<0.01$), thus have medium and statistically significant negative correlation between these two variables. The age of the participants also has statistically significant positive correlation ($r=0.31$, $p<0.01$) with number of manifestations. Binary linear regression analysis also identified MD adherence as the statistically significant predictor for number of manifestation (OR: 7.25, 95% CI: 6.39-8.11).

The association between disease/symptoms burden and independent variables were determined by chi-square analysis. Age, smoking habit, Asthma, Hypothyroidism, Cardiovascular problem, Acute kidney infection, ICU requirement, and Dietary adherence has statistically significant association with disease burden ($p<0.05$)(Table 1).

The multiple logistic regression analysis indicates, participants those does not have the habit of smoking (AOR: 0.43, 95% CI: 0.24-0.77), did not have Asthma during hospitalization (AOR: 0.34, 95% CI: 0.17-0.68), Hypothyroidism (AOR: 0.37, 95% CI: 0.15-0.93), ischemic heart disease (AOR: 0.33, 95% CI: 0.15-0.74), did not required ICU (AOR: 0.31, 95% CI: 0.15-0.64) are associated with lowering the symptom burden during post COVID period. Participants with low dietary adherence are at higher risk of more disease burden during the post COVID period (AOR: 3.56, 95% CI: 1.46-8.69) (Table II).

Table-I

Frequency distribution and bivariate analysis

Variables	Category	Frequency	No of Manifestation		P
		(%)	≤4 (%)	> 4 (%)	value
Age in years	24-40	39 (12.4)	33 (84.6)	6 (15.4)	0.02*
	41-60	161 (51.3)	110 (68.3)	51 (31.7)	
	61-90	114 (36.3)	68 (59.6)	46 (40.4)	
Gender	Female	106 (33.8)	69 (65.1)	37 (34.9)	0.57
	Male	208 (66.2)	142 (68.3)	66 (31.7)	
Habit of Smoking	No	213 (67.8)	155 (72.8)	58 (27.2)	<0.01*
	Yes	101 (32.2)	56 (55.4)	45 (44.6)	
Hypertension	No	195 (62.1)	137 (70.3)	58 (29.7)	0.14
	Yes	37.9 (Yes)	74 (62.2)	45 (37.8)	
Asthma	No	259 (82.5)	185 (71.4)	74 (28.6)	<0.01*
	Yes	55 (17.5)	26 (47.3)	29 (52.7)	
Hypothyroidism	No	283 (90.1)	200 (70.7)	83 (29.3)	<0.01*
	Yes	44 (14.0)	11 (35.5)	20 (64.5)	
Cardiovascular problem	No	240 (76.4)	194 (71.9)	76 (28.1)	<0.01*
	Yes	74 (23.6)	17 (38.6)	27 (61.4)	
Anemia	No	240 (76.4)	164 (68.3)	76 (31.7)	0.44
	Yes	74 (23.6)	47 (63.5)	27 (36.5)	
Acute kidney infection	No	269 (85.7)	187 (69.5)	82 (30.5)	0.03*
	Yes	45 (14.3)	24 (53.3)	21 (46.7)	
ICU requirement	No	249 (79.3)	186 (74.7)	63 (25.3)	<0.01*
	Yes	65 (20.7)	25 (38.5)	40 (61.5)	
Vaccinated	No	36 (11.5)	25 (69.4)	11 (30.6)	0.76
	Yes	278 (88.5)	186 (66.9)	92 (33.1)	
Dietary adherence	Low	65 (20.7)	15 (23.1)	50 (76.9)	<0.01*
	Medium	193 (61.5)	151 (78.2)	42 (21.8)	
	High	56 (17.8)	45 (80.4)	11 (19.6)	

Table-II

Multiple logistic regression analysis

Variables	Category	β	AOR (95% CI)	Significance
Age in years	24-40	-0.56	0.57 (0.19-1.66)	0.30
	41-60	-0.09	0.91 (0.49-1.71)	0.77
	61-90	Reference		
Habit of Smoking	No	-0.84	0.43 (0.24-0.77)	0.01*
	Yes	Reference		
Asthma	No	-1.07	0.34 (0.17-0.68)	<0.01*
	Yes	Reference		
Hypothyroidism	No	-0.98	0.37 (0.15-0.93)	0.04*
	Yes	Reference		
Ischemic heart disease	No	-1.11	0.33 (0.15-0.74)	0.01*
	Yes	Reference		
Acute kidney infection	No	-0.14	0.86 (0.38-1.96)	0.73
	Yes	Reference		
ICU requirement	No	-1.16	0.31 (0.15-0.64)	<0.01*
	Yes	Reference		
Dietary adherence	Low	1.27	3.56 (1.46-8.69)	0.01*
	Medium	-0.37	0.69 (0.32-1.48)	0.34
	High	Reference		

Discussion:

We have successfully completed a cross-sectional study targeting the health status of recovered COVID-19 patients. Here, we have assessed COVID-19 related manifestations and Mediterranean diet adherence. Our analysis has successfully revealed patterns of dietary adherence and other factors that are associated with a higher number of manifestations related to COVID-19.

The most common manifestation reported by the study participants is fatigue, followed by anxiety and joint pain. Fatigue was common among 74.2% of the study participants. A study previously conducted among Bangladeshi adults also reported a 63% prevalence of fatigue after two months of hospital discharge.[23] Joint pain was also highly prevalent in our study. The problem of muscle pain due to muscle weakness and skeletal muscle damage is very common for COVID-19 patients.[24] Both anxiety and depression were highly prevalent among our study participants. According to a previously conducted research, the COVID-19 pandemic has increased the prevalence of anxiety and depression worldwide by 25%.[25] Another study said that, the COVID-19 pandemic has led to a 27·6% increase of major depression.[26] Dementia and brain fog are also two common manifestations of COVID-19. If left untreated, brain fog can impact the quality of life and lead to other conditions such as Parkinson's disease, memory loss, and Alzheimer's disease.[27]

Despite being a respiratory or lung condition, COVID-19 can also affect the heart. Our analysis has reported a high proportion of people with problems in their hearts. Recovery can be hampered for those who have COVID-19, especially if those issues persist. Like other viral illnesses, the coronavirus may directly infect and harm the heart's muscular tissue. Thus, chest pain is experienced by 10% of patients afterrecovery.[28-30] A study reported the presence of chest pain among 27% ofpatients. Myocarditis has also been reported as a complication in patients with COVID-19. In April 2021, increased myocarditis incidence was reported in the United States after mRNA COVID-19 vaccination.[31]

Intermittent fever is also reported as one of the long COVID symptoms.[32] We have also seen a significant proportion of our study participants face this. The possibility of obsessive-compulsive disorder (OCD) being precipitated or brought on by COVID-19-related inflammatory stimuli. More than 14% of our study

participants also reported OCD after their recovery from infection. The prevalence of OCD has increased at a higher rate since the initiation of COVID-19 pandemic.[33]

Six months to a year after COVID-19, survivors often have persistent abnormalities on lung imaging. On pulmonary function tests, some people have chronic lung impairment.[34] Around 15% of our study participants also faced pulmonary fibrosis after their recovery from infection.

There were 12.7% newly diagnosed DM patients in our study, which is very alarming. Previous research also suggests that, those recovering from a severe SARS-CoV-2 infection may experience acute sequelae like newly diagnosed DM. Patients of all ages and genders are at risk of being newly diagnosed with diabetes following COVID-19.[35-37]

Cerebrovascular diseases are common among COVID-19 patients and also in the post COVID-19 period, especially in those who have existing vascular risk factors.[38] Studies have mentioned that, anticoagulation played an important role in the stroke during COVID-19. Even after the recovery from the infection, a high risk of stroke exists, which supports our study findings. When an acute ischemic stroke occurrs in patients with COVID-19, the probability of death increases by two-fold.[39]

Patients with COVID-19 have a high prevalence of kidney illness at admission, and AKI frequently develops during hospitalization and is linked to higher fatality rates. Survived COVID-19 patients also have a high risk of kidney disease in the post-acute phase.[40,41] These findings corroborated our observations, and clinicians should be more aware of kidney disease during the post COVID period.

The anti-inflammatory properties of the Mediterranean diet are essential during the struggling health condition of the body during the post-COVID. Essential steps needed to be taken to improve the adherence to dietary recommendations among the COVID-19 recovered patients. Previous studies have observed that MD adherence has a negative association with COVID-19 related deaths in various countries. We also observed a negative association between MD adherence and post COVID-19 symptom burden.[42,42]

The association of age with the severity and outcome of COVID-19 is widely known, and this study has demonstrated the relation between advanced age and complexity after the recovery from infection (44,45). On the other hand, smoking is a well-recognized risk factor for progression of COVID-19, which is also associated with a number of comorbidies (46). Our findings suggest the recovered patients those are smokers to immediately stop it even if they have no symptoms related to COVID-19.

Conclusion:

Persistent COVID-19 symptoms and post COVID chronic diseases are concerning public health issues in recent days. A large proportion of study participants showed low dietary adherence, which contributed to the high burden of symptoms during Post-COVID-19 for long term. People with low dietary adherence are also are at higher risk for chronic diseases. Patients who did not require ICU also had a lower risk of long-term COVID symptoms burden. Effective control of post-COVID symptoms is important to confirm a healthy and good quality of life. Therefore, it is important to maintain good dietary practices, avoid bad habits, and control chronic diseases.

Limitations of the study:

This study was conducted in a single center. A complete thrombophilia evaluation could not be performed in every patient due to financial constraints and genetic study was not done.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

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

Funding:

This research received no external funding.

Ethical consideration:

The study was approved by the Ethical Review Committee of of Ad-din Medical College Hospital, Dhaka, Bangladesh. Informed consent was obtained from each participant or caregivers of the patients.

Author Contributions:

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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ORIGINAL ARTICLE

EFFECTIVENESS OF TIZANIDINE AND INTENSIVE REHABILITATION IN SPASTIC CEREBRAL PALSY

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Abstract:

Background: *The treatment of cerebral palsy is multifactorial. The aim of the study is to find out the efficacy of tizanidine and intensive rehabilitation in the treatment of spastic cerebral palsy.* ***Methods:*** *This observational study was conducted over 35 patients in Sir Salimullah Medical Mitford Hospital from January 2022 to December 2022.The patients satisfying the inclusion and exclusion criteria were enrolled: total 35 patients received tizanidine (2mg) orally at a dose of 1 mg given at bed time under 10 years and 2 mg given at bed time more than 10 years of age, then after 1 week maintenance dose was given at 0.3 mg/kg/day, three times daily in combination with intensive rehabilitation 1 hour daily five times a week. Total 24 weeks of intensive rehabilitation was given. All patients were followed up at 4 weeks interval and were evaluated for a total of 24 weeks.* ***Results:*** *The study shows high efficacy in reducing tone in spastic cerebral palsy measured by using Modified Ashworth scale ($p<0.001$).Also there is improvement in physician rating scale crouch ($p<0.0001$) and foot contact, ($p<0.0001$) and also improvement in gross motor function ($p<0.01$).* ***Conclusion:*** *Combination of tizanidine and intensive rehabilitation is effective for reduction of generalized spasticity regarding muscle tone, range of motion of the joint and improvement of gait in cerebral palsy patients.*

Key words: *Cerebral Palsy, Spasticity, Tizanidine, Intensive Rehabilitation*

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Introduction:

Cerebral palsy is the most common disability of childhood that affects motor function as a result of injury to the developing brain.[1] It is now well known that the prime risk factors for cerebral palsy are delivery before 37 weeks and birth weight of less than 2.5 kg; however, there are some other problems evident in the literature which are found to be some of the prominent reasons for brain damage, some of which includes malformation of the brain in the developmental period, genetic causes, in utero mother and fetus infections, and various other issues.[2]

The presenting signs and symptoms of CP are diverse and mainly consist of motor disorders, sensory deficits, and associated comorbidities which occur due to a static lesion to the developing brain. These signs and symptoms change as the child ages and new features are added to the list. Thus, with advanced age, there is a worsening of the neuromuscular system and functional capability of the child even though the damage in the brain is static.[3]The most common movement disorders seen in cerebral palsy are spastic muscles and dystonia

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with difficulties in coordination, strength, and selective motor control. Spasticity is the major challenge in the management of CP children. It causes spasticity-induced bone and joint deformity, pain, and functional loss[4].Commonly used medicines found in the literature to relieve spasticity are baclofen, diazepam, clonazepam, dantrolene, and tizanidine. Baclofen and diazepam help in relaxing the muscles but have many side effects.[5] Treatment of spastic cerebral palsy includes physiotherapy along with antispastic medication. Tizanidine is similar to diazepam and baclofen in the effectiveness of tone reduction.[6] Tizanidine is readily absorbed after oral administration and metabolized in the liver. Alpha 2 adrenergic agonists have an anti-nociceptive effect, which may assist in their tone-reducing abilities because pain is known to increase spasticity; it is possible that this effect is mediated through the release of substance P in the spinal cord[7]. Tizanidine is possibly effective, but there are insufficient data on its effect on improvement of motor function and its side-effect profile. The tizanidine and baclofen are currently most promising drugs treated for cerebral palsy. Intensive rehabilitation may be defined as 1 hourly intervention, 5 days a week, as opposed to a therapy session once a week or once every second week[8]. It consists of neurodevelopmental treatment (NDT), therapeutic exercises (TEs) and activities of daily living (ADL) training.[9] The aim of this study was to find out the efficacy of tizanidineand intensive rehabilitation in reducing spasticity in cerebral palsy.

Methods:

Subjects:

An observational study was done in Sir Salimullah Medical College Mitford Hospital from January 2022 to December 2022. All the spastic cerebral palsy patients seeking treatment in outpatient department of Physical Medicine & Rehabilitation and Pediatrics were the reference population. From reference population, patients enrolled in the study who met the inclusion and exclusion criteria. Sample size estimates suggested that 35 subjects would be sufficient to detect a 5% level of significance. Patients aged between 12 months to 12 years; with disorder in the development of movement and posture presumably of cerebral origin started before 2 years of age, presence of spasticity associated with or characterized by increased tone reflexes, clonus or extensor plantar response, and delayed milestones of development which is improving over time were included in this study. Those with mixed type of cerebral palsy; receiving systemic anti-spasticity medications or had received phenol and/or botulinum toxin type A injections; past surgical intervention that might interfere with ankle joint movement; neurodegenerative disorders, chromosomal abnormality such as Down syndrome, inborn errors of metabolism such as galactosemia and presence of comorbidity such as epilepsy were excluded.

Procedure:

A total number of 35 patients were primarily selected. Complete history and clinical examination were done for all enrolled patients.

After taking written informed consent from parents,they were finally selected for the study. All patients received intensive rehabilitation (1 hour daily for 5 days a week) and oral tizanidine (2mg) orally at a dose of 1 mg given at bed time under 10 years and 2 mg 10 years or more, then after 1 week maintenance dose was 0.3 mg/kg/day three times daily was given for 24 weeks. Patients were first assessed with Modified Asworth Scale (MAS)[10] based on muscle tone to determine the extent of spasticity. Then Physician Rating Scale[11]to measure joint angle (crouch) especially by standard goniometer,knee recurvatum, foot contact and overall functional status by Gross Motor Functional Classification System.[12] Then intervention was done by giving oral tizanidine with intensive rehabilitation to reduce spasticity in the group and uniform intensive rehabilitation protocol was applied. After 4 weeks (1st follow up) during the continuation of drugs, patients were again assessed using before mentioned 3 scales and adverseeffect of oral tizanidine was recorded in follow-up sheet. After 8 weeks (2nd follow up), patients were again assessed using before mentioned 3 scales and adverse effect of oral tizanidinewas recorded in follow up sheet. Then follow upassessment was done every 4 weekly at 12th week, 16thweek, 20th week and lastly 24th week for total with continuing the drugs using same scales. Patients were advised intensive rehabilitation by an experienced physiotherapist at the department of Physical Medicine & Rehabilitation, Sir Salimullah Medical College Mitford Hospital, Dhaka.

Drug administration and titration:

After selection, tizanidine was given according to following dose schedule. Oraltizanidine (2mg) at a dose of 1 mg given at bed time under 10 years and 2 mg given at bed time more than 10 years of age, then after 1 week maintenance dose was 0.3 mg/kg/day three times daily.

Intensive rehabilitation:

One-hour intensive physiotherapy was given daily for 5 days a week. Activities included in each session

were body alignment weight transfer in various positions, bimanual activities and facilitation sequences of movements.

Ethical issues:

Ethical clearance has been obtained from the ethical committee of Sir Salimullah Medical College to conduct the research work.

Data analysis:

Data were collected through a pretested structured questionnaire. Data were processed and analyzed using SPSS (statistical package for social science) version 17. Test statistics used to analysis the data were chi square Test and student T test. The level of significance was set 0.05 and p-value of less than 0.05 was considered significant.

Results:

A total of 35 patients were recruited for the study. The mean age of the patients was 31.97 months. Patients receiving tizanidine and intensive rehabilitation were 39% inASscore-3 before starting treatment. However, 46.0%of patients later on began to show alower Ashworth score which at 3rd month in 2nd follow up shifted to ASscore-2 because of improvement. This improvement in the 4th month compared to the3rd month was found to be highly significant (p < 0.0001) (Figure-1).

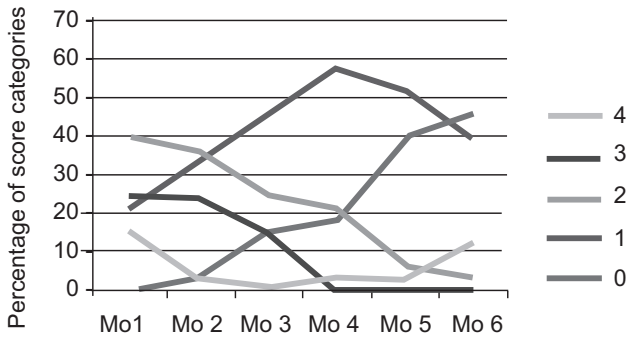

Fig.-1: *Monthly change of muscle tone by modified ash worth scores*

The patients showed variation in percentage of score of joint angle measured by crouch scores of physician rating scale. For example, 49% of the patients had severe spasticity in the first month. However, in the second month 61% patient had moderate angle, although the mean score improvement was not statistically significant (p = 0.21) from the 4th month another shift of improvement was observed among patients. 46% of the patients in the 4th month had mild variety, the condition lasting through the end of the follow up and significant change in mean scores at 5th month (p = 0.03) but nonsignificant from 5th to 6thmonth (p = 0.14). (Figure-2).

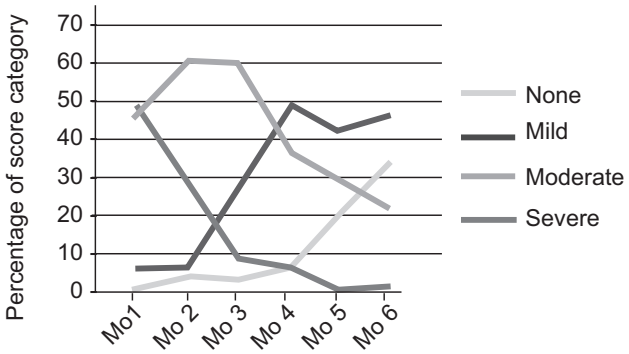

Fig.-2: *Monthly change of joint angle measured by crouch scores of physician rating scale*

Another component of physician rating scale of the patients had a score of 0 in month 1 and 2 (about 70% and 52% respectively), a change in score was seen in 3rd month (about 61% had score 1) of the follow-up, however, the change in mean score from 2nd to 3rd month was not statistically significant (p = 0.67). Statistically significant improvement (p < 0.0001in mean score began between 3rd to 4th month and the trend continued till the end of the follow-up (Figure-3).

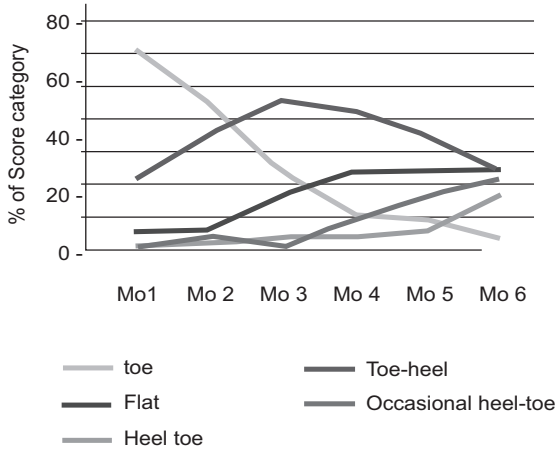

Fig.-3. Monthly change of gait measured by foot contact scores of physician rating scale.

Before starting treatment,52% patients were at level 5% and 32% patient were at level 4. In Month 4 follow-up it was found that over half the patients (56.0%) improved to Level 3. The difference in mean score was statistically highly significant (p = 0.001). Although a large proportion of these patients eventually improved towards level 2 (30.0%) or level 1 (9.0%), the majority of the sample remained in level 3 in the 4th (56.0%), 5th (56.0%) and 6th month (46.0%) of follow up time (Figure-4).

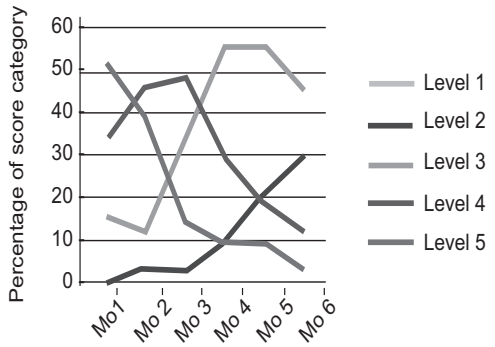

Figure 4.*Monthly change of gross motor function.*

Discussion:

The syndrome of spastic hypertonia develops when the supra segmental control over the spinal cord segmental reflexes is lost[13]. Spasticity can range from mild muscle stiffness to severe, painful, and uncontrollable muscle spasm. It is associated with some common neurological disorders: Multiple sclerosis, stroke, cerebral palsy, spinal cord and brain injuries, and neurodegenerative diseases affecting the upper motor neuron, pyramidal and extrapyramidal pathways[14]. Mean age of the patients was 31.97 months.

Nikkhahet al.[15] found mean age of 7.3 ± 3.4 years and Adam et al.[16] found mean age of 7.4 ± 2.3 years. The difference between this study and other study is that patients are not coming to physician after 5 years due to socioeconomic condition and false belief. Nikkhahet al.[15] found the mean Ashworth score decreased in 50% of the patients receiving tizanidine versus 6.7% of patients receiving the placebo ($p < 0.0001$). In a previous study by Vasqueset al.[17] found that in the group receiving tizanidine 78.8% reported having reduced spasticity compared with only 76% patients receiving the placebo ($p < 0.0001$). Alperet al.[18] found that the mean score of gross motor function measure is highly significant and modified Asworth is significant. This study suggests that adjuvant treatment with oral tizanidine is more effective than baclofen in combination with botulinum toxin for spastic equines foot deformity due to cerebral palsy. Significant improvement was demonstrated using gross motor and modified Asworth scale ($p < 0.05$). In present study in gross motor function score, it was found that the mean gross motor function score of the patients receiving tizanidine with Intensive Rehabilitation was lower. Physician ratings scales comprise crouch measure and foot contract score. A higher mean crouch score for patients receiving tizanidine with Intensive Rehabilitation was statistically highly significant ($p < 0.0001$).

Wagstaffet al.[19] found improvement in muscle tone occurred in 60% to 82% of tizanidine recipients compared with 60% to 65% of baclofen. Adam et al. [16] using Tardiew score found that score was 4.4 for baclofen and placebo. 49% of the patients had severe spasticity in the first month. However, in the second month 61% patient had moderate angle, although the mean score improvement

was not statistically significant ($p = 0.21$) from the 4th month another shift of improvement was observed among patients receiving tizanidine and Intensive Rehabilitation. 46% of the patients in the 4th month had mild variety, the condition lasting through the end of the follow up and significant change in mean scores at 5th month ($p = 0.03$) but non-significant from 5^{th} to 6^{th} month ($p = 0.14$).

During measuring crouch, patients receiving tizanidine with Intensive Rehabilitation showed remarkable variation in scores and accordingly change in severity of ankle compared to patients receiving intensive rehabilitation. For example majority of (about 49%) of the patients had severe spasticity in the first month. However in the second month majority of patient (about 61%) had moderate Ankle measure, although the mean score improvement was not statically significant ($p = 0.21$). Statically significant improvement of spasticity by change of mean score, using MAS score it is at 4th month. Using crouch score, there is statistically significant improvement in the patients getting tizanidine with Intensive rehabilitation in the 5th month. Nikkhah et al. [15] showed after 2weeks improvement of tizanidine group compared to placebo. Alper et al. [18] showed improvement after 3rd month comparing tizanidine with botulinum compared to baclofen with botulinum in GMFCS score & MAS score.

Conclusion:

Result of this study shows that basic motor abilities and self-care improved after intensive physiotherapy with tizanidine is effective for reducing generalized spasticity regarding muscle tone and joint angle stiffness and gait improvement in cerebral palsy patients. Further larger scale study is required to know the effectiveness of both tizanadine and intensive physiotherapy in the treatment of cerebral palsy patients.

Limitations:

Small sample size and this single hospital based study did not reflect exact scenario of the whole community. Patients from all socioeconomic status and all parts of the country did not come to seek medical attention in the study place.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

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

Funding:

This research received no external funding

Ethical consideration:

The study was conducted after approval from the ethical review committee. The study was approved by the Ethical Research Committee of Sir Salimullah Medical College The confidentiality and anonymity of the study participants were maintained.

Authors' Contributions:

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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ORIGINAL ARTICLE

STUDY OF LEFT VENTRICULAR DYSFUNCTION IN TYPE 2 DIABETES MELLITUS PATIENTS WITHOUT KNOWN CO-MORBIDITIES

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Abstract

Background: *Subclinical left ventricular dysfunction in type 2 diabetes mellitus (DM) patients may precede the development of symptomatic heart failure. Detecting this dysfunction early could potentially prevent its progression. However, there is a scarcity of studies on this topic in Bangladesh. Therefore, this study aimed to explore the left ventricular function status in type 2 DM patients without any known co-morbid conditions in a tertiary care hospital.* ***Methods:*** *A cross-sectional study was conducted at the Department of Internal Medicine in Sir Salimullah Medical College & Mitford Hospital over a one-year period. A total of 100 patients with a diagnosis of type 2 DM, meeting the inclusion-exclusion criteria, were enrolled. Written informed consent was obtained from each participant, followed by the collection of socio-demographic data, detailed clinical history, and routine investigations. Echocardiograms were performed on all participants to assess the presence of systolic and diastolic dysfunction using various modes. Data analysis was conducted using the statistical software SPSS 23.0.* ***Results:*** *The mean age of the study patients was 47.23±9.13 (SD) years, with the majority in the age group of 40-49 years (43%). Female patients accounted for 58% of the sample, while male patients comprised 42%. The frequency of left ventricular diastolic dysfunction (LVDD) was 65%. The presence of LVDD was associated with longer duration of diabetes mellitus, higher HbA1C levels, older age, and increased BMI (p<.05).* ***Conclusion****: The majority of type 2 diabetic patients in this study exhibited left ventricular diastolic dysfunction, with a prevalence of 65%. Further larger-scale studies are recommended to validate these findings.*

Keywords: *Diabetes mellitus, left ventricular dysfunction, Echocardiography.*

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Introduction:

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors (Chandey et al. 2020) .[1] Two broad categories of DM are Type 1 or Type 2. Type 1 is the result of complete or near-total insulin deficiency. Type 2 DM is a heterogeneous disorder characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production (Kumar et al. 2017; Masugata et al. 2008)[2]. Diabetes is a significant public health problem regionally and globally. It is a leading cause of death in most countries (Zimmet et al. 2014)[3]. In 2019, the International Diabetes Federation estimated that 465 million (9.3%) people worldwide had diabetes and by 2045, the number may rise to 700 million (10.9%). A progressive increase in the prevalence of diabetes and pre-diabetes has been observed both in urban and rural areas in South Asia, primarily due to lifestyle changes and the transition to urbanization and industrialization (Chowdhury et al. 2018; Patil et al. 2011; Akhtar et al. 2020)[4]. Bangladesh is not an exception; based on published studies, the prevalence of diabetes ranges from 2.21% to 35% in this developing country (Saquib et al. 2013; Akhtar et al. 2020).[5]

Metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that lead to long-term chronic complications, accounting for further morbidity and mortality attributed to the disease (Kumar et al. 2017).[6]

It is associated with many cardiovascular complications, e.g., increased atherosclerotic coronary artery disease, myocardial infarction, congestive heart failure, coronary microangiopathy, systemic arterial hypertension, and cardiomyopathy. An early diagnosis on that account can be of great help to prevent or delay the development of these complications (Chawla, Chawla and Jaggi 2016).[7]

Diabetic cardiomyopathy refers to a disease process that affects the myocardium in diabetic patients causing a wide range of structural abnormalities eventually leading to left ventricular hypertrophy and diastolic and systolic dysfunction or a combination of these. In diabetic cardiomyopathy, a long subclinical course can be present in most patients before the development of symptoms (Chandey et al. 2020).[8]

Left ventricular diastolic dysfunction (LVDD) represents the earliest pre-clinical manifestation of diabetic cardiomyopathy, preceding the systolic dysfunction and evolving to symptomatic heart failure. Diastolic dysfunction is the dominant cause of heart failure in patients having diastolic heart failure. In diabetes mellitus, diastolic dysfunction results from abnormal myocardial active relaxation and increased passive stiffness due to metabolic derangements, microvascular disease, autonomic dysfunction, and structural remodeling. However, the exact pathogenesis of diabetic cardiomyopathy is still unclear (Freire et al. 2007; Silbiger 2019; Yadava et al. 2017).[9]

Doppler echocardiography has emerged as a valuable noninvasive diagnostic tool for assessing cardiac function, including diastolic and systolic function. Advanced echocardiographic techniques, such as tissue Doppler and color M-mode, have improved the detection of moderate diastolic dysfunction, particularly the pseudonormal pattern. Given the cardiometabolic implications of DM, a comprehensive evaluation of cardiovascular function is essential in diabetic patients.

Previous studies have reported varying prevalence rates of LVDD in Type 2 DM, ranging from 47% to 71%, and in individuals with left ventricular systolic dysfunction, the prevalence ranges from 6% to 25%. However, there is considerable uncertainty regarding the correlation between glycemic control and LVDD, with conflicting results reported in the literature. Therefore, this study aims to investigate left ventricular function abnormalities in patients with Type 2 DM without known co-morbidities, shedding light on the presence and characteristics of LVDD in this population.

Methods:

This study employed a cross-sectional design and was conducted at the Department of Internal Medicine in Sir Salimullah Medical College & Mitford Hospital. The study period spanned from January 2021 to December 2021, following the acceptance of the protocol. A total of 100 patients diagnosed with Type 2 DM were enrolled based on predefined inclusion and exclusion criteria.

Upon enrollment, written informed consent was obtained from each participant. Socio-demographic data, along with a detailed medical history, were collected from each patient. A thorough clinical examination was performed, and routine investigations were conducted. The glycemic status of the participants was assessed using the measurement of HbA1C.

Furthermore, each participant underwent an echocardiogram to evaluate the presence of both systolic and diastolic dysfunction. Echocardiographic assessment was performed using 2D mode, M-mode, and Doppler mode with color flow mapping. The left ventricular function was specifically assessed using these techniques. The echocardiogram was conducted with the patient in a left lateral recumbent position, utilizing standard parasternal, short axis, and apical views. The pulsed Doppler spectrum of mitral flow was analyzed to measure the peak velocity of early filling (E) and peak velocity of atrial filling (A). The ratio of E/A was calculated.

Diagnosis of diastolic dysfunction was determined based on the E/A ratio measured by M-mode echocardiographic measurements. A ratio of E/A less than 1 or greater than 2 indicated left ventricular diastolic dysfunction. Left ventricular systolic function was assessed by estimating the left ventricular ejection fraction (EF) using the modified Simpson's method. An ejection fraction less than 50% indicated left ventricular systolic dysfunction.

Data collected during the study were tabulated and analyzed using the statistical package SPSS version 23.0. Categorical variables were presented as frequency and percentage, while continuous variables were presented as mean and standard deviation. The association between variables was established using appropriate statistical tests such as chi-square test, t-test, or non-parametric tests. A confidence interval of 95% and an error margin of 5% were employed for data analysis. A p-value less than 0.05 was considered statistically significant.

The study protocol received approval from the ethical committee of Sir Salimullah Medical College, Dhaka. Strict confidentiality measures were implemented to safeguard the information and records of the participants. Moreover, the participants had the right to withdraw from the study at any time during the research period.

Results:

This cross-sectional study was conducted in the Outdoor Department of Sir Salimullah Medical College Medical College and Hospital. The study patients were selected from the attending patients with a confirmed diagnosis of type 2 diabetes mellitus and no known co-morbidities. A total of 100 patients were selected according to inclusion and exclusion criteria. The aim of the study was to assess the left ventricular function status of the studied patients.

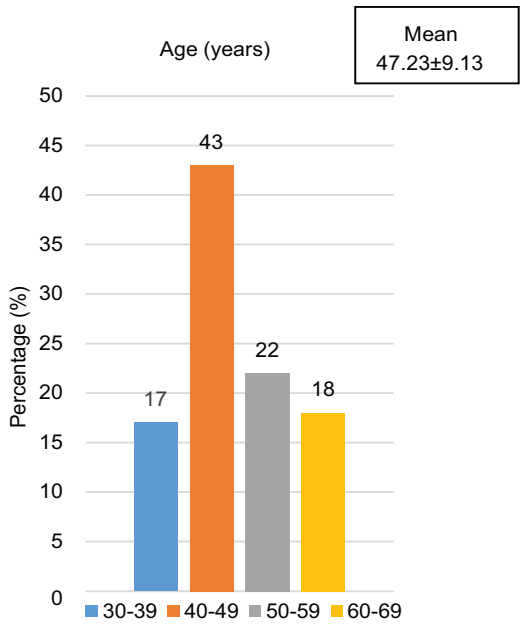

Figure 1: *Distribution of the study respondents according to age (n=100)*

The distribution of the study respondents according to age revealed that the majority of patients belonged to the 40-49 years age group (43%), followed by 50-59 years (22%), 60-69 years (18%), and 30-39 years (17%). The mean age of the patients was 47.23±9.13 (SD) years.

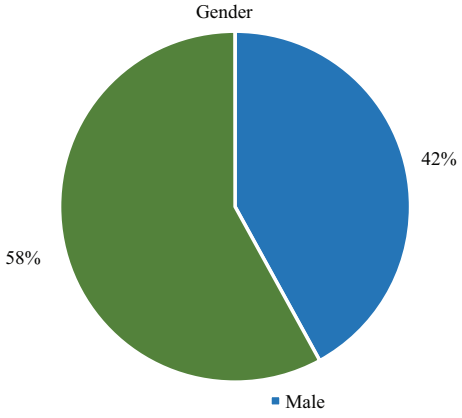

Figure 2: *Distribution of the study respondents according to gender (n=100)*

In terms of gender distribution, approximately 58% of the patients were female, while 42% were male.

Table-I

HbA1C among the study respondents (n=100)

H HbA1C (%)	n (%)	Mean±SD
<6.5	0	5.21±1.19
≥6.5	70	8.99±1.88

Regarding HbA1C levels, 30% of patients had HbA1C levels below 6.5% (mean 5.21±1.19%), while 70% had HbA1C levels equal to or above 6.5% (mean 8.99±1.88%)

Table II

Duration of type 2 DM among the study respondents (n=100)

Duration (years)	Percentage (%)	Mean±SD
≤5	59	5.79±4.0
6-10	32	
11-15	5	
16-20	4	

The mean duration of type 2 diabetes mellitus among the patients was 5.79±4.0 (SD) years. About 59% of the patients had type 2 diabetes for less than or equal to 5 years, 32% had it for 6-10 years, 5% had it for 11-15 years, and 4% had it for 16-20 years.

Table-III

Presence and type of left ventricular dysfunction among the study respondents (n=100)

LVD	Percentage (%)
Left ventricular diastolic dysfunction (present)	65
Left ventricular dysfunction (absent)	35
Left ventricular systolic dysfunction	00

In this study, about 65% of type 2 DM patients were observed with left ventricular diastolic dysfunction (LVDD).

Table IV

Association between the presence of LVD and HbA_1C among the study respondents (n=100)

HbA1C	LVD		Total	p value
	Yes n (%)	No n (%)		
<6.5	2(6.7)	28(93.3)	30	<.001*
≥6.5	63(90)	7 (10)	70	

p value was determined by chi-square test*

Patients with HbA1C levels equal to or above 6.5% had a higher prevalence of LVDD compared to those with HbA1C levels below 6.5%.

Table V

Relationship between the presence of LVD and duration of type 2 DM (n=100)

Duration of DM (years)	LVD		Total value	p value
	Yes n (%)	No n (%)		
d" 5	32 (54.2)	27 (45.8)	59	.044*
6-10	25 (78.1)	7 (21.9)	32	
11-15	4 (80)	1 (20)	5	
16-20	4 (100)	0	4	

p value was determined by chi-square test*

Values are expressed within parenthesis percentage (%) over row in total

Table VI

Relationship between the presence of LVD with age of the study respondents (n=100)

Age (years)	LVD		Total	p value
	Yes n (%)	No n (%)		
30-39	4 (23.5)	13 (76.5)	17	.001*
40-49	27 (62.8)	16 (37.2)	43	
50-59	19 (86.4)	3 (13.6)	22	
60-69	15 (83.3)	3 (16.7)	18	

p value was determined by chi-square test*
Values are expressed within parenthesis percentage (%) over row in total

The presence of LVD was statistically associated with the older age (p<.05).

Table VII

Comparison between the LVD and BMI (mean±SD) among the study respondents (n=100)

LVD	BMI (kg/m^2) mean±SD	*p* value
Yes	27.16±2.48	<.022*
No	24.83±2.71	

p value was independent student t test*

The mean BMI was also higher among the patients with LVD than the patients who didn't develop LVD (27.16±2.48kg/m^2 vs 24.83±2.71kg/m^2, p<.05).

Discussion:

This cross-sectional study focused on type 2 diabetic patients and provided insights into the prevalence of left ventricular dysfunction (LVDD) and its association

with various factors. The average age of the patients in this study was 47 years, with a majority falling in the 40-49 years age group. Additionally, female predominance was observed among type 2 DM patients, aligning with previous research by Safita et al. and Hira et al[10]. The influence of genetic factors, hormonal differences, and behavioral/environmental variations may contribute to the higher prevalence of type 2 DM in females (Kautzky-Willer, Harreiter, & Pacini)[11]

In terms of BMI, the majority of patients in this study were classified as obese (41%), followed by overweight (28%). A smaller percentage (12%) fell into the morbidly obese category, while only 19% had a normal BMI. These findings are consistent with studies by Mugharbel & Al-Mansouri, Al-Sharaf & Gunaid, Basukala, Sharma & Pandeya[12], which also reported high rates of increased BMI among type 2 DM patients.

The frequency of LVDD in this study was found to be 65%, with no cases of left ventricular systolic dysfunction (LVSD). This could be attributed to the fact that a significant portion (59%) of the type 2 DM patients had a disease duration of d" 5 years. Other studies, such as those conducted by Chandey et al[13]., Kumar et al[14]., Shrestha et al[15]., and Dike Ojji et al[16]., reported varying rates of LVDD, ranging from 66% to 81%. Dodiyi-manuel et al[17]. observed a lower prevalence of systolic dysfunction at 15.56%. These variations could be attributed to differences in study populations, diagnostic criteria, and patient characteristics.

The mean duration of type 2 DM in this study was 5.79±4.0 years. It was found that both longer disease duration and higher glycemic status, as indicated by HbA1C levels, were associated with the presence of LVDD. Older age and increased BMI were also identified as factors associated with LVDD. These findings are in line with previous studies highlighting the impact of glycemic control, disease duration, age, and BMI on the development of LVDD in type 2 DM patients.

Overall, this study provides valuable insights into the prevalence of LVDD among type 2 DM patients and its association with various factors. The findings underscore the importance of early detection, glycemic control, and lifestyle interventions, such as weight management, in preventing or managing LVDD in this population. Further research and larger-scale studies are warranted to validate these findings and explore additional factors contributing to LVDD in type 2 DM patients.

Conclusion:

The majority of type 2 diabetic patients in this study exhibited left ventricular diastolic dysfunction (LVDD) at a prevalence of 65%. The presence of LVDD was associated with longer duration of diabetes mellitus, higher HbA1C levels, older age, and increased BMI. These findings emphasize the importance of screening type 2 diabetic patients for subclinical LVDD using echocardiography to facilitate early interventions and prevent further deterioration.

Limitations:

Several limitations should be considered when interpreting the results of this study. Firstly, the samples were collected from a single site, which may limit the generalizability of the findings. Additionally, the sample size was small due to the constraints imposed by the Covid-19 pandemic. The study design was cross-sectional, which limits the ability to establish causal relationships. Furthermore, other parameters of diastolic dysfunction measurement, such as tissue Doppler imaging, were not included in the study.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

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

Funding:

This research received no external funding.

Ethical consideration:

The study was conducted after approval from the ethical review committee. The confidentiality and anonymity of the study participants were maintained

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ORIGINAL ARTICLE

MEASURING AND COMPARING CORTICAL SURFACE AREA OF PARACENTRAL LOBULE IN A TERTIARY CARE HOSPITAL, BANGLADESH

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Abstract

Background: *The paracentral lobule is the area on medial surface of the cerebral cortex which extends from precentral sulcus to postcentral sulcus. Any trauma, tumor, or cerebral ischemia cause lesions of motor and sensory cortex of paracentral lobule. The result of this study is very important to the radiologists and neurosurgeons for diagnosis of above mentioned diseases and the practice of safe neurosurgery. This study was carried out to observe the cortical surface area of paracentral lobule in adult male and female Bangladeshi population,may help for future research.* ***Methods:*** *This cross- sectional study was conducted in the Department of Anatomy, Dhaka Medical College, Dhaka, during the period of January 2017 to December 2017. Total 70 adult Bangladeshi male &female people were selected, among them 35 male and 35 female, age ranging from 20-65 years. CT scan image of brain in mid sagittal view was used for this study. Data were analyzed by Unpaired Student's 't' tests.* ***Results:*** *The surface area of motor cortex of right and left paracentral lobule was significantly higher ($p<0.01$) in male.Surface area of sensory cortex of both paracentral lobule was significantly higher ($p<0.05$) in male than female.* ***Conclusion:*** *The present study reveals significant difference in morphological measurements of right and left paracentral lobule between male and female of adult Bangladeshi population.*

Key words: *Paracentral lobule, motor cortex, sensory cortex, morphometric measurement.*

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Introduction

The paracentral lobule is located on the medial surface of cerebral hemisphere.[1] This specific area of cerebral cortex are concerned with specific parts of the body with specific types of input and activities.[2] This lobule extends from precentral sulcus to postcentral sulcus on superomedial border. On the medial surface of cerebral hemisphere, the paracentral lobule is bounded anteriorly by the paracentral sulcus, an ascending branch of the cingulate sulcus which is anterior to precentral sulcus. Posteriorly it is bounded by the pars

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marginalis, which is the ascending termination of the cingulate sulcus, inferiorly by the cingulate sulcus.[3,4] Its superior boundary corresponds to the superior margin of the hemisphere. The paracentral sulcus which is anterior to the precentral sulcus containing the supplementary motor area did not consider as a potential anterior boundary of the paracentral lobule.[4] In case of segmented cingulate sulcus there is a short transitional lobulo-limbic gyrus, which may complicate definition of the paracentral lobule boundaries.[5]

By the indentation of central sulcus, this lobule is divided into anterior and posterior parts.[6] The anterior part is continuous with the precentralgyrus and posterior part is continuous with the postcentralgyrus.[7]The anterior part contain primary motor area representing the muscles of leg and foot[4] and the perineal region of the opposite side.It is responsible for voluntary control of defecation and micturition.[6] The posterior part contains the primary somatosensory area, representing the leg and foot[(7)]. Ischemia and infarction occurs in cerebrovascular disease which causes lesions of motor cortex and produce contralateral lower limb weakness or paralysis and urinary incontinence.[8,1] This area may be a primary site for tumors and focal seizures making its surgical access of great importance for neurosurgery.[3]Thickness of cortex (gray matter volume) of paracentral lobule decreases with age and also in many diseases such as in Alzheimer's disease.[9] chronic Schizophrenia, and multiple sclerosis.[10]

Due to advances in the endoscopic neurosurgery, which has decreased the incidence of morbidity in conventional surgery, it has become extremely necessary to better understand the detailing of the paracentral lobule's anatomy and it'slocation with surroundings.[3]

This study was an attempt to contribute to the current knowledge regarding anatomy of the paracentral lobule, conducting an analysis of morphological measurements of this region in both cerebral hemispheres between adult Bangladeshi male and female population. For this study Computed tomography (CT) Scan of brain in mid sagittal view was used because it provided more detailed information about structure of brain than regular radiographs (x-ray).[11]

Methods:

This Cross sectional study was conducted in the Department of Anatomy, Dhaka Medical College, Dhaka, during the period from January 2017 to December 2017. Seventy adult Bangladeshi people, among them 35 male and 35 female, age ranging from 20-65 years were included in this study. The subject of this study were selected from the Radiology & Imaging Department of Dhaka Medical College & Hospital attending for CT scan of brain advised by their physicians. This study was carried after permission from Ethical Committee. Subject were selected purposively. The study subjects were assured of confidentiality of the study. Personal information of the subjects were recorded on questionnaire by the author. Informed written consent was taken. Those CT scan images of brain in mid sagittal view of both cerebral hemispheres were collected which were normal reported by the radiologists. For this study, reconstructed mid sagittal view of both cerebral hemispheres were taken since the paracentral lobule was visible in this way and these images were viewed on a computer monitor for editing and magnifying. Different dimensions of paracentral lobule were measured from these images by using computer with image measuring software program named DICOM (Digital Imaging and Communications in Medicine) version 4.0.3. (64-bit).

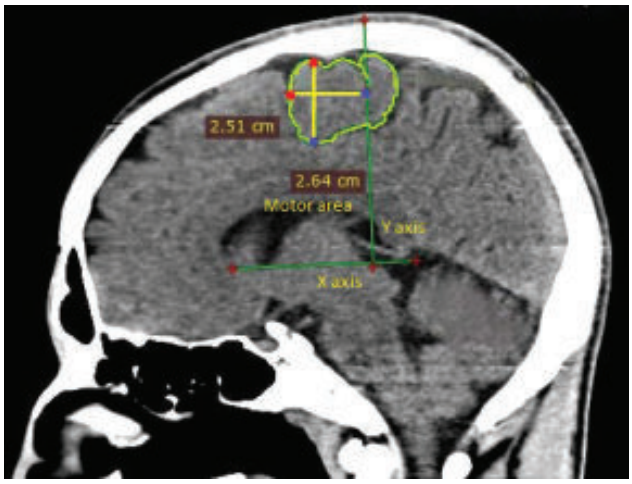

Figure: *Photograph showingsurface area of motor cortex of paracentral lobule.*

Due to a total absence of clear morphological landmarks, measurement was standardized by using intercommissural or CA-CP line (CA- anterior commissure, CP- posterior commissure)) line system in order to increase precision of data[4].

Statistical analysis:

Unpaired student's't' test was done for statistical analysis of the results. P value <0.05 was taken as of significance.

Results:

In male,mean surface area of motor cortex of the right paracentral lobule was 6.17±0.85 cm^2&the left paracentral lobule was 6.47±0.74 cm^2. In female, mean surface area of motor cortex of the right paracentral lobule was 5.52±0.81 cm^2& the left paracentral lobule was 5.97±0.72 cm^2. From Table I foundstatistically significant difference in mean surface area of motor cortex of right (p=0.002) and left (p=0.005) paracentral lobule between male and female.

Table I

Surface area of motor cortex of right & left paracentral lobule between male and female

Variables	Male (n=35)	Female (n=35)	p value
Right motor cortex (cm^2) (Mean±SD)	6.17±0.85	5.52±0.81	0.002**
Left motor cortex (cm^2) (Mean±SD)	6.47±0.74	5.97±0.72	0.005**

Comparison of values between male and female was done by Unpaired Student's 't' test,

** = significant at p<0.01.

In male, meansurface area of sensory cortex of the right paracentral lobule was 2.21±0.43 cm^2&the left paracentral lobule was 2.07±0.37 cm^2. In female, the meansurface area of sensory cortex of the right paracentral lobule was 1.94±0.41 cm^2&the left paracentral lobule was 1.88±0.41 cm^2. Table II showingstatistically significant difference in mean surface area of sensory cortex of right (p=0.010) and left (p=0.047) paracentral lobule between male and female.

Table II

Surface area of sensory cortex of right & left paracentral lobule between male and female

Variables	Male (n=35)	Female (n=35)	p value
Right sensory cortex (cm^2) (Mean±SD)	2.21±0.43	1.94±0.41	0.010*
Left sensory cortex (cm^2) (Mean±SD)	2.07±0.37	1.88±0.41	0.047*

Comparison of values between male and female was done by Unpaired Student's 't' test,

* = significant at p<0.05, ** = significant at p<0.01.

Discussion:

In this study, mean surface area of motorcortex (right (p=0.002) and left (p=0.005))and sensory cortex (right (p=0.010) and left (p=0.047))of the right & left paracentral lobule were found significantly higher in male than female.Statistically significant difference was also observed between male and female.Surface area of motor cortex of left paracentral lobule was significantly largerthan right both in male and female.Mean surface area of sensory cortex was larger in right paracentral lobule than the left both in male and female. Spasojevic[4] recorded the surface area of right and left paracentral lobule and revealed that mean surface area of left paracentral lobule was significantly larger (p<0.05) both in male and in female than the right paracentral lobule in their study subjectswhich corresponds to the predominance of right handed people (90-95%).After comparing the surface area of paracentral lobule between male and female,they did not find statistically significant sex differences(p>0.05).The findings of the present study were almost within normal range and also similar to the findings of that study.

Review of existing literature reveals that few works have been done on this topic in other countries. The studies concerning measurements of the paracentral lobule did not carried out in our country previously. So, the result of the present study was compared with the findings of other researchers of abroad. Some dissimilarities were noticed among the findings of present study and the studies conducted byother researchers.This dissimilarities may be due to mixture of different age and races, different geography, use of cadaveric brain instead of CT scan image from living subject, variation in the radiograph and taking the measurement in different technique.

The adult paracentral lobule study is very important to the radiologist and clinicians for the diagnosis and treatment of related diseases. The result of the present study can be used as a baseline anatomical normative data for future researches and the findings of this study might be useful in providing data for the anatomists, radiologist, neurosurgeons, and forensic experts.

Conclusion:

The study findings suggest thatthere are significant differencein cortical surface area of right and left paracentral lobule between adult Bangladeshi male and female subjectthat may have anatomical and clinical importance.

Limitations:

In this study, the samples were not distributed into age groups. The present study was conducted in a single center, may not be fully representative of whole community of Bangladesh. So far known, no published article was available on the paracentral lobule among Bangladeshi people, so comparison could not be done here. Few numbers of publications of similar study were available done by researchers of other countries to compare with the findings of present study. So, morphological parameters could not be compared

properly with the present study.The result of this study might be more accurate if correlation could be done with some other variables such as age, height, race, education and occupation etc.

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

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Authors' Contributions:
Mahfuza Chowdhury were responsible for conception and design, obtaining funds, data interpretation, manuscript drafting and manuscript editing, and final approval data acquisition, data interpretation and critical revision for important intellectual content conception and design, obtaining funds, data interpretation, manuscript editing, and final approval. Ferdausi Rab was responsible for data analysis and statistical analysis. Mahfuza Chowdhury Tunajjina Kawsar and Aminur Rahman were responsible manuscript writing and editing. Mahfuza Chowdhury was responsible for data collection. All authors have read and approved the final version of the manuscript.

Data Availability:
The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

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

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Ethical consideration:
The study was conducted after approval from the ethical review committee. The study was approved by the Ethical Research Committee of Dhaka Medical College The confidentiality and anonymity of the study participants were maintained.

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CASE REPORT

TYPHOID DENGUE COINFECTION: 2 CASE REPORTS

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Abstract:

Dengue and typhoid fever are different entities with overlapping signs and symptoms. The resemblance of symptoms makes clinical diagnosis and treatment difficult. Both are major health problems mainly during monsoon. If they are not diagnosed timely and treated, outcome can be fatal. We report 2 cases of dengue virus co-infection with typhoid fever during this outbreak of dengue. The aim of this report was to create awareness about this co-infection.

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Introduction:

Dengue fever is a viral exanthematous febrile illness. It is transmitted to humans by the insect Aedes Aegypti.[1] Similarly typhoid infection is also an important leading cause of morbidity and mortality worldwide.[2]Like many developing countries, Bangladesh is also endemic to malaria and enteric fever. In Bangladesh, dengue malaria co-infection is relevant, but the same is not true for dengue-Salmonella co-infection [3]. Viral illnesses can be complicated by secondary bacterial infections and the dengue virus is no exception.4 Here, we report two cases; both were treated in hospital.

Case 1:

A 14-year-old young lady presented with the complaints of high-grade fever for 5 days and lose stool. On examination, she was mildly dehydrated and just palpable spleen was present. Blood for culture and sensitivity report showed Salmonella typhi. Ceftriaxone was started with appropriate dose. 3 days later she became afebrile. But again after 2 days, she developed high grade fever, vomiting, anorexia and lose stool. She presented to us on the 3rd day of second episodes of fever. At presentation, she was febrile (102 degrees F) and tachycardic (pulse rate 100/min). Her blood pressure was 120/80 mmHg with a respiratory rate (RR) of 16/min. Her abdomen was soft but tender on deep palpation. There was no clinical evidence of organomegaly or ascites. The rest of the physical examination was unremarkable. Her labs revealed a recent sudden drop in leukocyte (3.1 × 109/L. NS1 was positive. And her platelet count showed progressive thrombocytopenia, SGOT was 209u/l. After hospital admission, her blood pressure was low 90/60, there was mild pleural effusion and ascites. Her lowest platelet level was 25k/µl. She was treated with proper fluid therapy along with antibiotic Ceftriaxone for 14 days. Patient improved completely and discharged from the hospital.

Case 2:

23-year-old man presented to us with the complaints of fever for 8 days which was associated with headache and vomiting, highest recorded temp was 104°F.After admission, one day later he developed breathlessness and subsequently upper abdominal pain. His SO_2 level dropped below 86% in room air. On Examination, his temperature was 101,pulse showed tachycardia, BP was low, Abdomen showed epigastric tenderness, chest examination showed wide spread crepitation. Chest Xray done immediately and showed bilateral interstitial pneumonitis. Injectable antibiotic started immediately and 2 days later he became stable and

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shifted from ICU. Other Investigation showed leucopenia with thrombocytopenia. Dengue Ig M was positive. SGOT was 692U/L, lipase was 1175U/L, CRP was 324, Procalcitonin was 8.00ng/ml, S. bilirubin was 3.8, Albumin was 2.65mg/dl, HBsAg and Anti HCV was negative. USG of whole abdomen revealed mild ascites. Blood culture showed salmonella typhi. He was treated with Inj ceftriaxone along with judicial fluid management. 5 days later he was discharged from hospital.

Discussion:

Though dengue fever was first recognized in early 1780s.[5] The incidence of both dengue and typhoid fever peaks during the monsoon season. Early clinical signs of both the diseases are non-specific and similar. It is important to distinguish typhoid fever from dengue as early antibiotic therapy in the former leads to a favorable outcome, while dengue as such has no specific treatment and is treated symptomatically. Lee et al. also observed concurrent bacteremia in a patient with dengue fever who had a fever prolonged for more than 5 days and suggested a predominance of microflora in this case.[6]A possible interaction between dengue and typhoid may arise through intestinal endothelial damage or intestinal hemorrhage, or through immunosuppression superimposed by virtue of the initial virus illness.[7,8] Both patients presented with a sudden onset of high fever, myalgia and gastrointestinal disturbances including nausea, abdominal pain and loss of appetite. According to WHO guidelines, the acute febrile phase of dengue usually lasts 2–7 days.[9] In both cases, Dengue was graded as group B. Clinicians should be alert to a progressive leucopenia in the early phase of dengue fever. In both cases fever persisted in the second week of illness. There was, thus, a possibility of some concurrent infection. Owing to a high prevalence of both dengue and typhoid in Bangladesh, a high degree of suspicion for the latter must be maintained.

Conclusion:

Change in the pattern of fever in the setting of a dengue outbreak should raise the suspicion of co-infection with dengue virus. Prompt diagnosis, early recognition of plasma leakage and appropriate management of DHF can reduce morbidity and mortality.

Conflict of Interest:

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

Funding:

This research received no external funding.

Ethical consideration:

The study was conducted after approval from the ethical review committee of Popular Medical College Hospital , Dhaka, Bangladesh. 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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CASE REPORT

DISSEMINATED HERPES ZOSTER IN AN IMMUNOCOMPETENT PATIENT ON LONG-TERM CLOZAPINE: CASE REPORT

NIKHIL DAS[1], FARZANA HOQUE[2]

Abstract:

Disseminated herpes zoster is characterized by more than 20 herpetic lesions distributed across other body parts outside the affected dermatome. Disseminated herpes zoster occurs more frequently in immunocompromised patients and only a handful of case reports highlighted itsoccurrence in immunocompetent individuals. Clozapine use has been linked to decreased immune functioning, but no conclusive evidence to categorize clozapine as an immunosuppressive drug has been published. Here we report a case of a 65-year-old immunocompetent man on long-term clozapine who presented with vesicular lesions in a non-dermatomal distribution and was diagnosed to have disseminated zoster.

Keywords: *Disseminated zoster; varicella-zoster virus; herpes zoster; clozapine.*

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Introduction:

Reactivation of varicella-zoster virus is known to cause herpes zoster commonly known as shingles. Herpes zoster typically presents as a painful, unilateral, vesicular eruption restricted to a singledermatome.[1] Disseminated herpes zoster is characterized by more than 20 herpetic lesions distributed across other body parts outside the affected dermatome. Dissemination occurs nearly exclusively in immunocompromised patients, but a handful of cases of disseminated zoster in immunocompetent individuals have been reported.[2]

Clozapine is a highly effective antipsychotic generally reserved for treatment-resistant schizophrenia. This is due to the potential for drug-induced agranulocytosis which requires regular blood count monitoring. The precise mechanism behind this serious adverse effect remains uncertain.[3] Clozapine use has been linked with attenuated immune functioning with studies showing an association with increased risk of pneumonia and tuberculosis,[4] decreased immunoglobulins in patients taking clozapine compared to those taking other antipsychotics,[5,6] and suppressed immune function through modulation of the production of multiple cytokines including IFN-ā in CD4+ T-cells.[7,8.9] Prolonged utilization of clozapine may heighten the propensity for immunosuppressive effects.[10] The response in varicella reactivation has been shown to involve similar adaptive immune functions as those that are diminished with clozapine administration.[11] However, no prior literature to the authors' knowledge has implicated clozapine use with herpes zoster reactivation. Here we describe a case of disseminated varicella-zoster virus in an immunocompetent individual on long-term clozapine.

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Case Report:

A 65-year-old deaf and nonverbal black male with a history of schizophrenia on clozapine for over 10 years, seizures, hypertension, history of multiple falls, and cervical myelopathy presented with falls and acute encephalopathy. A right subscapular and flank wound was noted during his admission, and the dermatology team was consulted. He was afebrile and denied any itching or pain associated with the skin lesions. A physical exam revealed a large, ulcerated plaque with irregular and hyperpigmented borders along with peripheral collarette scales on the right subscapular region (Figure 1).

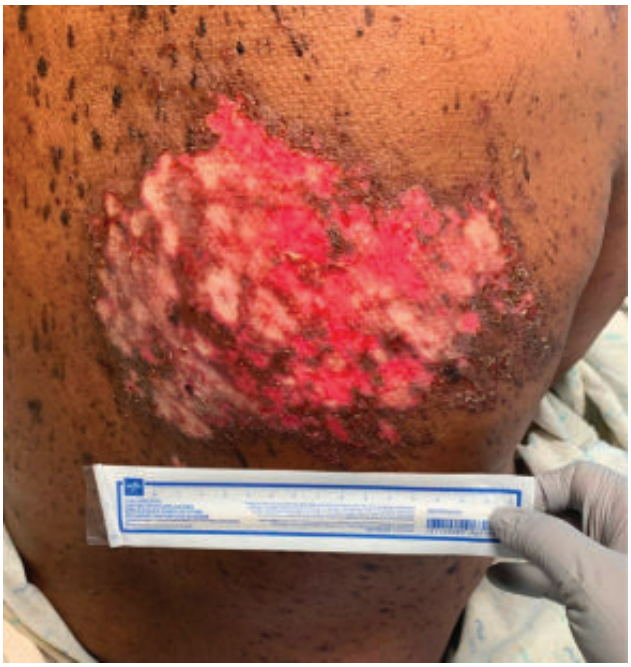

Fig.-1: *Large, ulcerated plaque with irregular and hyperpigmented borders along with peripheral collarette scales on the right subscapular region*

Hyperpigmented papules with peripheral collarettes of scale, yellow crusting, and peripheral flaccid pseudovesicles were also seen along the right chest (Figure 2). Additionally, scattered vesicles on the left arm and lower legs were noted. Due to the nondermatomal distribution of lesions with more than 20 vesicles outside of the dermatome as well as the presence of intact vesicles, the patient was started on intravenous acyclovir at immunosuppresseddosage (10 mg/kg three times daily) for seven days based on clinical diagnosis. Clozapine levels were normal at 715 ng/mL and the complete blood count was negative for leukopenia. No biopsies of skin lesions were taken. Four days later the patient's vesicles had crusted over, and he was transitioned to oral valacyclovir 1000 mg three times daily for the remainder of the seven-day course and was later discharged. At follow-up, his rash had resolved three months later, and he complained of postherpetic neuralgia.

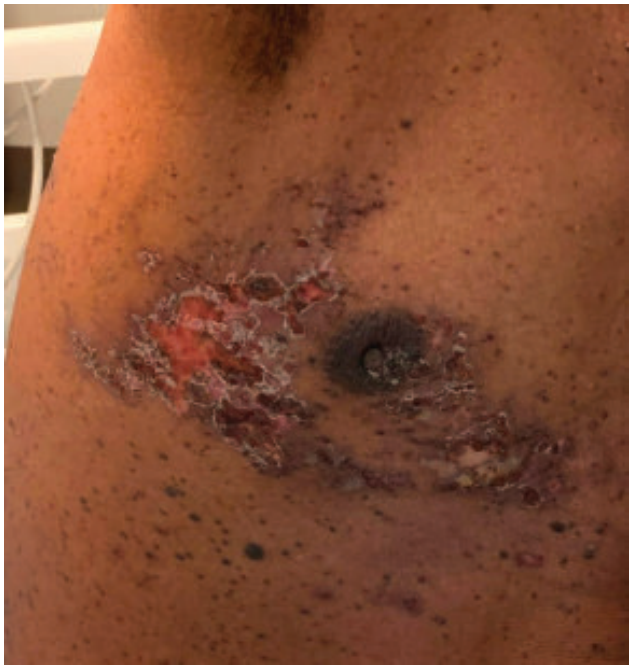

Fig.-2: *Hyperpigmented papules with peripheral collarettes of scale, yellow crusting, and peripheral flaccid pseudovesicles along the right chest*

Discussion:

Disseminated zoster is a rare diagnosis in immunocompetent individuals. A total of 25 cases of disseminated herpes zoster in immunocompetent patients have been reported to date. A recent case review from 2022 detailed 22 prior case reports of disseminated herpes zoster. [12] Since that analysis in 2022 one additional patient has been reported.[13] A study looking at hospital visits by patients in Canada prior to 2016 found 2 immunocompetent patients per million had disseminated zoster.[14] A phase 3 trial of the recombinant subunit zoster vaccine in immunocompetent subjects found reduced rates of herpes zoster complications with none of the vaccinated individuals developing disseminated zoster and 0.042% of the unvaccinated individuals developing disseminated zoster.[15] This patient received Zostavax (Zoster Vaccine Live; Merck) 14 years prior to presentation, but never received Shingrix (Recombinant Zoster Vaccine; GlaxoSmithKline) which was approved in 2017. However, the live vaccine only provides protection

against herpes zoster for 8 years and is less efficacious than the recombinant vaccine in preventing shingles.[16]

Immune function disturbances have been described in patients with schizophrenia[17] as well as those with clozapine use.[5,7,8,9] Larger doses of clozapine seem to have greater impacts on immune functioning[8] with one review finding increased clozapine serum levels to be associated with infection.[18] While this patient had normal clozapine levels, he had been receiving clozapine for over 10 years increasing the probability of immunosuppressive effects.[10] This patient's clozapine use could have caused the dissemination of herpes zoster as he had no other clinically significant reason to be immunosuppressed.

Conclusion:

Disseminated varicella is well known to appear in immunocompromised individuals. However, disseminated herpes zoster has been reported to occur rarely in immunocompetent patients. This case report highlights the possibility of developing disseminated zoster in patients on long-term clozapine therapy. Clinicians should keep disseminated zoster in mind when examining non dermatomal skin lesionson an immunocompetent patient, especially in patients that are taking clozapine.

Conflicts of interest: None

Financial support: None

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CASE REPORT

PARADOXICAL REACTIONS IN THE FORM OF OPTOCHIASMATIC ARACHNOIDITIS AND STROKE IN AN IMMUNOCOMPETENT GIRL WITH TUBERCULOUS MENINGITIS- A CASE REPORT

MD. ALAMGIR HOSSAIN[1], AMINUR RAHMAN[2], AJAY KUMAR AGARWALLA[3], MUHAMMAD JAMIL AHMED[4], ABUL HASNAT MD. RUSSEL[5], SHAHJADA MOHAMMAD DASTEGIR KHAN[2], MOHAMMAD MOSHIUR RAHMAN[2], BIPLAB PAUL[2] , PALLAB KANTI SAHA[2], ZAHED ALI[6]

Abstract

The paradoxical response is characterized by clinical or radiologic worsening of pre-existing lesions or the appearance of new lesions following initiation of treatment for tuberculosis (TB). The paradoxical response has raised questions about the accuracy of the diagnosis, the potential for treatment failure, and the presence of an underlying disease, making it an important topic of care for clinicians. In this case report, we present the paradox reaction of a 14 year old girl diagnosed and treated for TB meningitis. This healthy immune girl is successfully treated with steroids, and we discuss the importance of treating the paradox of tuberculosis progression despite the use of effective anti-TB drugs.

Key words: *Paradoxical Reactions, Optochiasmatic Arachnoiditis, Immunocompetent, Tuberculous Meningitis*

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Introduction:

Patients with tuberculosis (TB) experience paradoxical reactions, which are clinical or radiological exacerbations of lesions or new lesions arising after treatment.[1] Paradoxical reactions are most commonly observed in the lungs, lymph nodes and in the central nervous system (CNS) affected by TB [2].There is limited literature on paradoxical responses in HIV-positive children. In a study of 115 HIV-positive children with pulmonary (and extrapulmonary) TB, 12 (10%) patients experienced paradoxical reactions 3.It is important for clinicians to be aware of the clinical nature of paradoxical reactions, especially in patients with treatment failures or underlying diseases [4]. Paradoxical reactions present serious challenges in the management of CNS TB. Drug resistant TB is

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always a question when the patient is worsening, and paradoxical reactions often lead to inappropriate increment(s) or addition(s) of more toxic newer anti-tubercular drugs with multiple side effects [4]. This case of a child highlights this situation and increases clinicians' awareness.

Case Report:

A 14-year-old girl was admitted to the department of neurology, sir salimullah medical college Mitford Hospital. She had been complaining for 5 months, losing weight for 4 months, suffering from headache for 1 month, and was disoriented for last 1 day. On inquiry, she did not have a history of chronic cough or chest pain or breathing difficulty. She had joint pain and skin rash. She had oral ulceration and skin pigmentation. She was also in contact with a TB patient. Her father was diagnosed with pulmonary tuberculosis in 2018 and recovered completely with 6 months anti-tuberculosis drugs. She was diagnosed as Tuberculous meningoencephalitis (TBM) on the basis of physical examination, and laboratory findings, including CSF study, and radiological findings, including chest X-ray MRI of brain. The chest X ray showED inhomogeneous opacity in both lung fields (Fig-a). MRI of brain demonstrated multiple tuberculoma in both cerebral hemisphere and cerebellum (Fig 1: b, c, d). Anti-TB treatment (isoniazid, rifampicin, ethambutol, and pyrazinamide) and 0.2mg/kg Inj. Dexamethasone was given. As the treatment progressed, her complaints improved and the dexamethasone was decreased gradually.

After a month of hospitalization, the patient was discharged with a GCS of 15, cranial nerves normal, muscle power normal, fundus normal, and planter-flexor. However, 7 days later at home, the patient developed sudden right side weakness and blurred vision. She was again admitted to that hospital and upon examination had a GCS of 12 with a slurred, indistinct speech. She also had visual acuity (VA) finger counting and a bilateral dilated, poorly reacting pupil. Her fundal photograph showing bilateral optic atrophy (Figure: 2a) .Perimetry showing profound visual loss (Figure:2b).

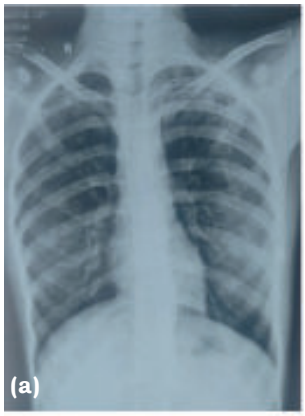


Fig.-1: (a) *Chest X ray showing inhomogeneous opacity in both lung fields.*

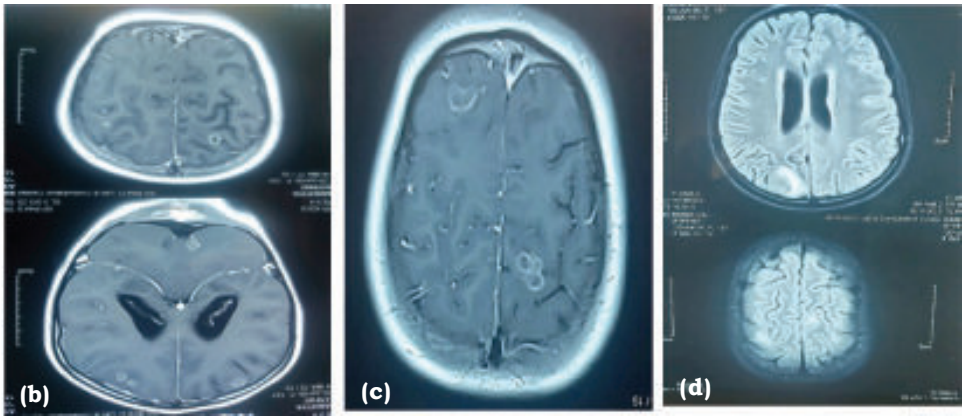


Fig-1: *b,c,d MRI of brain showing multiple tuberculoma in both cerebral hemisphere and cerebellum.*

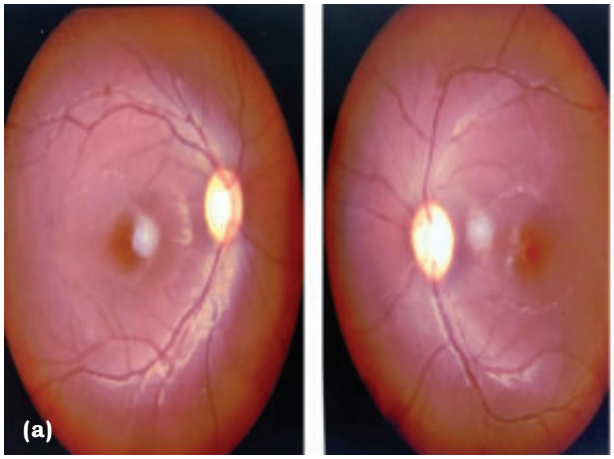


Fig-2a : *Fundal photograph showing bilateral optic atrophy*

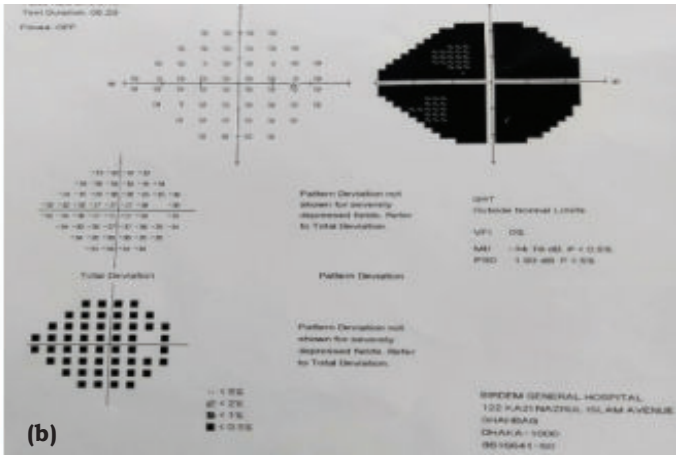


Fig:2b *Perimetry showing profound visual loss.*

She was also diagnosed with right upper motor facial palsy and right side extensor planter response. At the hospital, an MRI of the brain was performed with contrast. The MRI showed that there was a large, growing, and absent-inhabiting tuberculoma on the right side of the brain in comparison to the previous film, and an increasing number surrounded by edema. In the current film, there was an infarct in the anterior cerebral artery territory (ACA) that was completely absent in the previous film (Figures-3: a, b, c, d). in MRI of brain showed small, single tuberculoma in right cerebellar hemisphere without edema Fig-3 (a). (b) Multiple conglomerated tuberculoma surrounded by perilesional edema Fig-3 (b) (c) No evidence of infarct before starting treatment Fig-3 (c). A large ACA territory infarct after one month 7 days after starting treatment Fig-3 (d).

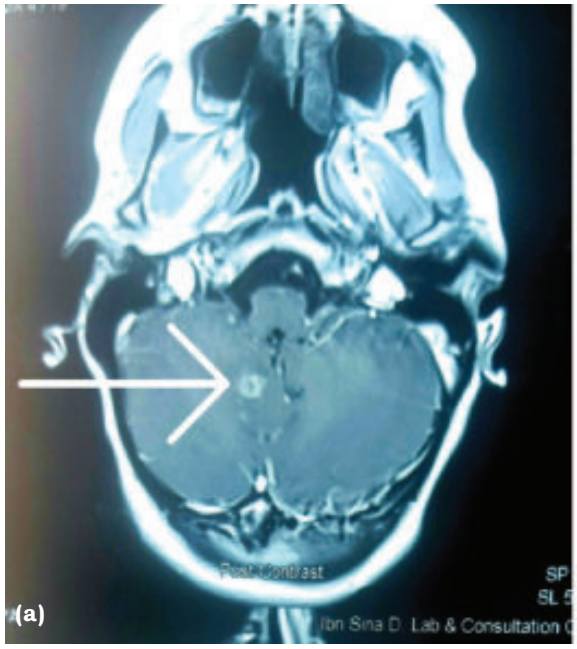


Fig-3: *(a) Small, single tuberculoma in right cerebellar hemisphere without edema.*

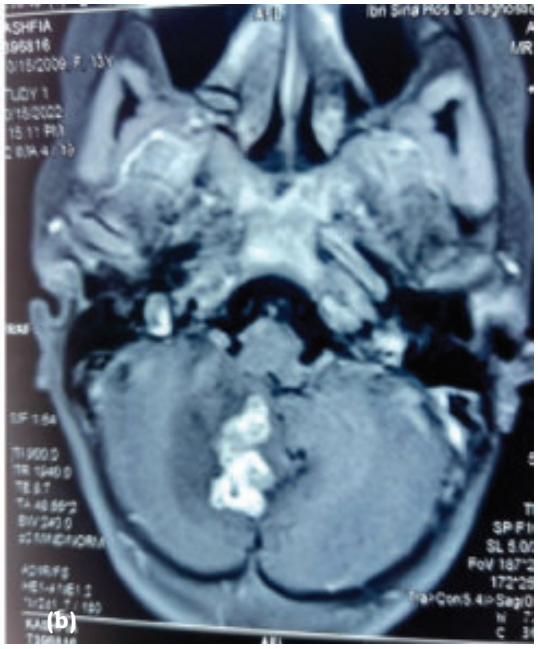


Fig-3: *(b) Multiple conglomerated tuberculoma surrounded by perilesional edema*

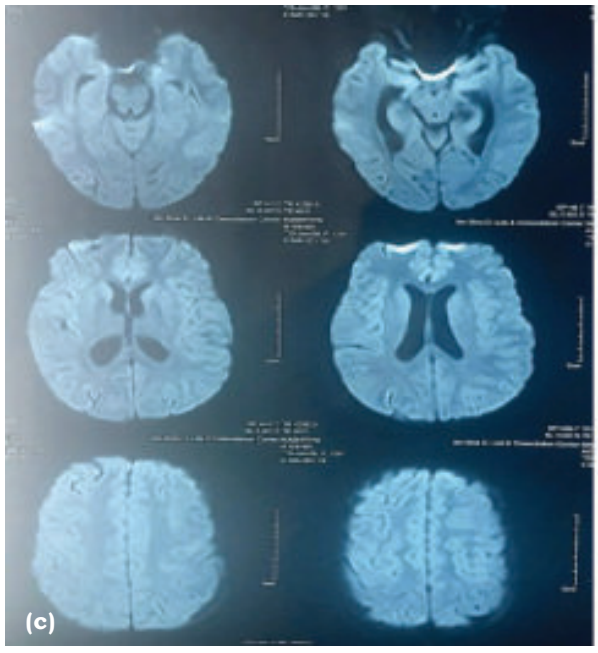


Fig-3: *(c) No evidence of infarct before starting treatment.*

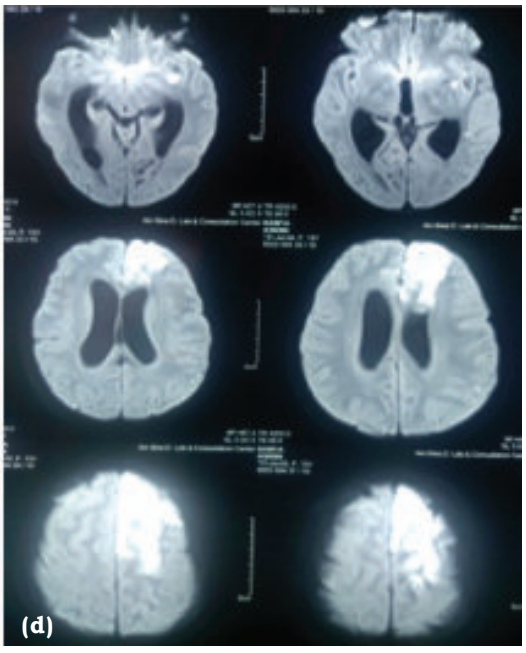


Fig-3: *d) A large ACA territory infarct after one month 7 days after starting treatment.*

While assessing profound visual loss Ethumbutol induced retrobulbar neuritis was our primary consideration. But new MRI features was a little bit surprising for us.

Simultaneously we keep examining her fundus several times. At one stage we found disk pallor in both eye. Then we went for fundal photograph and HVFA. (Figure: 2 a,b)

After comparison to previous MRI, the following findings were found in the most recent MRI (Fig-4a-c): Fig-4 : (a)Before starting treatment (b) Optochiasmatic arachnoiditis—Dense plaque-like basal exudates especially around the optic chiasm and cisternal part of optic nerve). (c) T1W contrast sagittal images; shows multiple ring and nodular enhancing lesions and exudates in the suprasellar cistern involving the optochiasmatic region., increased exudation in the basal cisterns resulting in communicating hydrocephalus and trans-ependymial migration of CSF, robust meningeal enlargement compared to the previous MRI. Extensive investigations were conducted to exclude alternative diagnosis. CBC, CRP - normal, ANA - negative, p ANCA – normal, ANCA - normal, S Protein C & S - normal, S Homocysteine - normal, Anti HIV 1 & 2 - negative, S. Calcium - 8.7 mg / dl, MRV of brain - normal. No alternative/ differential diagnosis was found after extensive investigations. Less/no chance of Multidrug-resistant TB (MDR TB) , presence of Paradoxical reactions IN TB (female gender) risk factors, disseminated/extra pulmonary Tuberculosis with high mycobacteriostatic antigen load, time association between initiating anti tubercular therapy and deterioration in clinical and radiological features-finally we considered our patient as case of Paradoxical Reaction (PR) to Anti-tubercular therapy..

To overcome the paradoxical reactions, we correct dose of Inj. Dexamethasone in tapering mode. Tab. Intravenous administration of 500 mg of Levofloxacin (0 + 0+1) was initiated as previously treated patient. Drug Susceptibility Testing (DST) not performed according to 2021 National TB Guideline. We found Clinical status at 2 months of post treatment:, her GCS found 15, VA 5/60 (both eyes), Optic disc pallor and facial palsy improved .Her muscle power found 3 on right side. She walked independently. Her MRI of brain (Figure: 5 a-f) features showed significant improvement. Fig-5:(a) and (b) showing improvement of cerebellar lesions. (c) and (d) showing improvement of Optochiasmatic arachnoiditis (e) and (f) showing improvement of ACA infarct

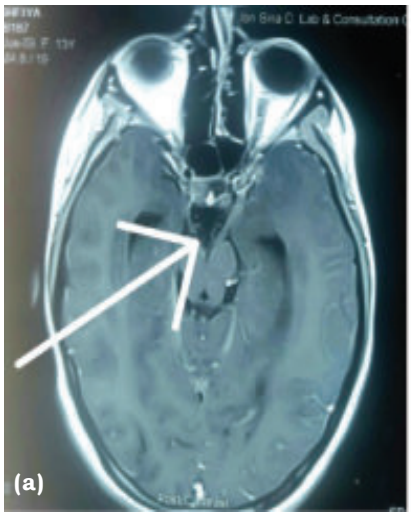


Fig-4a Before starting treatment

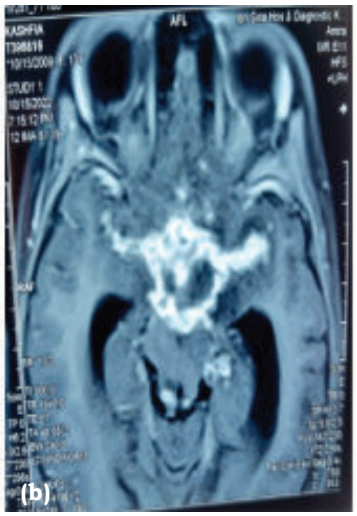


Fig-4: b Optochiasmatic arachnoiditis — Dense plaque-like basal exudates especially around the optic chiasm and cisternal part of optic nerve).

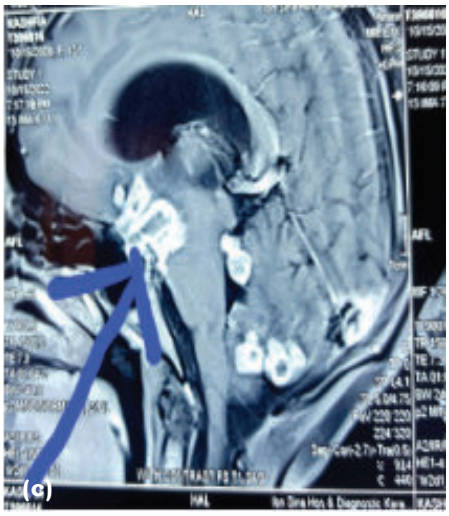
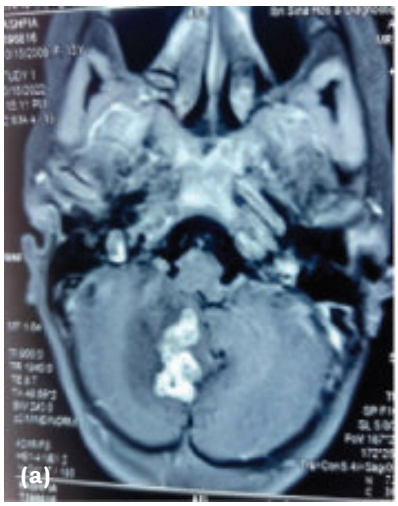


Fig-4: c T1W contrast sagittal images; shows multiple ring and nodular enhancing lesions and exudates in the suprasellar cistern involving the optochiasmatic region.



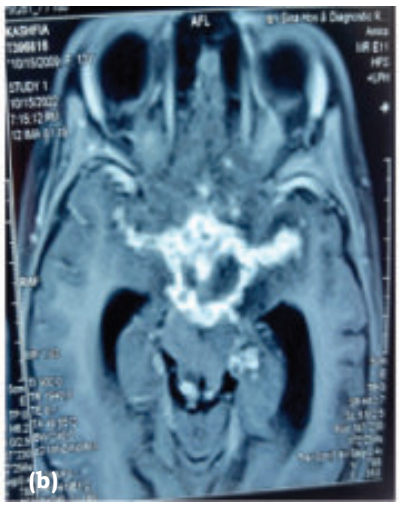


Fig-5: *(a) and (b) showing improvement of cerebellar lesions*

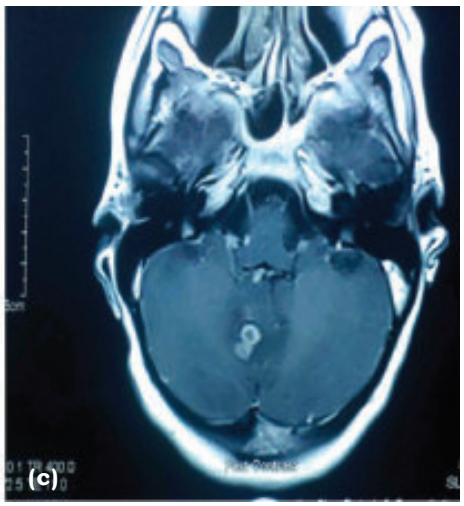
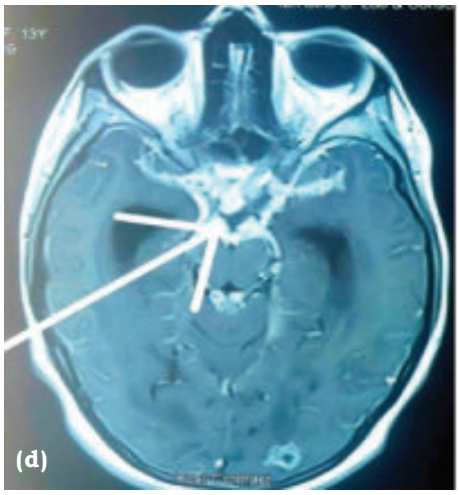
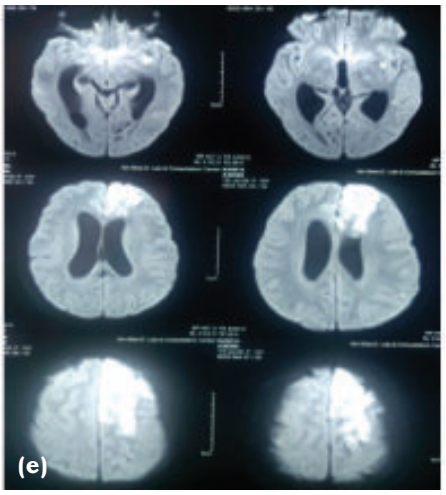


Fig.-5: *(c) showing improvement of Optochiasmatic arachnoiditis*





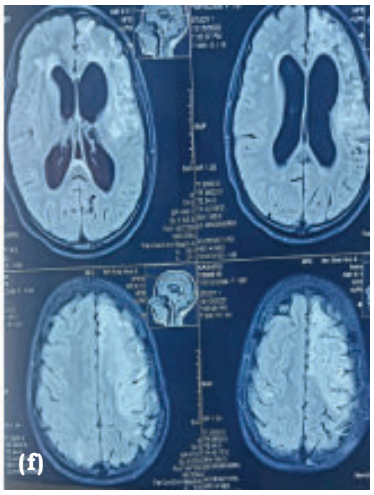


Fig.-5: *(d) showing improvement of Optochiasmatic arachnoiditis* **Fig:5** *(e)& (f) showing improvement of ACA infarct*

Discussion:

Paradoxical reactions are mostly described in case reports and in small number of cases. They include a wide range of clinical symptoms and abnormalities in neuroimaging, as well as a change in the cerebral fluid picture. Changes in cerebral fluid may be lymphocytic, polymorphonuclear dominant or elevated protein. Paradoxical reactions do not always mean treatment failure. Corticosteroids have been shown beneficial effect.[4,5]

Paradoxical reactions occur in 6 to 30% of patients receiving treatment for tuberculosis [6]. These reactions are most common in adults and in immunocompetent patients. Very rarely, paradoxical reactions have been observed in children, and the earliest time at which it occurred was in a 21-day old child who was receiving treatment for congenital pulmonary tuberculosis [7]. Paradoxical reaction manifestations, such as Optochiasmatic, Spinal Arachnoid, and a Large Brain Tumor, are serious conditions with severe disabilities and a high risk of death [8]. These conditions necessitate immediate treatment with immuno-modulatory drugs. Currently, high-dose corticosteroid therapy is the preferred treatment. Other immuno-modulating drugs such as TNF-A Antagonists, Thalidomide and Interferon–ã are also used [8].

While paradoxical reactions in adults are rare in Bangladesh, paradoxical reactions in children have never been reported in TB meningitis cases. In our case, a child had a paradoxical reaction (ACA stroke) causing profound visual loss, which was rarely

observed and reported. In contrast, the reported rate of paradoxical response in HIV infection patients is 35%, which is less than 5% in normal immune system TB patients [9] However, in our case, HIV was negative. Risk factors for paradoxical reactions include anemia; hypoalbuminaemia; lymphopenia; female gender; and disseminated / extrapulmonary TB [10] Our patient also had some risk factors. Anti-TB treatments do not need to be changed or stopped when paradoxical reactions occur. 95% of Mycobacteria is sensitive to the treatment [11] Resistance to anti- TB drugs is still a concern, especially in my country where the spread of resistant TB strain is a constant development.

Paradoxical reactions can be treated with systemic corticosteroids and/or surgical procedures. Corticosteroids reduce intracranial pressure, which helps in reducing any of the neurological symptoms of the disease [3]. Surgical alternatives include a ventriculoperitoneal shunt implementation in case of hydrocephalus or surgical *lyses* of adhesion in case of devastating Optochiasmatic arachnoiditis; however, no surgical treatment is required in our case. In our case we treated with Anti-tubercular therapy with Inj Dexamethasone started to overcome paradoxical response and continued proper dosage in tapering manner. This paradoxical response occurs 3 – 12 weeks after initiation of treatment for TB; however, this response may take up to 18 months [12]. We observed this paradoxical response in our patient at 5 weeks post-treatment with several central nervous system (CNS) symptoms. At 2 months post-treatment, her clinical status improved as follows: Glasgow Coma Scale (GCS) found 15 , Visual acuity (VA) was 5 / 60 in both eyes Optic disk pallor was improving Facial Palsy was improved Muscle power was found 3/5 on right side and walked independently.

Drug resistant CNS TB was not a concern in our patient, as she demonstrated significant improvement in the first month of antiretroviral therapy. Complete improvement in her father's TB may suggest reduced risk of infection with a resistant organism.

Conclusion:

The paradoxical response results in either an exacerbation of lesions clinically or radiological, or new lesions after initiation of treatment in patients with TB, which occurs in approximately one third of patients with TB. This has caused physicians to worry about whether the diagnosis is correct, if treatment will not work, or if there is another underlying disease. So this is a difficult situation for clinicians.

Conflict of Interest:

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

Funding:

This research received no external funding.

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.

Acknowledgments:

The authors were grateful to the staffs and management of the Department of Neurology in Sir Salimullah Medical College Mitford Hospital, Bangladesh.

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CASE REPORT

SEPSIS, AN UNUSUAL PRESENTATION OF TYPHOID FEVER - A CASE REPORT

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Abstract:
Typhoid fever is an infection caused by Salmonella typhi. *The common complications are intestinal perforation and typhoid encephalopathy. Cases of typhoid fever with sepsis and/or disseminated intravascular coagulation (DIC) are rarely reported. A 20 yr old male presented with grade fever, vomiting, diarrhoea.His Dengue NS1 was negative, procalcitonin was high,coagulation profile was altered and developed subclinical DIC along with septicemia within a short period of time which is very rare. Sepsis and DIC are rare complications of typhoid fever. Typhoid fever can be presented with profound bleeding manifestation other than gastrointestinal bleeding, since it is a common symptom of typhoid fever. Further research should be conducted to postulate association between typhoid fever and DIC. Here we reported an unusual case of sepsis which a caused by case of typhoid fever.*

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Introduction:
Typhoid fever is a serious systemic disease caused by Salmonella *enterica* serotype typhi. The prevalence of typhoid in worldwide are near about 12–33 million cases a year.[1] It is more common in children and young adults than in older patients. Though gastrointestinal manifestation are common but some rare presentation are sepsis, disseminated intravascular coagulation (DIC), multiorgan failure, and rhabdomyolysis-related acute renal failure.[2,3]Here we are discussing a case of typhoid fever presenting with rapidly progressive sepsis.

Case report:
A 20-yr-old male presented to us with high grade fever which was 104F, generalized body ache and vomiting for 3 days.As now dengue is endemicinitially, we thought this may be a case of dengue fever or any other viral disease. One day after admission, he developed severe watery diarrhea along with high fever. On examination patient was toxic, drowsy, dehydrated. His pulse was feeble along with low blood pressure. Spleen was just palpable. Initial CBC showed leucopenia. NS1 came negative. Liver enzymes were deranged and S. electrolyte showed hyponatremia.Further CBC report showed progressive leucopenia and thrombocytopenia (Table-I).

His condition was detoriating. Abnormal blood coagulation (PPT 40.3 s, APTT 44s, Fibrinogen <7 mg/dL, D-dimer 2.5mg/dl), lactatemia (lactate 5.42 mg/dL), and increased level of procalcitonin (procalcitonin 28.98 ng/ml). DIC score was 7. Meanwhile report of Dengue IgM and IgG was negative. We started inj ceftriaxone 2gm intravenously 12 hrly.1 day later, report of Blood culture showed salmonella typhae. Patient became afebrile 3 days later and his condition was improving. Based on clinical and laboratory findings, the patient was diagnosed with typhoid fever with septicaemia with DIC.

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Table-I

Serial Laboratory reports of the patient

Date	07/06/23	08/06/23	09/06/23	10/06/23	12/06/23
White Blood Cell (WBC)	2.33 K/µL	2.06 K/µL	2.69 K/µL	2.80 K/µL	7.87 K/µL
Red Blood Cell (RBC)	5. 18 million/µl	4.50 million/µl	4.21 million/µl	4.25 million/µl	4.03 million/µl
Platelets	150 K/µL	100 K/µL	80 K/µL	50 K/µL	80 K/µL
Haemoglobin	15.40 g/dL	13.70 g/dL	12.60 g/dL	12.70 g/dL	12.10 g/dL
Neutrophils	71%	82 %	77 %	80 %	48 %
Lymphocyte	25 %	15 %	20 %	17 %	46 %
Monocyte	03 %	02 %	02 %	02 %	05 %
Eosinophil	01 %	01 %	01 %	01 %	01 %
Basophil	00%	00 %	00 %	00 %	00 %
ESR	06 mm/ hr	16 mm/ hr	22 mm/ hr	21 mm/ hr	19 mm/ hr
HCT	42.60 %	36.20 %	34.40 %	35.30 %	32.90 %
MCV	82.2 fl	80.1 fl	81.7 fl	83.1 fl	81.6 fl
MCH	29.7 pg	30.3 pg	29.9 pg	29.9 pg	30.0 pg
MCHC	36.2 g/dL	37.8 g/dL	36.6 g/dL	36.0 g/dL	36.8 g/dL

Discussion:

In typical cases, a gradual increase of body temperature, known as “step ladder”, relative bradycardia, and hepatomegaly are common in the first week of onset. Sustained high temperature with apathetic facial expression is observed in the second week of onset. In the third week, intestinal perforation and GIT bleeding are common manifestations. The fourth week is normally the recovery phase. The most common complications due to typhoid infection are hepatitis, bone marrow suppression, and paralytic ileus [4]. Here we diagnose the case on the basis of blood culture.

Sepsis due to *Salmonella typhoid* is uncommon [5]. Adu-Gyamfi et al. reported a 28 year-old male with Salmonella sepsis in November 2019. The patient came to hospital and presented with septic shock after a ten-day history of abdominal pain, malaise, vomiting, and diarrhea. Laboratory investigation showed septicaemia. [6]. Another case reported by Nishida et al. was a 7 year-old boy with typhoid fever complicated by sepsis and DIC[7].

DIC is mostly a subclinical event, and the severe bleeding complications are not typically found in typhoid fever, although DIC score indicates an imbalance of coagulation and fibrinolysis which are markedly elevated in patients with typhoid [8]. Coagulation problems involve three major processes: pro-coagulation, anti-coagulation, and fibrinolysis. A typhoid patient usually demonstrates increased plasma prothrombin fragments as well as D-dimer level, prolonged prothrombin time, and lower protein C and anti-thrombin concentrations. Repeated tests of coagulation markers during convalescence showed a return toward normal values [8]. DIC in this patient can be a part of the multi-organ dysfunction due to sepsis syndrome[4].

Acute infection can also result in systemic activation of coagulation. Thrombocytopenia is one of hematological features of typhoid; 18–44.9% of patients with typhoid fever suffer from thrombocytopenia[9]. The mechanism of thrombocytopenia in typhoid patients remains vague. It has been postulated that there are defects in production of platelets due to the direct effect of the toxin produced by Salmonella on the bone marrow, while others have suggested the destruction of non-immune platelets due to DIC.[8]

Conclusion:

Salmonella infection can present as fulminant sepsis which can mimic acute viral illness.Outcome can be worse. There should be a high index of suspicion of typhoid fever during this season of dengue fever. Typhoid vaccine is now a burning issuein our country now a days.

Conflict of Interest:

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

Funding:
This research received no external funding.

Ethical consideration:
The study was conducted after approval from the ethical review committee of Popular Medical College Hospital , Dhaka, Bangladesh. 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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SHORT COMMUNICATION

PLASTIC AND HEALTH ISSUES IN BANGLADESH: CURRENT SCENARIO

GOUTAM SAHA

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Citation: *Saha G. Plastic and Health Issues in Bangladesh: Current Scenario. Bangladesh J Medicine 2023; 34: 255-.256.*

The plastic industry in Bangladesh has a multifaceted and significant impact on the country's economy. A report by the Asian Development Bank (ADB) highlights that the growing plastic industry in Bangladesh plays a major role in both domestic demand and export trade. The plastic industry already holds a prominent position within the chemical industry sector. Currently, this sector employs around 2 million people directly and indirectly across around 3,000 manufacturing units. The annual sales of plastic products in the local market alone reach approximately 150 billion BDT. The Bangladesh Plastic Products Production and Export Association reports that 300 domestic manufacturing companies export around 30 billion plastic products annually, valued at approximately 30 billion BDT. Furthermore, the domestic market value of plastic products is estimated to be around 200 billion Bangladeshi taka.

According to a study by the National Oceanic and Atmospheric Administration of the United States, it takes 20 years for grocery store bags to decompose in nature. Plastic cups used for beverages can last up to 50 years, while diapers and plastic bottles take 450 years to decompose. A research study conducted by the non-governmental organization Environment and Social Development Organization in Bangladesh revealed that 35 percent of single-use plastic is used by the 15-25-year-old, and 33 percent is used by the 26-35-year-old. Bangladesh generates 87,000 tons of single-use plastic waste annually, primarily from restaurants, residential hotels, airlines, and super shops. The study also showed an increase in the amount of single-use plastic in the garbage from three percent in 2014 to around 21 percent in 2019.

The recycling capacity of Bangladesh for plastic waste is not prepared to handle the increasing amount of plastic waste generated. PET plastic recycling is the most developed sector of the plastic recycling industry in the country, while other types of plastic recycling are not as well established. Estimates vary regarding the percentage of plastic waste recycled in Bangladesh, ranging from 38 percent to 83 percent for recyclable plastic waste. The per capita plastic consumption in Bangladesh has been increasing over the years. In Dhaka, the annual per capita plastic consumption was reported to be 24 kg in 2017, significantly higher than the national average. The annual per capita plastic consumption in urban areas outside Dhaka was 3 kg in 2005, which tripled to 9 kg in 2020. Experts predict that by 2030, it may reach 34 kg.

Plastic pollution has had a detrimental impact on the Sundarbans and coastal areas, with single-use plastics posing a threat to public health and the environment. According to Transparency International Bangladesh (TIB), Bangladesh, polythene shopping bags are still widely used, although Bangladesh is the first country that enforced a complete ban on their usage. Regrettably, Bangladesh also faces the challenge of being responsible for 2.47 percent of the world's plastic pollution. Research has shown that 20 species of fish in the Sundarbans area are contaminated with microplastics. Plastic production contributes to greenhouse gas emissions, and the manufacturing process involves the use of harmful chemicals. Polyethylene, a commonly used plastic, is a non-recyclable one-time-use product that breaks down into particles, posing a serious risk to public

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health when it enters the food chain. The persistence of plastic, being a specific type of chemical polymer, poses a long-lasting threat to the environment, leading to chronic damage. Non-biodegradable plastic waste endangers the existence of flora, fauna, and aquatic life. Microplastic particles, present in soil, hinder land fertility and reduce fruit production. Similarly, airborne microplastics, inhaled by animals and humans, particularly, contribute to respiratory function decline and an increase in asthma cases. Furthermore, plastic particles in water are associated with cancer, hormonal issues, and even infertility. This harmful waste also enters the human body through the food chain, with pregnant women, young children, and respiratory patients being particularly vulnerable. Notably, a 2015 World Bank report highlighted that approximately 28 percent of annual deaths in Bangladesh are attributed to plastic pollution. To sustain development while addressing these challenges, it is imperative to prioritize effective waste management practices alongside plastic production.

Source: The information presented in this article has been compiled from various media sources in Bangladesh.

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PHYSICIANS IN PRACTICE

SCARS OF EXPERIENCE: UNLEASHING HOPE

CHOWDHURY H AHSAN

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It was a relatively quiet, routine post call night. I was with my co-intern Dr. Ashraful Hannan Shaheen in the medical ward of Prof Waliullah on the first floor of Dhaka Medical College Hospital. It was a cold winter night in 1985. A man from the end of the medical ward was walking towards our table. He appeared pale and somewhat distressed, with his hand across his chest. We directed him to his bed, where he coded just minutes after we were able to perform an ECG). It was not the standard 12 lead EKG A4 size print that we see today. It was a long, narrow EKG paper strip with tracings of myocardial depolarization and repolarization changes denoted as P Q R S T. It took only seconds for us to evaluate the strip and correctly interpret the ST changes in the ECG for our patient. He had acute ST elevation myocardial infarction. We gave him oxygen and tried our best to comfort him and the family. We prayed together but unfortunately lost him an hour later. Other patients were looking at us and we looked at them in silence, defeated. We knew we had most likely destroyed all the trust they had in us. My friend and I mourned in private. No, we were not in "House of God."[1]

Years later in 1995, I was in Royal Liverpool University Hospital in the UK. I had started my clinical career in Merthyr Tydfil, a small coal miners' town in South Wales, after which I moved to Royal Gwent Hospital, New Port, Wales, home of the famous Dr. John Davies. All MRCP Part 2 students had to read Dr. Davies' books in those days. Dr Davies was the first specialist cardiologist at the Royal Gwent Hospital in his native South Wales. Soon after, he recommended me to Dr Silas in Arrowe Park Hospital in Wirral and Dr Steven Saltissi at the Royal Liverpool University Hospital for the position of Registrar in Cardiology. Dr. Saltissi was the chief of cardiology at Royal Liverpool. He was rounding one day and diagnosed a man in mid-60's with Tietze Syndrome and asked me to give local injection with lidocaine. Shortly afterwards he went to his outpatient clinic,and I ignored his earlier instructions. In the following hour, I asked the nursing staff and my interns to do serial ECG's. The ECGs started to progress until the man showed significant ST elevations in the precordial leads at which point, I immediately gave him tPA. GUSTO trial[2] was published a couple years earlier. We were then following ISIS studies.[3] I went to see Dr Saltissi in the afternoon and briefed him about his patients. He asked me if I had given the lidocaine and I replied, "no."Instead, I had administered tPA. He went back to the patient, told him that he had made a mistake, and I had diagnosed him correctly. The patient smiled at me, and I promptly acknowledged that the chief had trained me well. On that day, Dr Steven Saltissi earned the most respect of any of my mentors. Royal Liverpool University Hospital did not have Cath Lab back then and Primary PCI[4] (Percutaneous Coronary Intervention) was not the first line therapeutic choice to benefit survival. Our patient did well, went home, and my team had full faith in me. We thought to ourselves, we were in House of God.[1]

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Then it happened. I lost him. I lost my best friend. My friend who would ask me to sit in his clinic in Pabna, a district town in Bangladesh. He would routinely almost force me to see some of his patients, to listen to their stories and make me feel baffled, challenged and helpless. Many of the patients would have significant valve disease, particularly mitral valve disease, as well as congestive heart failure, atrial fibrillation, and of course, coronary artery disease. There was hardly anything I could do for them. Meanwhile my friend would order a cold coca cola drink for me to calm me down. He would be doing an ultrasound examination on a lady who might soon be facing obstructed labor ~~and~~ he would say to me in his soft voice, "one day we will be able to take care of these challenges, however today, all we can do is to face them". A few months later, he had chest pain, nausea, vomiting and collapsed. Within hours, he was gone. Dr Mostafa Kamal Selim was an outstanding physician committed to serving the community he had lived in. At that time, I was preparing for my presentation on Door to Balloon Time in ST elevation Myocardial Infarction. American College of Cardiology and American Heart Association have been promoting ACLS and advocating for triaging patients with suspected myocardial Infarction, championing the use of defibrillators to avoid unnecessary deaths. In many district towns in Bangladesh, even today, one can hardly find any cardiac defibrillators.

Access to healthcare and putting patients under a system of care is the fundamental basis for a successful healthcare delivery organization. We must have an oversight for the delivery of care, and we need to look into all of the contemporary clinical data with our experience and knowledge to strive for excellence at an affordable cost. We can adopt this mantra of:

A. Access to HealthCare and System of Care: One can get the care.

B. Accountability: there is an oversight for the quality of care and outcome matrix

C. Affordability: To contain cost and keep the quality of care.

We looked into the outcome data of the patients with acute myocardial infarction presenting in different areas of the state of Nevada and assigned them into groups with geographic advantage where Cath lab and cardiac care are readily available vs difficult disadvantageous areas. We observed a fourfold higher mortality in patients who presented to areas with no readily accessible healthcare (see figure 1).

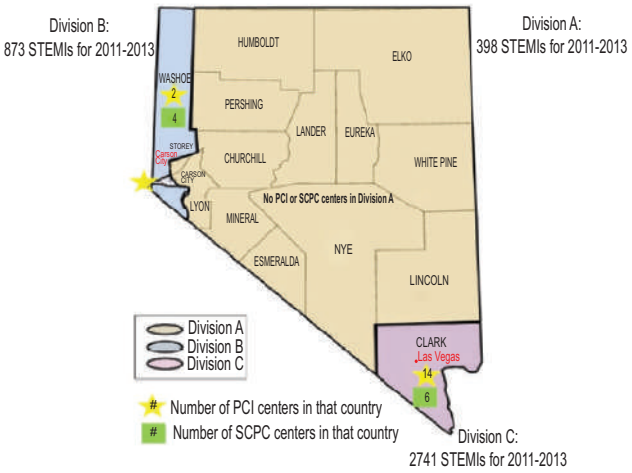

Fig.-1: *We divided the areas of the state of Nevada into 3 groups with immediate access to cardiac catheterization laboratories to get Primary PCI, access to thrombolytics and remote areas where access to health care is limited* (Fig.-1).

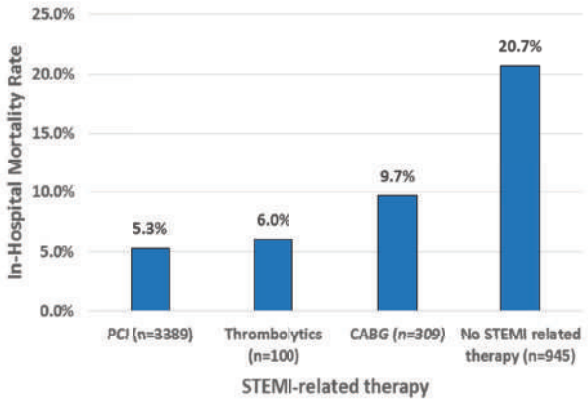

Fig.-2: *Those who did get Primary PCI or Pharmaco-invasive therapy with initial lytics at the* ***point of careservice centers*** *followed by transfer (Drip and Ship) to invasive strategy for areas with no immediate access to Cath lab had very similar outcomes. Pharmacotherapy is now a recognized strategy with comparable outcomes [5]. However, when we compare the group who did not receive any therapy with those who received Primary PCI or Pharmaco-invasive Therapy, the no therapy group had a fourfold increase in mortality.*

Hundreds and thousands of studies have been done in different disciplines all around the world to establish disease specific standards of care. Society guidelines and clinical pathways have been drafted to outline the care plan and provide guidance to healthcare providers for delivery of care.

We therefore definitely can:

Triage—the patients at the **Point of Care Service Centers** and upload all the info to sort out the

emergency, urgency and time sensitivity in terms of delivery of care at any corner of the country by utilizing current technology at hand with the help of an army of physicians and

Treat: we can start treating the patient without delay: Our pharmaceutical industries have developed and have made over 90% of the medications prescribed available in Bangladesh. We have a task to educate our healthcare providers who are in urban and rural areas and make them fully aware and confident to seek help from experts for the initiation of treatments and make a Care Plan

Transfer: Forward to secondary or tertiary higher care centers as needed or back to General Practitioner for the follow up care. The whole process can be organized in the electronic health record system with the help of our IT sector.

More and investments in healthcare systems keeping in mind the above fundamental principles of delivery of care will see a significant impact in the GDP and build confidence and trust among the people.

Bangladesh has made significant progress in economic fronts. The country's infrastructure has been strengthened more than ever, and the mighty projects have allowed our country to turn the page towards the next best thing for the explosive growth of opportunities and avenues for changing the fate of our people. The IT sector has significant advancement to match other developed countries of the world, whereas the health sector has been unable to utilize these resources to meet the challenges and expectations achievable in healthcare field in today's world. We already have preventive strategies for non-communicable and communicable diseases. Now we need a comprehensive plan on delivery of care for all the people of our country by involving the Government and Non-Government agencies, financial institutions, healthcare providers in all disciplines, healthcare delivery institutions and agencies so that we can build a solid healthcare delivery system. A system that gives access to the patient when needed, opens up a system of care to receive the standard of care, and provides accountability for the care provided so the care is affordable at least to the majority of its recipients.

"We shall forget by day, except
The moments when we choose to play
The imagined pine, the imagined jay."
—Wallace Stevens, "*The Man with the Blue Guitar*"

"Now is no time to think of what you do not have.
Think of what you can do with what there is."
—Ernest Hemingway, *"The Old Man and the Sea".*

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CLINICAL IMAGE

MEDICAL QUIZ: IMAGE-1

AMINUR RAHMAN

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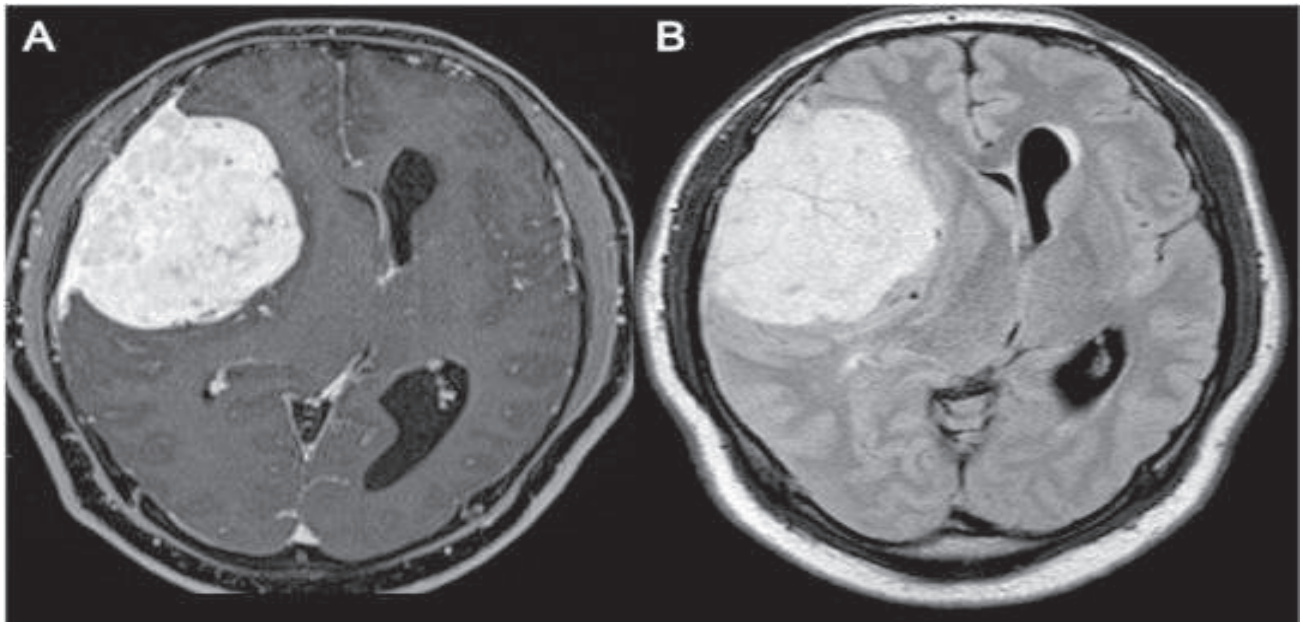
Citation: *Rahman A. Clinical Image-1. Bangladesh J Medicine 2023; 34: 260.*

A 62-year-old female with no medical history, presented 3 months' ago headaches resistant to usual analgesics with behavior disorders. Symptoms worsened with an onset of vomiting, without sensory-motor deficit or seizures. She undergoes a contrast enhanced MRI (A) and FLAIR (B). Ans the following questions.



Questions

1. Describe the film (3 important features)
2. What is the most likely diagnosis ?
3. What are the treatment modalities ?

Address of Correspondence: Dr Aminur Rahman, Assistant professor, Department of Neurology ,Sir Salimullah Medical College, Mitford, Dhaka, Bangladesh, email: draminur@yahoo.com; Cell no: +08801711189092; Orcid.org/0000-0001-9261-7734

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CLINICAL IMAGE

MEDICAL QUIZ: IMAGE - 2

MUHAMMAD ABDUR RAHIM

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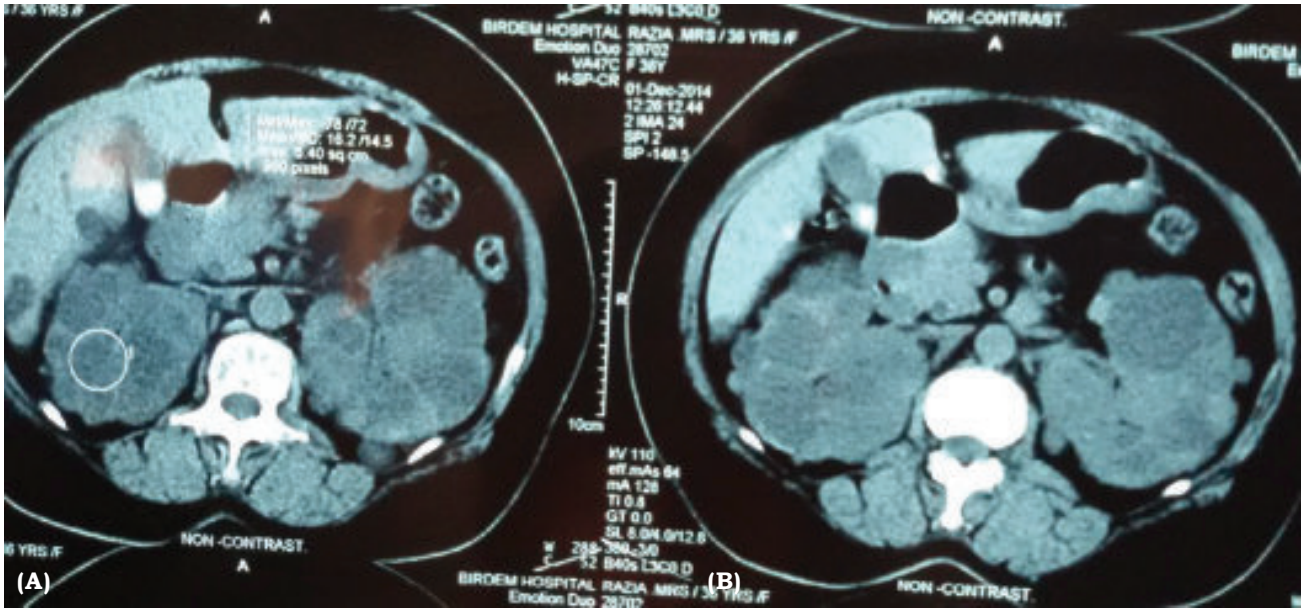
Citation: *Rahim MA. Medical Quiz: Image-2. Bangladesh J Medicine 2023; 34: 261.*

A 50-year-old male patient, with family history of kidney failure, presented with hypertension and vague upper abdominal discomfort. Clinically, he had bilateral ballotable kidneys. A non-contrast, computed tomography (CT) scan, axial film of his abdomen is shown. Read the film and answer the following questions.



Questions

1. Mention 2 abnormal radiological findings.
2. What is the most likely diagnosis?
3. Mention 1 cardiovascular association.
4. Patient developed sudden severe headache followed by unconsciousness. Mention possible cause and pathogenesis.

Address of Correspondence: Dr. Muhammad Abdur Rahim, Associate Professor, Department of Nephrology, BIRDEM General Hospital, Dhaka-1000, Bangladesah. Email: muradrahim23@yahoo.com

Answer to Medical Quiz - 1

AMINUR RAHMAN

Answers:

1. Homogeneously enhanced mass within the right Frontoparietal lobe
2. A dural tail sign
3. Compression of the left lateral ventricle and midline shift to the left
4. Meningioma in the right Frontoparietal lobe
5. Surgical resection of the tumor

Review:

Meningioms are the most prevalent meningeal tumors, which are extra-axial tumors. They are a kind of non-glial neoplasm that develops from meningocytes or arachnoid cap cells of the meninges and can be detected anyplace that meninges are present, even those locations where it is thought that only rest cells exist. MRI with contrast provides the most precise delineation of the tumor, presence of intra- and trans-osseous extension, and connection to the underlying brain for meningiomas.

MRI is the investigation of choice for the diagnosis and characterisation of meningiomas, as it is with the majority of other intracranial pathologies. The diagnosis may be determined with an extremely high degree of accuracy when both the look and location are usual. However, in other cases, the appearances are uncommon, necessitating careful interpretation in order to determine the proper preoperative diagnosis.

Typically, meningiomas take the form of extra-axial masses with a wide dural foundation. Although various variations are seen, they are typically homogenous and well-defined. It appears that the histological subtypes correlate with the signal strength of meningiomas on T2-weighted imaging.

Surgery is typically used as a kind of treatment. External-beam radiation treatment (or even brachytherapy) can be given if only partial resection is achievable, particularly towards the base of the skull it has been demonstrated that radiation increases local control and lengthens overall survival.

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Answer to Medical Quiz - 2

MUHAMMAD ABDUR RAHIM

Answer

1. Enlarged kidneys with multiple cysts, hepatic cysts
2. Autosomal dominant polycystic kidney disease (ADPKD)
3. Mitral valve prolapse
4. Rupture of intra-cranial aneurysm

Review

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited kidney disease accounting for 1 in 800 live births in western world with 5-10% patients in end-stage renal disease (ESRD) programm.[1,2] Mutations may be in PKD-1 gene (located in chromosome 16, common and have relatively aggressive disease) and PKD-2 gene (located in chromosome 4). Defective synthesis of polycystin-1 and 2 results in cyst formation in kidneys and other organs. Patients may remain asymptomatic; common presentations include hypertension, abdominal heaviness, pain, haematuria, renal failure, etc.[3] Ultrasonography is the investigation of choice and also used for screening of first degree relatives over 20 years of age. Abdominal pain may result from cyst infection, expansion, haemorrhage and stone. Treatment is directed towards control of hypertension by angiotensine blocking agents, treatment of infection and monitoring. Newer agents may help reduce cell proliferation.[1] Patients with progressive kidney failure may require kidney transplantation. As the disease has an autosomal dominant inheritence, each of the off spring has a 50% chance of being affected and this issue should be discussied during counselling.

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