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EDITORIAL

DENGUE VACCINE UPDATE

SHOHAEL MAHMUD ARAFAT

Dengue, the most common arbovirus infection, affects four billion people in at least one hundred twenty-eight countries and is most prevalent in Southeast Asia, Central and South America[1]. Since 2023, continued transmission and an unanticipated surge have led to over five thousand dengue-related deaths in over eighty countries[2].

Three key findings have challenged dengue vaccine design nearly 50 years after its development; antibody-dependent boost, cellular immunity safeguarding[3], and the nonstructural protein 1 (NS1) antigen pathogenicity[4]. Dengue vaccinations should include structural and nonstructural antigens (including NS1) of all four DENV serotypes for maximum protection[5].

The dengue vaccines that WHO has licensed are Dengvaxia (CYD-TDV) by Sanofi and Qdenga (TAK-003) by Takeda[6], but only Dengvaxia is approved by the US-FDA[7]. Another vaccine which is in the pipeline just successfully completed phase 3 trial, which is a single administration tetravalent vaccine, Butantan-DV (Instituto Butantan), developed in the National Institute of Allergy and Infectious Diseases laboratory may provide protective immunity against all four DENV serotypes[8].

Yellow fever virus-derived Dengvaxia is a three-dose vaccine fused chimerically with the structural areas of the four DENV serotypes[9]. Dengvaxia is now accessible to children, adolescents, and adults with laboratory-confirmed prior dengue infection[7]. This vaccine is not widely used due to the need for pre-vaccination dengue screening of previous dengue infection.

The two-dose dengue vaccine TAK-003, commonly known as Qdenga (Takeda), comprises live, attenuated DENV-2 and structural region chimaeras of DENV-1, DENV-3, and DENV-4 (10). WHO does not advocate systematic use of the TAK-003 vaccine in low dengue prevalence areas as the efficacy–risk profile for DENV3 and DENV4 in seronegative people is not well understood.

The dengue vaccine is only a part of a structured protective plan against dengue infection, including vector control, patient care, community education, and engagement.

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REVIEW ARTICLE

POSITRON-EMISSION TOMOGRAPHY (PET) AND SINGLE-PHOTON-EMISSION COMPUTED TOMOGRAPHY: DIAGNOSIS OF NEUROLOGICAL DISORDERS

AMINUR RAHMAN

Abstract:
Functional neuroimaging is a major tool in the study of neurological illnesses. It plays a role in diagnosis, therapy, and surgical planning. It can aid in the identification and understanding of functional movement impairments, as well as their differentiation from other diseases. It can also aid in detecting co-morbid organic illnesses. Positron-emission tomography (PET) and single-photon-emission computed tomography (SPECT) are well-known nuclear-medicine imaging techniques utilized in current neurological diagnostics. PET (Positron Emission Tomography) and SPECT (Single Photon Emission Computed Tomography) are two imaging procedures that use radioactive tracers to analyze the brain and other organs. They are essential in both clinical research and treatment development, and can aid in the early detection and treatment of neurological diseases. So, the combination of PET with 18F-fluorodeoxyglucose (FDG) and SPECT with a 111 In-labeled ligand provides clinicians with information an other kind of neurological disorders.

Keywords: *Positron-emission tomography, PET, Single-photon-emission computed tomography, SPECT, Diagnosis of Neurological disorders*

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Introduction:

Functional neuroimaging is the use of neuroimaging technology to assess a specific element of brain function, generally in order to better understand the relationship between activity in certain brain areas and specific cognitive functions.[1] Common approaches of functional neuroimaging include: Single photon emission computed tomography (SPECT), Positron Emission Tomography (PET), Functional magnetic resonance imaging (fMRI), Electroencephalography (EEG), Magnetoencephalography (MEG), Functional Near-Infrared Spectroscopy (fNIRS) and Functional Ultrasound Imaging (fUS).[1,2]

PET (positron emission tomography) and SPECT (single photon emission computed tomography) scans are two medical imaging procedures that use radioactive tracers to provide 3D images of the body's interior functioning.[3] PET scans employ radiotracers to emit positrons, whereas SPECT scans use radiotracers to release gamma rays. PET provides superior spatial resolution than SPECT. PET scans offer higher resolution than SPECT scans, with pictures averaging 5 mm against 10-20 mm for SPECT. PET has a better sensitivity, which means it can detect smaller levels than SPECT. [4]

In general, SPECT radioisotopes may be measured for hours to days, whereas PET radioisotopes can be measured for minutes to hours. PET provides superior spatial resolution than SPECT PET devices require an on-site cyclotron to supply radioisotopes, whereas SPECT machines are more generally available. PET scans are effective for cancer diagnosis and brain

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imaging, whereas SPECT scans are commonly utilized for bone scans and heart/blood flow imaging.[5]

Both scans use very small amounts of radioactive tracers that are quickly removed by the body, and radiation exposure is negligible and comparable between the two. A single photon emission computed tomography (SPECT) scan is an imaging technique that reveals how blood flows to tissues and organs. It may be used to diagnose seizures, strokes, stress fractures, infections, and spinal malignancies. [4]

Positron Emission Tomography (PET) Imaging:

Introduction:

Positron Emission Tomography (PET) is a non-invasive imaging method that produces three-dimensional (3D) images of the interior of the body using radioactive tracers.[5] It is frequently employed to evaluate blood flow, metabolic activity, and chemical composition of organs and tissues. Using radioactive isotopes, this imaging method can examine a range of chemical or functional characteristics in both healthy and diseased brains that are not available with other imaging techniques. A biological tracer is identified by a positron-emitting radionuclide in positron emission tomography (PET) imaging.[6] A positron is a positively charged electron (Fig.-1).

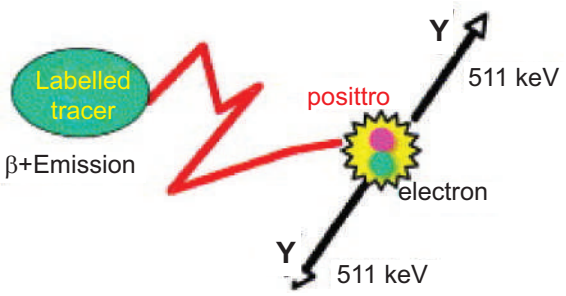

Fig.-1: *A positron is a positively charged electron*

Source: semnuclmed.2011.11.003. doi: 10.1053/j. PMCID: PMC3586419.

PET scans of the brain are used to identify or highlight tumors and diseased tissue, measure blood flow, measure cellular and/or tissue metabolism, assess patients with seizure disorders that do not improve with medication, assess patients with specific memory disorders, and identify changes in the brain after trauma or drug abuse. It is clinically proven that brain metabolism can be visualized indirectly through perfusion directly utilizing PET and [F-18] fluorodeoxyglucose (FDG). [7]

In vivo measurements of cerebral blood flow and metabolism have been made possible using radio-isotopes like [15O] or [18F] deoxyglucose (Figure: 1). The tracer is administered by gaseous inhalation or intravenous injection, and tomographic images show where it is distributed throughout the brain. PET studies that assess receptor binding, such as those that examine dopaminergic receptors in extrapyramidal disorders, also include radioisotope labels.[8]

Advantages:

PET studies have shed a great deal of light on the pathophysiology and pathogenesis of diseases as well as elements of normal brain activity. Important information has been gathered about the different anatomical patterns of altered flow and metabolism in a variety of neurodegenerative illnesses, as well as the patterns of flow and oxygen use in infarcts and the ischemic penumbra that surrounds them. Figure 5 shows amyloid PET in Alzheimer's Disease and Frontal Lobe Dementia.[9]

Disadvantages:

It is an expensive tool, requires immediate access to a cyclotron. The opportunity for serial examinations is limited by the constraints of radiation exposure.[10]

Limitations of Positron emission tomography (PET) scans:

PET scans can generate erroneous results if a patient's chemical balance is abnormal. Patients with diabetes, for example, or those who ate within a few hours of the scan, may have inaccurate results. The radioactive chemical used in PET scans decays quickly, so be on time for your appointment. PET scans may not have the same image resolution as CT or MRI scans. Patients may need to fast for a few hours prior to the scan. PET and CT scans have difficulty detecting cancers less than one centimeter in diameter. PET scans have limits in certain types of cancer, such as breast and thyroid cancer. Patients who suffer from claustrophobia or anxiety may struggle to complete the scan.[11]

PET in Dementias:

Positron Emission Tomography (PET) scans are used to determine the levels of specific chemicals in the brain. There are several distinct types of PET scans. An amyloid-PET scan detects the accumulation of aberrant amyloid protein in the brain, which is one of

the hallmarks of Alzheimer's disease. An ^{18}F]fluorodeoxyglucose, FDG) ; FDG-PET scan assesses the concentration of glucose in the brain, demonstrating how the brain uses energy(Fig.-2). ^{18}FDG PET scan, reveals areas of the brain where nutrients are not being used effectively for energy. A brain with Alzheimer's disease exhibits a loss of red color and an increase in yellow, blue, and green colors, indicating diminished metabolic activity.[12] Several other PET tracers have also been created to investigate the neuropathology and changes in neurotransmitter systems that underpin dementia, to further our understanding of the pathophysiology of dementia, and to improve diagnostic accuracy (Table:1).

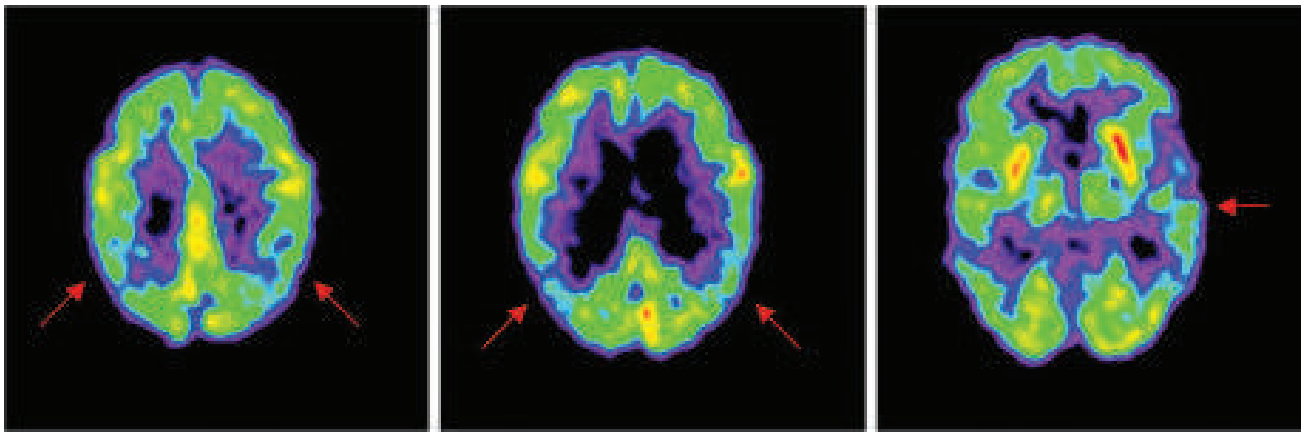

Fig.-2: *8F-FDG PET images of early AD. Early Alzheimer's typically affects the parietal, temporal, and posterior cingulate cortices. Brain images of this 80-y-old woman demonstrate hypometabolism of the parietal cortex, bilaterally (left and middle), with relative sparing of the primary visual cortex, sensorimotor cortex, thalamus, and basal ganglia. In the early stages of AD, deficits often appear asymmetrically, as evidenced here by mild hypometabolism of the left temporal cortex (right). In later stages of the disease, degeneration will be apparent bilaterally.*

Source: Daniel H.S. Silverman ; Journal of Nuclear Medicine April 2004, 45 (4) 594-607;

Table I

Major findings in dementia for PET tracers mainly used in clinical practice

Disease	[18F]FDG	[11C]PiB/[18F]FDDNP	Dopaminergic system tracers
AD	Parietotemporal, posterior cingulate, medial temporal hypometabolism, accompanied by frontal hypometabolism in advanced disease	high cortical uptake, mostly in frontal, parietal, and temporal association cortices	Normal
FTLD	Frontal lobe hypometabolism, accompanied by temporal and subcortical hypometabolism in advanced stages; SD: temporal hypometabolism, associated with frontal hypometabolism; PNFA: left frontotemporal hypometabolism	Low cortical [11C] PIB retention; high [18F] FDDNP uptake in frontal and prefrontal regions	Normal
LBD	Widespread hypometabolism with marked metabolic reductions in occipital cortex	DLB: high cortical [11C]PiB retention; PDD: low cortical [11C] PiB retention	Marked reduction in striatum, more prominent in putamen

PET scans in Parkinson's Disease:

The brain's dopamine-producing neurons' capacity to generate dopamine is reflected in 18F-DOPA absorption. Research has indicated that elevated bradykinesia and rigidity, but not tremor, are associated with 18F-DOPA uptake.[13]

PET tracers like 18F-DOPA and radiolabeled tracers tailored for dopamine transporters (DaT) and vesicular monoamine transporters (VMAT) can be used to evaluate motor dysfunction. At the synapse—the junction of two nerve cells or a nerve cell and a muscle cell—both DaT and VMAT are membrane-embedded proteins that aid in the uptake of monoamine neurotransmitters like dopamine. PET can detect abnormal activity of these transporters, which is used to diagnose Parkinson's disease early.[14]

Additionally, PET can be used to distinguish Parkinson's disease from other movement diseases. As an illustration, 18F-DOPA PET has been used to distinguish between idiopathic Parkinson's disease and drug-induced Parkinson's disease(Fig.-3). Taking antipsychotics can cause drug-induced Parkinsonism, a reversible illness. In contrast to idiopathic Parkinson's patients, who have diminished DaT activity even in the early stages of the disease, drug-induced Parkinson's patients' brains do not exhibit any changes in presynaptic DaT activity.[15]

Since the uptake of 18F-FDG in the brains of patients with multiple striatal atrophy (MSA) is low and that of people with Parkinson's disease is either normal or elevated, PET with this tracer can be utilized to distinguish between patients with MSA and those with Parkinson's disease.[16]

Dementia, linked to alterations in the brain's cortical region, affects about 40% of patients with Parkinson's disease. Due to their low cortical area activity, people with dementia can be distinguished from those without dementia using PET tests using 18F-FDG, even in the early stages of Parkinson's disease. Research also revealed that individuals with dementia from Parkinson's disease have lower glucose metabolism, as measured by the uptake of 18F-FDG in the frontal, temporal, and parietal regions of the brain, as compared to those without dementia.[16,17]

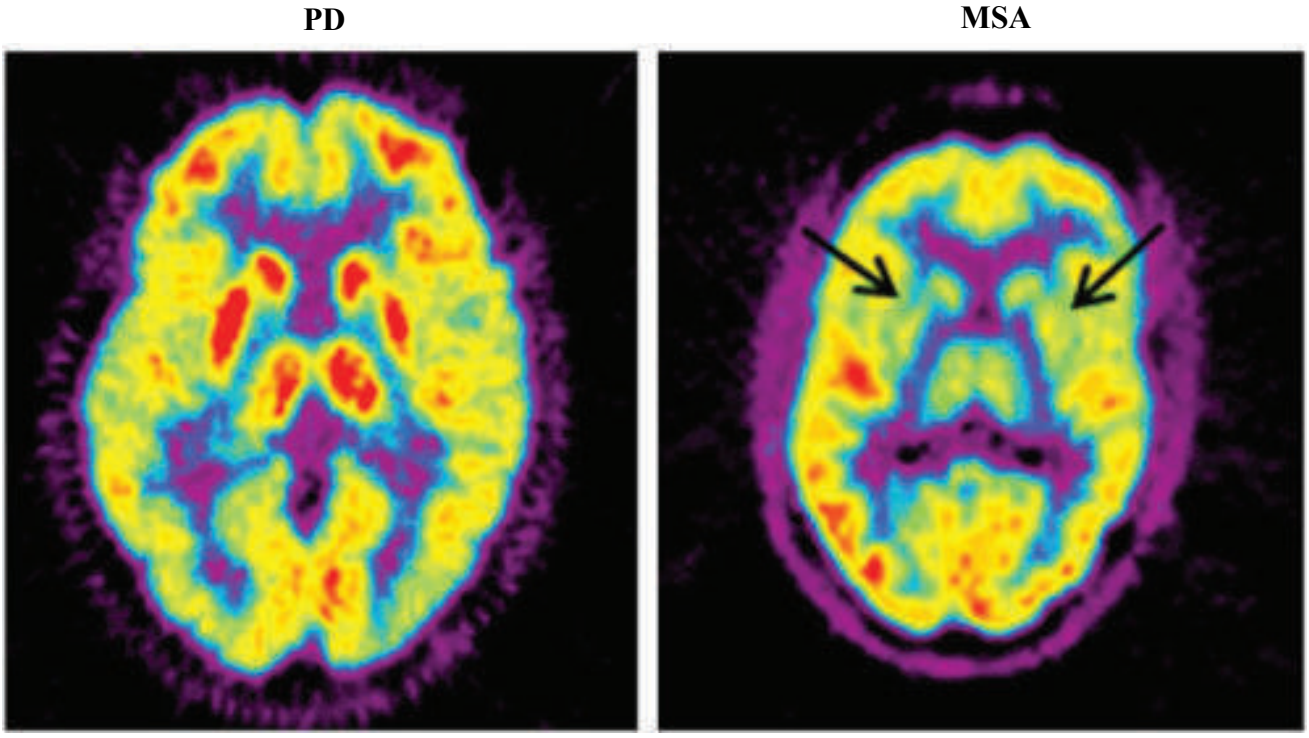

Fig.-3 *F-18-FDG PET in Parkinson's disease (PD) & Multiple-system atrophy(MSA). 18 F-FDG PET images of PD and multiplesystem atrophy patient. Multiple-system atrophy patient shows significant striatal reduction of glucose metabolism. MSA multiple-system atrophy.*

Source: Journal of Nuclear Medicine ;2010;51(4):596-609. DOI:10.2967/jnumed.108.059998

PET in Multiple Sclerosis:

Neurodegeneration results from inflammation and demyelination in the central nervous system (CNS), which are linked to the pathology of multiple sclerosis (MS). These processes have been imaged using a variety of positron emission tomography (PET) tracers. Neuro-inflammation has been measured using PET tracers for 18-kD translocator protein (TSPO) receptors, which are overexpressed on activated microglia, macrophages, and astrocytes. Increased activation of inflammatory cells was shown by PET imaging of TSPO expression in normal appearing white matter (NAWM), grey matter (GM), and MS lesions (Fig. 4). One of the key factors influencing the effectiveness of treatment was found to be a decrease in inflammation in MS lesions. Recently, myelin visualization with PET has advanced.[18]

First clinical trials using PET to visualize myelin yield encouraging findings. When evaluating neuronal damage in various neurodegenerative illnesses, [18F] FDG remains the primary PET tracer. PET's current clinical use in MS are primarily limited to supporting differential diagnosis or assessing the effectiveness of immune-suppressive therapies. The initial metabolic and structural alterations in MS neurons can be found by PET imaging of the mitochondria and synaptic vesicles. In clinical trials of medications intended to postpone or stop neurodegeneration in multiple sclerosis, PET imaging of pathological processes may offer reliable outcome markers.[19]

PET scan in brain tumor:

A positron emission tomography (PET) scan is a type of brain imaging examination used to detect tumors of the brain A PET scan employs a radioactive tracer that binds to brain tumor cells, making them visible on the image (Fig.-5). PET scans are very efficient at detecting rapidly growing brain cancers like glioblastomas and some oligodendrogliomas. However, they are less effective at detecting slow-growing brain tumors, which are more common in benign tumors. So, to produce even more detail three dimensional images for highly exact diagnosis, the scans can be merged in a PET-MRI scan or a PET-CT scan.[20]

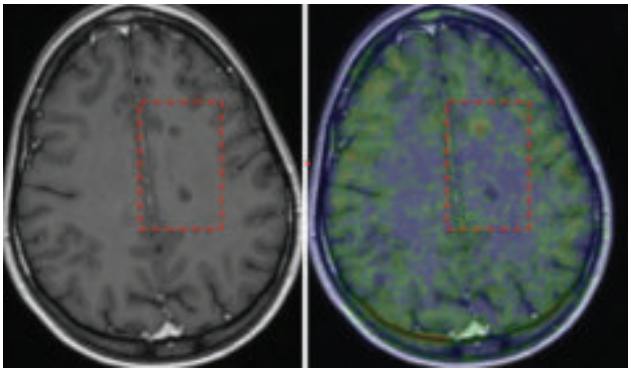

Fig.-4: *TSPO-PET imaging for neuroinflammation in multiple sclerosis. Chronic T1 lesions were differentiated in vivo using TSPO-PET. The left image shows a T1-weighted MRI image with two T1 black holes that appear comparable (no gadolinium enhancement). TSPO-PET (on the right) demonstrates that in the upper lesion, there is microglial activation, confirming this lesion as a chronic active lesion, but in the lower lesion, there is no radioligand uptake, confirming this lesion as a chronic inactive lesion.*

Source: Frontiers in Neurology, *9*, 341831. https://doi.org/10.3389/fneur.2018.00181

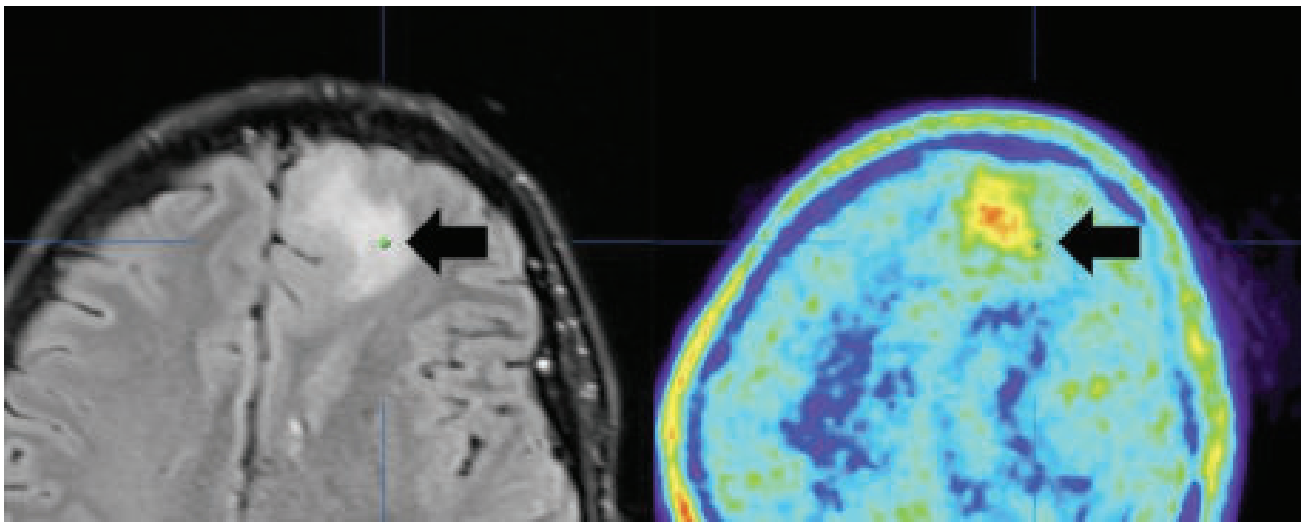

Fig.-5: *On the left, an image of the brain obtained using magnetic resonance imaging; on the right, using a new tyrosine PET procedure. The location of the tumor is indicated by the arrow.*

Source: Franciszek Lukaszczyk Oncology Center; Harat et al., Nature Communications 2023 (CC BY 4.0)

Single Photon Emission Computed Tomography (SPECT) Scan:

A single photon emission computed tomography (SPECT) scan is a functional nuclear imaging method used to assess regional cerebral perfusion. Because cerebral blood flow is directly related to neuronal activity, the activity distribution is thought to reflect neuronal activity levels in various parts of the brain. Although structural magnetic resonance imaging (MRI) and computed tomography (CT) provide fine anatomical detail, SPECT offers additional functional information. Frequently, brain pathology manifests as functional abnormalities before physical changes may be seen.[21] SPECT has clinical applications in diagnosis, therapeutic treatment, and patient follow-up. A basic discussion of the clinical utility of this technology is followed by pertinent information on cerebral physiology and pathology for accurate interpretation of brain SPECT pictures.[22]

Clinical applications of SPECT:

Cerebral disorders can be diagnosed and monitored using a SPECT scan, including strokes, seizures, and neurodegenerative diseases such as Alzheimer's. It can also aid in diagnosing vascular brain illnesses such as moyamoya disease. A SPECT scan can assist in assessing memory loss. Detecting changed blood flow: A SPECT scan can reveal which parts of the brain are the most and least active. It can assist pinpoint epileptic foci prior to surgery and map cerebral perfusion during surgical procedures. It can assist measure vascular spasm following a subarachnoid hemorrhage and assist predict the prognosis of patients who have had a stroke. It scan can support the clinical diagnosis of brain death.[23]

Limitations of SPECT:

The major limitation of brain SPECT study is the attenuation by the skull. The commonly used Chang method of attenuation correction is based on a simple mathematical formula, which is susceptible to technical variation. In diagnosis of dementia with SPECT, it can be difficult to separate the real defect from the attenuation artifact. SPECT is technically less sophisticated and demanding when compared with positron emission tomography (PET), but provides lower-resolution images. It can be used to evaluate regional variations in blood flow, but its role in everyday clinical practice is, like that of PET, a small one.[24]

SPECT in Epilepsy:

Patients with intractable focal epilepsy who are candidates for surgical excision of the epileptogenic focus may benefit from SPECT imaging (12-13). MRI is also important in the care of these individuals, albeit not all epileptogenic foci can be precisely localized using this modality, and not all anatomical foci are the source of a patient's seizures. As a result, SPECT can correctly pinpoint the epileptogenic focus, which is useful for neurosurgical procedures. (Fig.-6).

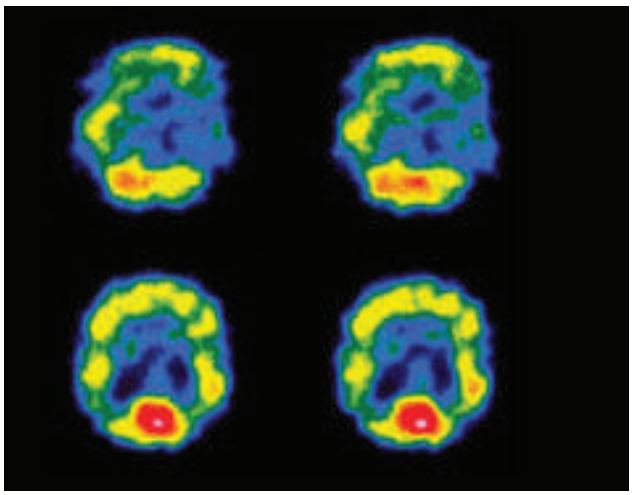

Fig.-6: *A SPECT scan of a patient with uncontrolled complex partial seizures. The temporal lobe on the left side of the brain shows less blood flow than the right, confirming for the surgeon the nonfunctioning area of the brain causing seizures.*

Source: Dinesh, E. et al. "Instinctive classification of Alzheimer's disease using FMRI, pet and SPECT images." 2013 7th International Conference on Intelligent Systems and Control (ISCO): 405-409.

SPECT in Dementias:

Anatomical imaging in dementia patients often indicates little or no change. However, employing SPECT scans to identify functional involvement patterns allows for more reliable distinction of these forms of dementia (Fig. 7).[26] Regional cerebral blood flow is reduced in Alzheimer's disease, particularly in the bilateral temporal lobes (Fig. 7A). The posterior parietal lobes may also exhibit hypometabolism. These changes can arise early in the disease process and may serve to identify AD from other types of dementia. In vascular dementia, many asymmetrical lesions impact the anterior and posterior cortex, as well as the right striatum (Fig. 7B), and in frontotemporal dementia, there is frontal hypoperfusion. (Fig. 7C).

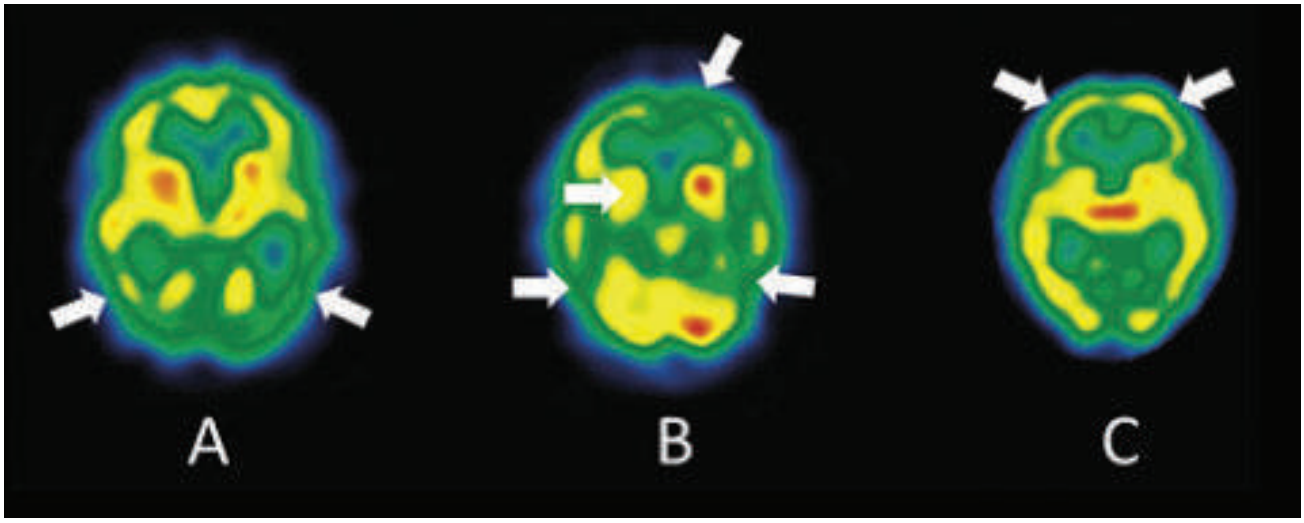

Fig.-7: *Tc-99m HMPAO SPECT scans in 3 patients with dementia showing perfusion patterns suggestive of Alzheimer's disease, with bilateral temporo-parietal hypoperfusion (A), vascular dementia with multiple asymmetrical lesions affecting the anterior and posterior cortex and right striatum (B) and fronto-temporal dementia with frontal hypoperfusion (C).*

Source: Warwick, J. "Brain imaging with SPECT and PET." Continuing Medical Education "2013; 31.8: 307-309.

SPECT in Stroke:

SPECT tests can determine the position and degree of lesions caused by blood supply abnormalities. This approach is more sensitive than CT in determining the existence and size of myocardial infarction [27] (Fig: 8&9). SPECT was found to be positive in 90% of cases within the first 8 hours following a stroke, with sensitivity of 61%-74% and specificity of 88%-98% reported 13. Within 6 hours of symptom onset, transient ischemic episodes can be distinguished from ischemic strokes by SPECT counting rate densities of 70% when compared to the contralateral side (perfusion in stroke tissue 35%-60% of contralateral values).[28]

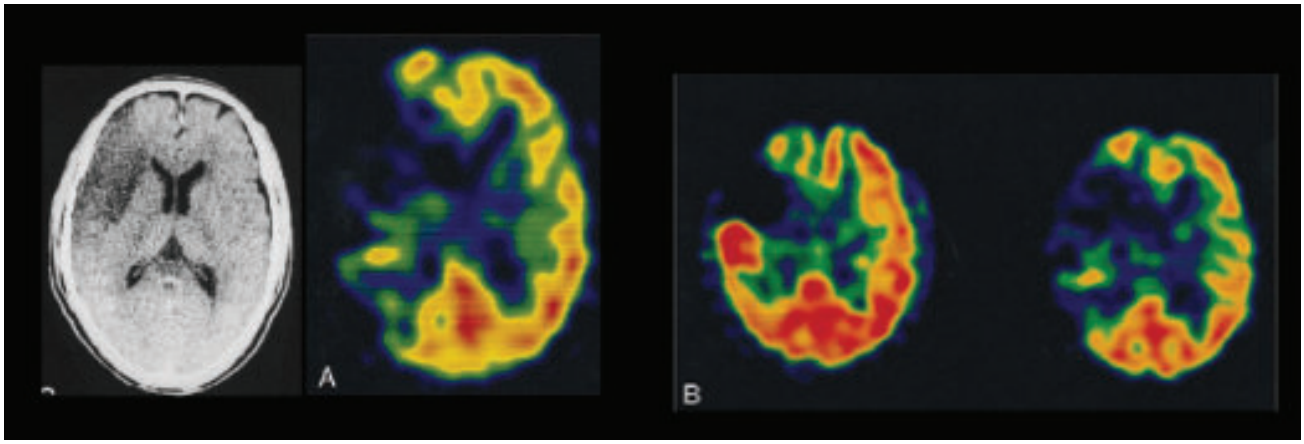

Fig.-8: *54-year-old man with atrial fibrillation and sudden onset of left-sided hemiparesis. Figure (A) CT scan of brain and 99mTc-HMPAO SPECT image 4.5 hours after the onset of stroke shows hypoactivity in the right frontal and temporal lobes. (B) 99mTc-HMPAO SPECT image (left) obtained 12 hours after the initial study shows hyperactivity in the right temporal lobe; a 99mTcECD SPECT image (right) shows hypoactivity in the same area.*

Source: Ogasawara, K., Mizoi, K., Fujiwara, S., & Yoshimoto, T. (1999). 99mTc-bicisate and 99mTc-HMPAO SPECT imaging in early spontaneous reperfusion of cerebral embolism. AJNR., 20 4, 626-8.

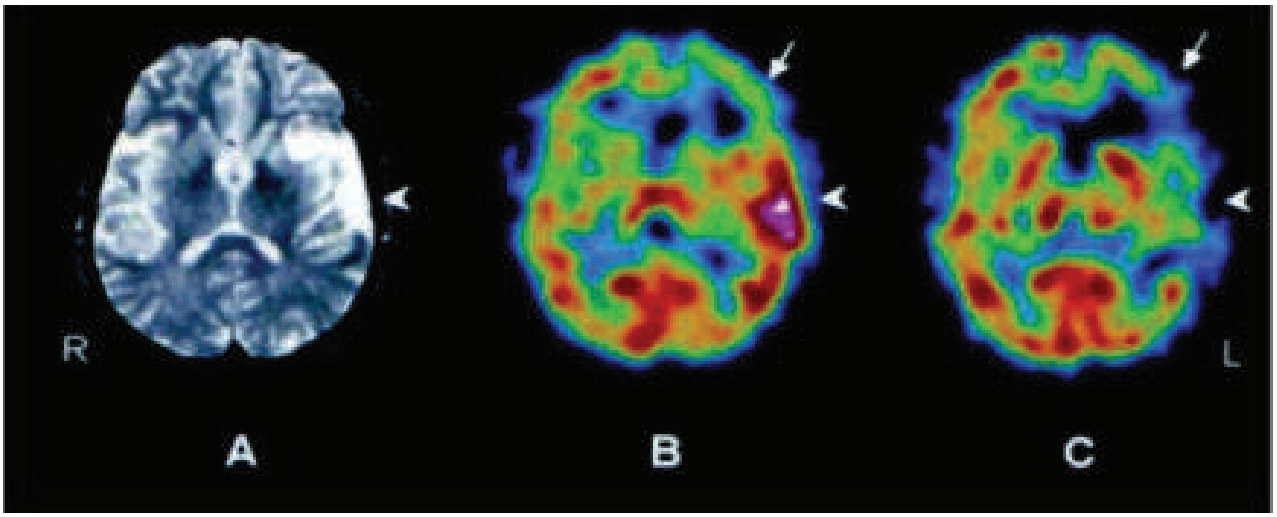

Fig.-9: (*A) MRI (T2-weighted) at admission shows hyperintensity at site of infarction (arrowhead). (B) 99mTc-HMPAO SPECT image obtained 1 wk after stroke shows increased tracer uptake (hyperperfusion) in left temporal lobe caused by luxury perfusion (arrowhead). Hypoperfusion is also seen in left frontal cortex (arrow), intrepreted as ischemia in anatomically preserved region. (C) 99mTc-HMPAO SPECT image obtained 1 mo after stroke shows left temporal lobe hypoperfusion (arrowhead) corresponding to initial MR image of ischemia. Perfusion changes in left frontal lobe are also seen: improvement in anterior and mesial aspects caused by recovery of ischemia, as well as perfusion impairment in lateral aspect caused by extension of the infarction (arrow).*

Source: Ana M. Catafau "Brain SPECT in Clinical Practice. Part I: Perfusion" J Nucl Med 2001; 42:259–271

SPECT in Traumatic Brain Injury:

SPECT scans reveal more abnormalities in traumatic brain injury (TBI) patients than MRI and CT scans.[29]Hypoperfusion is most common in the frontal and parietal lobes (Fig. 10), although it can also impact the basal ganglia, occipital, parietal, and cerebellar areas. SPECT has a high sensitivity and negative predictive value for TBI, and a normal study predicts a good recovery.[30] However, due to its low specificity, SPECT alone is insufficient to diagnose TBI.

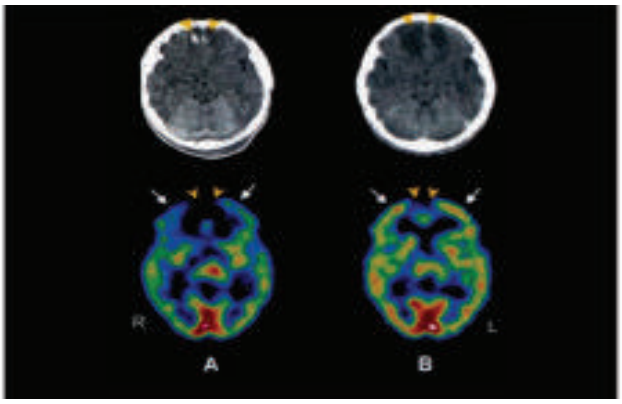

Fig.-10. *CT (top) and 99mTc-HMPAO SPECT (bottom) images from 16-y-old patient with traumatic brain injury after traffic accident. (A) CT at time of admission shows subarachnoid hemorrhage with small contusional hemorrhagic foci in both frontal lobes (orange arrowheads). SPECT was subsequently performed and shows absence of tracer uptake (cold areas) in anteromedial aspect of both frontal lobes corresponding to hemorrhagic lesions, in addition to global hypoperfusion, more marked in both frontal cortices (white arrows). (B) CT and SPECT images obtained 1 mo later at time of discharge after clinical recovery. Hypodense images in both frontal lobes can be seen on CT as consequence of hematoma's resolution. Corresponding cold areas persist on SPECT image (orange arrowheads) but show improvement in global cerebral perfusion, particularly in both frontal lobes (white arrows).* Source: Ana M. Catafau "Brain SPECT in Clinical Practice. Part I: Perfusion" J Nucl Med 2001; 42:259–271

SPECT in Parkinsonism:

SPECT is routinely used to diagnose Parkinson's disease.[31] 123I-Ioflupane-SPECT imaging offers information based on the local binding of presynaptic dopamine transporters (DaTs) with 123I-Ioflupane, which has been demonstrated to be highly linked with Parkinson's disease progression.[31,32] This binding metric is quantitative and measures the geographic distribution of dopamine transporters. Furthermore, 123I-Ioflupane-SPECT is an imaging technique that can differentiate between Parkinson's disease and essential tremor.[33] SPECT imaging can help identify PD from drug-induced Parkinsonism. [34,34] However, any condition that causes the loss of presynaptic dopamine neurons would appear aberrant when compared to normal controls (NCs)24. Thus, SPECT cannot distinguish between Parkinson's disease, progressive supranuclear palsy, multiple system atrophy, and other neurodegenerative illnesses that

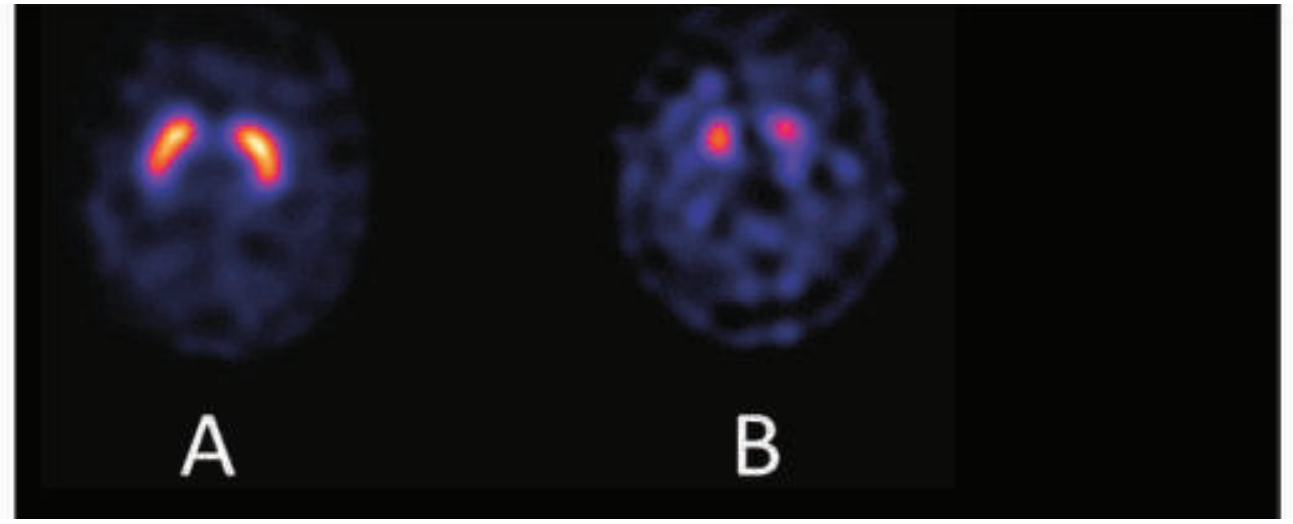

Fig.-11: *Scans of two patients with parkinsonism. In one case, DaT SPECT shows normal striatal DaT density, virtually ruling out Parkinson's disease or other causes of presynaptic dopaminergic neuron degeneration (A). The second scan shows a patient with Parkinson's disease with marked loss of striatal uptake, particularly in the putamen, and a high level of background activity (B).*

Source: Warwick, J. "Brain imaging with SPECT and PET." Continuing Medical Education, 2013; 31.8:307-309.

damage dopamine neurons.[35] The majority of 123I-Ioflupane-SPECT studies have focused on the striatum (putamen and caudate) [36-38]. Researchers found that Parkinson's disease reduces DaT levels in the striatum, which are linked to disease progression and clinical scores. [39.40] DaT imaging shows reduced presynaptic neuronal degeneration in PD and kindred parkinsonian syndromes, even when clinical symptoms are mild, whereas essential tremor has normal striatal DaT density29 (Fig. 11).

SPECT in Brain tumour:

SPECT is used in brain tumor patients to assess tumor aggressiveness, distinguish between therapy-induced necrosis and tumor recurrence, evaluate treatment response, and estimate prognosis.[41] It also implies that it has a high sensitivity and specificity for localizing ICSOLs and can be employed in patients who are unable to undergo CECT/CEMR due to contraindications or long waiting lists. The most commonly used SPECT radiopharmaceuticals are Tc-99m diethlyenetriaminepentaacetic acid (DTPA) and Tc-99m glucoheptonate (Tc-99m GHA), which are well-known renal radiopharmaceuticals that lack the drawbacks of Tc-99m pertechnetate.

Tc-99m GHA SPECT can discriminate between high- and low-grade gliomas, as well as metastases.[42] Similarly, thallium-201, Tc-99m tetrofosmin, and Tc-99m sestamibi were discovered to delineate brain tumors through multiple mechanisms of uptake other than blood-brain barrier (BBB) disruption; however, their high cost and the availability of morphological imaging techniques put these modalities on the back burner (Fig.12).[43] SPECT has also been used to diagnose brain cancers and assess tumor response to radiation therapy using the radioactively labeled amino acid 3-(123I) iodo-a-methyl-L-tyrosine.

Comparison of PET and SPECT:

PET (Positron Emission Tomography) and SPECT (Single Photon Emission Computed Tomography) scans are two imaging procedures that use radioactive tracers to produce 3D images of the body's interior functioning. The primary distinction between the two is the type of radiotracer utilized and the ensuing resolution and sensitivity. PET scans use radiotracers to produce positrons, whereas SPECT scans detect gamma rays.[44]

PET scans provide more spatial resolution than SPECT scans. For example, a heart PET scan has a resolution of 5 to 7 mm, whereas a cardiac SPECT scan has a resolution of 12 to 15 mm. PET scans have more sensitivity than SPECT scans, allowing them to detect lower amounts. SPECT scans are typically cheaper than PET scans.[45]

PET scans are frequently used to assess the function of organs like the heart and brain, diagnose cancer, and assess the effectiveness of cancer treatment. SPECT scans can reveal bone malignancy, brain activity, and cardiac blood flow, among other indicators of organ function. MRI scans are frequently coupled with PET and SPECT scans. When combined, the

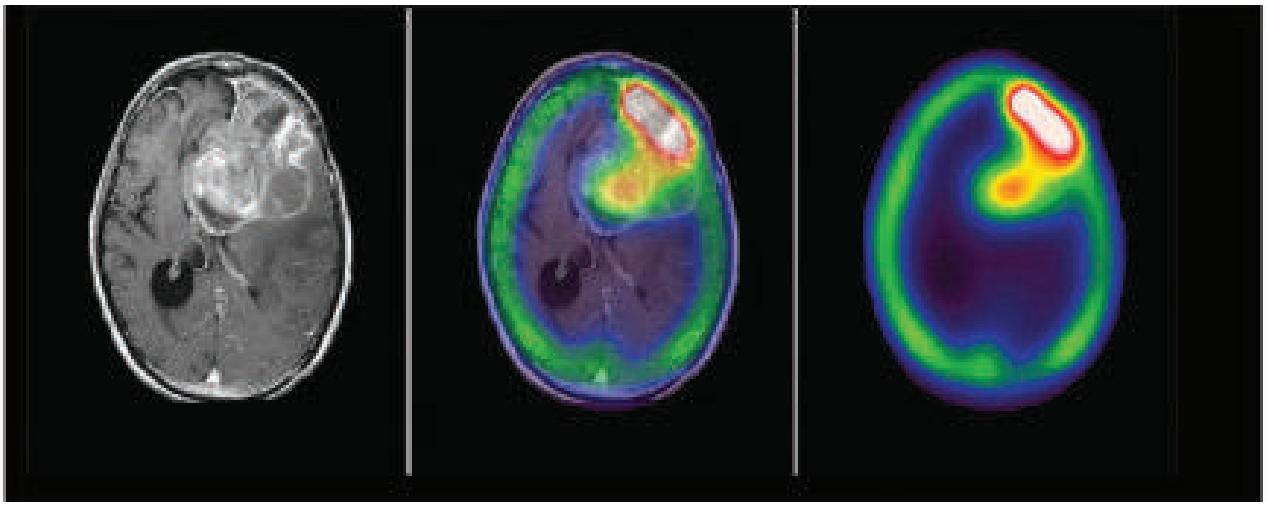

Fig.-12: *Tc-99m GHA SPECT (Tc-99m glucoheptonate) shows anaplastic oligodendroglioma of the left prefrontal region.*

Source: Alam S.S, Junaid S., Ahmed S.M" Evaluation of Technetium-99m glucoheptonate single photon emission computed tomography for brain tumor grading"Asian J Neurosurg. 2016 Apr-Jun; 11(2): 118–128.

information from these scans can yield more precise diagnoses. PET can measure radioisotopes in a matter of minutes to a few hours, while SPECT can measure them in a matter of hours to days.[46]

Conclusion:

Functional imaging such as SPECT or PET, which is used to diagnose metabolic diseases and lesions on a finer scale (such as dementia, PD etc.), and also for neurological and cognitive-psychology research. SPECT is technically less sophisticated and demanding when compared with positron emission tomography (PET), but provides lower-resolution images. SPECT can be used to assess regional differences in blood flow, but its utility in ordinary clinical practice is limited, as are PET's. PET provides more spatial resolution than SPECT. PET has a better sensitivity, which means it can detect smaller levels than SPECT. In general, SPECT radioisotopes may be measured for hours to days, whereas PET radioisotopes can be measured in minutes to hours.

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REVIEW ARTICLE

NONTUBERCULOUS MYCOBACTERIAL INFECTION: AN ACHILLES HEEL FOR CLINICIAN

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Abstract:
Nontuberculous mycobacterial (NTM) o Atypical mycobacterial (ATM) infection is becoming an upcoming challenge for the clinicians. Atypical Mycobacterial infections range from pulmonary to extra pulmonary including skin and soft-tissue infections, traumatic and surgical wound infections, catheter and implant-associated infections. They are commonly misdiagnosed as tuberculosis caused by M. tuberculosis *(MTB). Appropriate diagnostic methods and tools are essential in order to facilitate the differential diagnosis of Atypical Mycobacterium from MTB infections. We aimed to collect data available on Atypical Mycobacterium for diagnosis and appropriate treatment and to create awareness among the physician to combat with challenges.*

Keywords: *Nontuberculous Mycobacterial Infection, Achilles heel for Clinician*

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Introduction:

Nontuberculous mycobacteria (NTM) or Atypical mycobacteria (ATM) are a diverse group of more than 190 species. Among them a few are associated with human infection. They are pervasive environmental bacteria that include mycobacterial species other than *Mycobacterium tuberculosis complex* (MTBC) and *Mycobacterium leprae.*[1]

NTM are found in the environment globally, specifically in water and soil. NTM disease and its localization frequently interplay between organism pathogenicity and host susceptibility. The most commonly encountered atypical mycobacteria that cause the majority of infection in humans are the *Mycobacterium avium complex bacteria (MAC), Mycobacterium avium, and Mycobacterium intracellulare,* also referred to as *Mycobacterium avium-intracellulare (MAI), Mycobacterium kansasii, Mycobacterium marinum, Mycobacterium ulcerans, Mycobacterium abscessus complex bacteria (abscessus, massiliense, and bolletii), Mycobacterium chelonae,* and *Mycobacterium fortuitum.*[2]

Because of their morphological appearance as MTB in sputum smears and their similar clinical presentation, they often misdiagnosed. Due to this, they are also under-reported, misclassified and improperly treated. With these given challenges, NTM have gained more attention in recent years and understanding of their biology, epidemiology, diagnosis, and management of infections caused by them has undergone considerable research globally. However, in our country, NTM are still struggling to get their importance due to their misdiagnosis or incorrect diagnosis. In resource-constrained settings, NTM are rarely diagnosed or sometimes given appropriate attention only after obtaining a history of failed anti-TB treatments[9]

The search terms included "Pulmonary NTM," "Extra pulmonary NTM," and "Antimicrobial susceptibility of NTM" in PubMed. We initially collected abstracts of 78 articles according to the relevance of the topic. After evaluation, 24 papers have been selected finally to write this review article.

The purpose of the review is to elucidate their importance and to establish the need for research in future studies.

Epidemiology:

Estimates of the rate of pulmonary disease are between 5 to 10 per 100,000 per year. Various studies have estimated the rate of all causes of atypical mycobacterial infection in children to be between 0.6 to 3.3 per 100,000. Estimates of the rate of all causes of infection in adults are between 20 to 47 per 100,000.[5]

The reported incidence of NTM species in pulmonary and extra-pulmonary clinical samples from India range from 0.7% to 34%[6].

Pathophysiology:

Nontuberculous mycobacteria are usually taken up by macrophages, causing them to release IL-12 and

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TNF-alpha. IL-12 release activates the IL-12-interferon gamma pathway. The macrophages, neutrophils, and T-cells recruited to the site of infection and result in granuloma formation and creates fibrinous mass walling off the infection. This isolating it from the rest of the body.

Histopathology:

Nontuberculous mycobacterium has a hydrophobic mycolic acid layer in their cell wall. They are not typically seen using Gram staining due to this reason. The best method for detecting atypical mycobacteria is fluorochrome staining which is a type of acid-fast staining and here these bacteria will appear as yellow to orange bacilli. Rapidly growing mycobacteria are noted to be more sensitive to the decolorization process in acid-fast staining. Using more delicate methods for decolorization can increase the chance of visualizing these bacteria. Other less sensitive staining method can also be used include the Ziehl-Neelsen method and the Kinyoun stain[8].

Classification of Atypical Mycobacteria:

The microbiological classification of NTM depends on two main factors[8].

1. Rate of growth (rapid growing or slow growing) and
2. Pigment production.

Table-I

Lists some of the clinically important NTM organisms[8]

Rapid growing	Slow growing
Mycobacterium abscessus	*Mycobacterium avium-intracellulare complex*
Mycobacterium chelonae	*Mycobacterium hemophilum*
Mycobacterium fortuitum	*Mycobacterium kansasii*
	Mycobacterium malmoense
	Mycobacterium marinum
	Mycobacterium scrofulaceum
	Mycobacterium ulcerans
	Mycobacterium xenopi

Clinical presentation:

Pulmonary NTM infections are often misdiagnosed as tuberculosis. In case of NTM, fever is less common and the chest X-ray images shows the nodular lesions and pulmonary infiltrations. Clinical presentation usually found more commonly in middle-aged males with the risk factors of long-term alcohol and tobacco abuse. In these patients, they tend to form large fibro-cavitary lesions in the apex of the lung. The MAC lung disease more commonly affects postmenopausal Caucasian women. In this case, the bacteria form small pulmonary nodules and cylindrical bronchiectasis with a concentration of nodules in the right middle lobe and lingula of the left upper lobe of the lung. *Mycobacterium kansasii* and *Mycobacterium abscessus* tends to form large fibro cavities in the apex of the lung.

Lymphadenitis: The progression of atypical mycobacterial lymphadenitis has four stages. The first stage describes a unilateral lymphadenopathy that progress slowly over several days to months. Stage one is unlikely to show systemic symptoms. Then it shows tenderness indicative of necrosis within the lymph node & in stage three shows erythematous discoloration of the overlying skin & stage four describes the breach of skin and formation of sinus tracts.

Skin and soft tissue disease:

Atypical Mycobacteria enter into the skin and soft tissue through trauma, surgical procedures, or via indwelling medical equipment. Skin and soft tissue infection can be caused by all species. The most common species are *Mycobacterium chelonae, abscessus, fortuitum, ulcerans, and marinum. Mycobacterium marinum* infection is also known as the fish tank granuloma. They usually cause soft tissue infection in fish tank workers/enthusiasts. It most commonly causes localized erythema and granuloma formation of the digits and it can progress to develop nodular lymphangitis of the hands and forearms. They can also affect tendons, joint spaces and cause osteomyelitis. Immunocompromised patients also recorded cases of disseminated infection. Another atypical Mycobacteria "*Mycobacterium ulcerans"* cause Buruli ulcer. They cause large areas of skin involvement, deep ulceration, and marked cosmetic disfigurement. They present as a small, painless nodule, which slowly begins to ulcerate. These ulcers are characterized by poorly defined and irregular borders and can cover extensive sections of the body. *Mycobacterium ulcerans* infections can also cause osteomyelitis in 15% cases. *Mycobacterium fortuitum* most commonly presents as a solitary subcutaneous nodule. They usually cause low morbidity and limited infection. *Mycobacterium abscessus* most commonly causes painful sinus tracts, and progress to ascending lymphadenitis. *Mycobacterium chelonae* also presents as disseminated painful cutaneous nodules.[10]

Diagnosis and Drug-susceptibility Testing:

According to 2017 BTS and 2020 ATS/ERS/ESCMID/IDSA Guidelines, NTM infections is considered positive when more than one expectorated sputum culture is positive and the same NTM species/subspecies must be isolated in more than two sputum cultures. In Broncho alveolar lavage (BAL), NTM can also be found. These are suitable when patients are unable to expectorate. In Trans-bronchial/ lung biopsy, mycobacterial histopathological features are usually present (defined as granulomatous inflammation or presence of acid fast bacilli) this must be combined with a positive culture result. Radiological criteria include nodular or cavitary opacities on a chest X-ray. Bronchiectasis with multiple small nodules on HRCT.

Prior to initiating treatment, it is also now recommended that baseline drug susceptibility testing must be done[11].

Clinical considerations and decision to treat:

The most recent guideline recommends that careful assessment of the patient's clinical status, radiological findings, pathogenicity of the organism, risks and benefits of therapy, the patient's wish and ability to receive treatment as well as the goals of therapy should be discussed with patients prior to initiating treatment'. Depending on the above factors a 'watchful waiting' during clinical review, sputum cultures/bronchoscopy and imaging may sometimes be preferred to treatment. Treatment plan must include follow-up[11].

Treatment:

Treatment of NTM lung required at least three drugs should be used in order to minimize drug resistance and all patients should receive a minimum of 12 months of treatment after sputum conversion. The new guidelines suggest using three times weekly rather than daily treatment in patients with mild/moderate non-cavitary, less progressive, susceptible disease, which has been shown to be better tolerated. Expert advice should be sought where possible to treat species and subspecies accordingly, reduce toxicity, improve adherence and reduce development of resistance. This is particularly true in cavitary, severe, resistant or treatment-refractory disease (those who remain culture positive after 6 months of guideline-based treatment). Table 2 summarizes management of the four main disease classes based on the 2020 ATS/ERS/ESCMID/ IDSA guidelines. The guidelines were established based on currently available evidence and expert opinion. More detail on individual drugs follows, drawing on recent publications where available[11].

Disease characteristics	Guideline-based treatment	Treatment duration
MAC		
Macrolide susceptible, non-cavitary, non-severe	Macrolide+ Ethambutol+ Rifamycin -Three times weekly	≥12 months after culture conversion
Macrolide susceptible, cavitary/ severe	Macrolide+ Ethambutol + Rifamycin + parenteral aminoglycoside Daily (except aminoglycoside may be given three times weekly)	
Refractory	Macrolide+ Ethambutol+ Rifamycin+ ALISDaily (except aminoglycoside maybe given three times weekly)	
Macrolides resistant	Clofazimine OR Moxifloxacin OR linezolid+ Ethambutol+ Rifamycin+ parenteral aminoglycoside Daily (except aminoglycoside may be given three times weekly)	
M. Kansasii		
Non cavitary	Macrolide or Isoniazid+ Ethambutol+ Rifamycin, Macrolide-containing regimen three times weekly or INH-containing regimen daily	≥12 months
Cavitary	Macrolide or Isoniazid+ Ethambutol+ Rifamycin Daily	
Severe	Macrolide or Isoniazid+ Ethambutol+ Rifamycin+ parenteral aminoglycosideDaily (except aminoglycoside maybe given three times weekly)	
Rifampicin resistance/ intolerant	Macrolide+ Ethambutol+ fluoroquinolone Daily	
M. Xenopi		
Non-cavitary	Macrolide OR fluoroquinolone+ Ethambutol+ RifamycinDaily	≥12 months after culture conversion
Cavitary/ severe	Macrolide OR fluoroquinolone+ Ethambutol+ Rifamycin+ parenteral aminoglycosideDaily (except aminoglycoside maybe given three times weekly)	
M. Abscessus		
No mutational/ inducible macrolide resistance	Intensive phase:One or two parenteral agents: Amikacin/ Imipenem or Cefoxitin/ Tigecycline+ two oral agents' Macrolide/Clofazimine/ linezolid.Continuation phase:Two oral/ inhaled agents: Macrolide/ Clofazimine / linezolid/ inhaled amikacin Daily (except aminoglycoside maybe given three times weekly)	2 to 3-month intensive phase then continuation totaling ≥12 months
Macrolide resistant	Intensive phaseTwo or three parenteral agents: Amikacin/ Imipenem or Cefoxitin/ tigecycline+ two or three oral agents: Macrolide/ Clofazimine/ linezolidContinuation phase Two or three oral agents: Macrolide/ Clofazimine/ linezolid/ inhaled Amikacin.	

Treatment of lymphadenitis:

Treatment based on a two-drug regimen of one macrolide combined with rifampin or ethambutol. Antibiotics are dosed daily and taken until the resolution of symptoms.

Surgical resection of infected lymph nodes and tissue is typically used in combination with antibiotic therapy with significantly increased cure rates.

Duration of treatment: In case of Mild infections duration are usually 2-4 months of treatment, while severe ones can require 6 months or even longer. But Specific type of atypical mycobacteria have varying levels of resistance to antibiotics and duration of treatment according to the resistance pattern.

Response to therapy: Regular monitoring is crucial to assess progress and adjust the treatment plan if needed.

Skin and soft tissue infection:

Skin and soft tissue infections are treated with combination antibiotic therapy with a variety of options available, including macrolides, doxycycline, fluoroquinolones, trimethoprim/sulfamethoxazole, cephalosporins, or linezolid.

Empiric therapies are adjusted once susceptibility testing yields results; however, combination antibiotic therapy is continued due to inducible antibiotic resistance.

Surgical debridement is required for infections that are extensive and associated with necrosis.

Duration of treatment: In case of Mild infections duration are usually 2-4 months of treatment, while severe ones can require 6 months or even longer. But Specific type of atypical mycobacteria have varying levels of resistance to antibiotics and duration of treatment according to the resistance pattern. In case of musculoskeletal infections treatment are usually continued for 6-12 months. Immunocompromised individuals also need longer treatment durations.

Response to therapy: Regular monitoring is crucial to assess progress and adjust the treatment plan if needed[13].

Conclusion:

Due to rising incidence of NTM in recent years, there is a need for extensive research. A differential diagnostic test is required to discriminate the contaminants and pathogenic NTM for treatment options and in case of mixed infection to distinguish TB. Now a days, A well-formulated guideline is burning need for our country.

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ORIGINAL ARTICLE

PATTERN AND OUTCOME OF PULMONARY AND EXTRA-PULMONARY TUBERCULOSIS IN CHILDREN: TWO YEARS STUDY OF A TERTIARY CARE HOSPITAL

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Abstract :

Background: *Bangladesh faces a significant tuberculosis burden, ranking among the highest globally. The country has a high incidence of both tuberculosis and drug-resistant tuberculosis, especially in densely populated urban areas and among marginalized populations. The objective of this study was to evaluate the pattern and outcome of pulmonary and extra-pulmonary tuberculosis in children.* ***Methods:*** *This was a descriptive type of study that was conducted in the Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh, from August 2021 to August 2023. A total of 280 diagnosed children of tuberculosis were enrolled purposively. Data were analyzed by using MS Office tools.* ***Results:*** *Among the participants, 51.1% (143) had pulmonary tuberculosis (PTB), while 48.9% (137) had extra-pulmonary tuberculosis (EPTB). Most patients were young girls aged 5-10 years. All presented with fever, followed by cough with sputum (51%), anorexia, and weight loss (51%). A history of TB contact was common. Of the participants, 185 (66%) completed treatment and were cured; 10 (3.6%) completed treatment but weren't cured; 14 (5%) were still undergoing treatment; 25 (8.9%) stopped treatment; 7 (2.5%) defaulted; 6 (2.1%) were lost to follow-up; and 3.8% died. The treatment success rate was 94.9%.* ***Conclusion****: Pulmonary tuberculosis (TB) is prevalent in pediatric patients, commonly presenting with fever and cough. Despite some discontinuing treatment, most are cured with appropriate antiTB drugs. The DOTS strategy is effective, showing no adverse effects from the drugs.*

Keywords: *Tuberculosis, Anti-tubercular therapy, Extrapulmonary TB, TB lymphadenitis, Gene X-pert ultra.*

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Introduction:

Tuberculosis (TB) remains a major global public health problem. According to the World Health Organization (WHO), 10 million people developed TB disease in 2017, including 1 million children under the age of 15 years.[1] Pediatric tuberculosis is currently diagnosed based on a history of contact, clinical symptoms, chest radiography, tuberculin skin testing (TST), and microbiological analysis. However, children with tuberculosis can have vague clinical symptoms and abnormalities on chest X-rays.[1] A precise diagnosis of pediatric tuberculosis is challenging. Sputum for acid-fast bacilli smear positivity occurs in less than 15% of patients, while mycobacterial culture yields range from 30% to 40%.[2,3]

Childhood TB accounts for around 9% of global cases, rising to 15% in low-income countries.[4] Unfortunately, TB control programs primarily focus on identifying

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highly infectious adult cases with sputum smear-positive results, leading to neglect of childhood TB due to diagnostic challenges and overestimation of the effectiveness of the BCG vaccine.[5] Additionally, TB diagnosis is more complicated in resource-poor settings like Bangladesh. Concerns have also arisen regarding TB among HIV-positive children. [6] Various studies from different countries have explored the epidemiology and clinical aspects of childhood TB, with clinical presentations and diagnostic methods influenced by the local TB and HIV situations. Diagnosis of childhood TB can be particularly challenging in resource-limited settings, such as Nepal, which has a high TB burden.[7] Obtaining sputum samples, especially in children under 7 years old, can be difficult, as they may not produce enough or good-quality samples for testing. Diagnosing active TB in children is more complex than in adults due to its less frequent presence of bacteria and differing symptoms.

In the absence of bacteriological confirmation, a triad of (1). close contact with an infectious index patient, (2). a positive tuberculin skin test (TST), and (3). the presence of suggestive abnormalities on a chest radiograph is used to diagnose childhood tuberculosis (TB).[8]

These criteria, however, have limited application in TB-endemic countries because case detection and contact tracing activities are not routine in national TB programs, transmission is not limited to the household, and most individuals become infected and TST-positive during childhood and adolescence.[9,10] As a result, this study was conducted to provide insights into the clinical and epidemiological characteristics of pediatric PTB and EPTB patients and the diagnostic procedures involved. The objective of this study was to investigate the prevalence of pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB), assess their clinical profiles and diagnostic methods, and observe the outcomes of anti-tubercular therapy up to 6 months after enrollment.

Methods :

It was a descriptive type of study. This study was conducted in the Department of Pediatrics at the Sir Salimullah Medical College Mitford Hospital (SSMCMH) Dhaka, Bangladesh, from August 2021 to August 2023. Ethical clearance for the study was obtained from the institutional ethical clearance committee of the mentioned hospital. After obtaining informed consent, participants were selected according to the inclusion and exclusion criteria of this study.

All children clinically suspected and newly diagnosed cases of tuberculosis and Children within the age of 12 years were included and the Children who do not fulfill the diagnostic criteria of TB were excluded in this study. A total of 280 children diagnosed with tuberculosis were enrolled, including both outpatients and inpatients.

A total of 280 diagnosed TB patients aged up to 12 years met the inclusion and exclusion criteria for this study. They were informed about the study's purpose and benefits. All consecutive children attending the outpatient department of SSMCMH with clinical symptoms suggestive of tuberculosis were investigated to confirm TB disease. After obtaining written informed consent, demographic data, detailed clinical history, family contact history, and physical examination results for each child were recorded. Complete blood count, Mantoux test, and chest X-ray were performed for all the children. Additional tests such as fine needle aspiration cytology (FNAC), ultrasound (USG) of the whole abdomen, chest and spine X-rays, lumbar puncture (LP), CT scan, MRI, and other necessary investigations were conducted based on diagnostic needs. Sputum and stool samples were tested for gene X-pert and gene X-pert Ultra as required. In some cases, gastric lavage was performed for acid-fast bacilli (AFB) staining and gene X-pert testing. Children attending the outpatient (OPD) and inpatient departments were evaluated and enrolled in the study. Of the 280 cases, 209 children came for follow-up at regular intervals: after one month, at two months, and just before the completion of six months of Anti-TB (ATB) treatment. Reminders were sent to the parents via mobile phone to ensure follow-up. All cases received Anti-TB treatment at the DOT Center in the hospital or another feasible treatment source. The information was entered into SPSS 23 for analysis.

Results:

Table 1 presents the sociodemographic statistics observed in our study. Out of 280 patients, the largest proportion (44.29%) were in the age range of 5 to 10 years. There were 86 patients (30.71%) older than 10 years, while 70 patients (25%) were younger than 5 years. Females comprised 153 cases (54.64%), and males comprised 127 cases (45.36%). Regarding socioeconomic status, 134 patients (47.86%) were from the middle class, 106 patients (37.86%) were from the low-income category, and 40 patients (14.28%) were from the upper class.

Table I

Socio-demographic data (n=280)

Variables	Frequency	Percentage
Age (Year)		
<5	70	25%
5-10	124	44.29%
11-12	86 Sex	30.71%
Male	127	45.36%
Female	153	54.64%
	Socio economic status	
Low	106	37.86%
Middle	134	47.86%
High	40	4.28%

Table II shows that all 280 individuals exhibited fever (100%). Among these, 143 (51.07%) experienced both cough with sputum and anorexia, which was subsequently accompanied by weight loss. Additionally, 30 cases (10.71%) presented with ascites, 21 (7.5%) experienced back discomfort, 8 (2.86%) reported shortness of breath, 3 (1.07%) exhibited confusion, and only 2 (0.71%) had headaches.

Table II

Presenting symptoms (n=280)

Presenting symptoms	n	%
Cough with sputum	143	51.07%
Anorexia and weight loss	143	51.07%
Fever	280	100%
Shortness of breath	8	2.86%
Back pain	21	7.50%
Headache	2	0.71%
Disorientation	3	1.07%
Ascites	30	10.71%

Figure 1 shows that the majority of our cases, specifically 143 (51.07%), were diagnosed with pulmonary TB, while the remaining 137 (48.93%) had extrapulmonary TB.

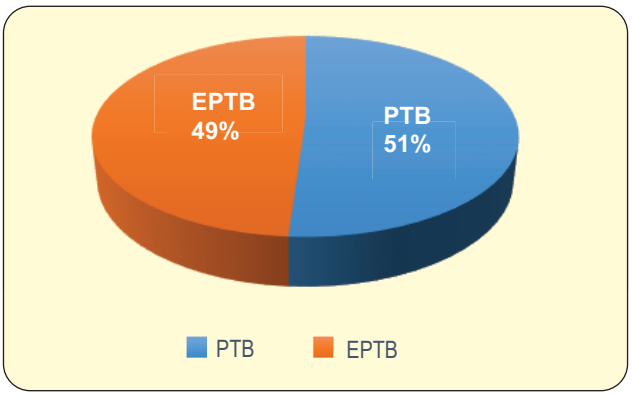

Fig.-1: Types of Tuberculosis(n=280)

Table III lists the various types of extrapulmonary tuberculosis. The majority of cases (44.52%) presented with TB lymphadenitis. This was followed by abdominal TB in 30 cases (21.90%), Pott's disease in 20 instances (14.60%), miliary TB in 17 cases (12.41%), tubercular pleural effusion in 8 cases (5.84%), and just 1 case (0.73%) of TB meningitis.

Table-III

Types of EPTB in our study cases (n=137)

Types of EPTB	Frequency	Percentage%
TB lymphadenitis	61	44.52%
TB meningitis	1	0.73%
TPE	8	5.84%
Pott's disease	20	14.60%
Abdominal TB	30	21.90%
Miliary TB	17	12.41%

TPE: Tubercular pleural effusion

Figure 2 shows that out of the total 280 cases, 267 (66.43%) had a confirmed history of contact with TB, while 33.57% had no confirmed history of contact with TB.

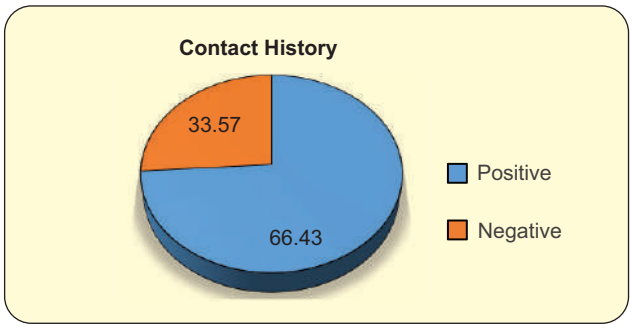

Fig.-2: *History of TB contact in our study cases (n=280)*

Figure 3 displays the initial clinical diagnosis of 156 patients (55.71%) and the bacteriological detection of TB in 124 patients (44.29%).

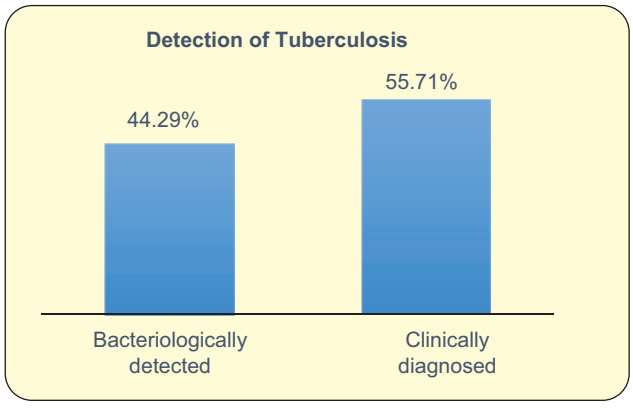

Fig.-3: *Initial detection of Tuberculosis in our study cases(n=280)*

Table III presents a comprehensive account of multiple investigations. A significant proportion of patients (23.57%) tested positive for the sputum GeneXpert test, while a slightly lower percentage (19.6%) had positive results for the MT test. Positive findings were also observed in the FNAC of different specimens, such as lymph nodes, in 20% of cases. Chest X-rays showed features suggestive of tuberculosis in another 20% of cases. A smaller percentage (12.14%) tested positive for the GeneXpert Ultra test. Positive findings in pleural fluid studies were observed in 2.86% of cases, while only 0.36% had positive findings in their CSF study.

Table IV

Different investigations in our study total percentages cases(n=280)

Variables	n	%
CBC with ESR	4	1.43%
Sputum for Gene X-pert	66	23.57%
MT	55	19.60%
Chest X-Ray P/A view	56	20%
FNAC & LN biopsy	56	20%
Gene x-pert Ultra	34	12.14%
CSF study	1	0.36%
Pleural fluid study	8	2.86%

Table V reflects the treatment outcomes of 280 TB patients. Out of these, 143 (51.1%) had pulmonary tuberculosis (PTB) and 137 (48.9%) had extrapulmonary tuberculosis (EPTB). Overall, 258 (92.1%) underwent treatment—133 (51.6%) with PTB and 127 (48.4%) with EPTB. Among these, 69.2% (99) of the PTB patients and 62.8% (86) of EPTB patients recovered after completing the treatment, representing an overall recovery rate of 66% (185). In terms of treatment results, 66% (185) of patients finished the course and were cured: 69.2% (99) of PTB and 62.8% (86) of EPTB. Meanwhile, 3.6% (10) of the total cases—3.5% (5) of PTB and 3.6% (5) of EPTB—completed the course but were not cured. A total of 7.9% (22) of patients did not receive any treatment: 7% (10) of PTB and 8.8% (12) of EPTB. Treatment was continued in 5% (14) of cases—0.7% (1) of PTB and 9.5% (13) of EPTB. Moreover, 8.9% (25) of patients discontinued treatment: 10.5% (15) of PTB and 7.3% (10) of EPTB. Notably, 2.5% (7) defaulted on their treatment—2.8% (4) of PTB and 2.2% (3) of EPTB. Additionally, 2.1% (6) were lost to follow-up—2.1% (3) of PTB and 2.2% (3) of EPTB. Unfortunately, 3.8% of patients passed away during the follow-up: 4.2% (6) of PTB and 3.6% (5) of EPTB. Among the TB patients who completed their treatment, the overall success rate was 94.9%—95.1% (99) for PTB and 94.5% (86) for EPTB.

Table V

Treatment outcomes of pulmonary TB and extra-pulmonary

TB cases Outcomes	Types of TB		
	Pulmonary (143) % (n)	Extra-pulmonary (137) % (n)	TB patients (280) % (n)
Treatment completed & cured	69.2% (99)	62.8% (86)	66% (185)
Treatment completed but failed	3.5% (5)	3.6% (5)	3.6% (10)
Treatment ongoing	0.7% (1)	9.5% (13)	5% (14)
Switch off	10.5% (15)	7.3% (10)	8.9% (25)
Defaulted	2.8% (4)	2.2% (3)	2.5% (7)
Lost to follow-up	2.1% (3)	2.2% (3)	2.1% (6)
Death	4.2% (6)	3.6% (5)	3.9% (11)
Treatment not received	7% (10)	8.8% (12)	7.9% (22)

Discussion:

Among our total participants, the highest percentage (44.29%) belonged to the age group of 5 to 10 years. In contrast, R Ksoo et al. found that most patients [11] were under 5 years of age, and Wang et al. reported the mean age of their patients as 9.11 ± 4.39 years.[12] Environmental differences or geographic location may account for these variations in findings. We found a nearly equal ratio of male to female participants, with a slightly higher number of females. However, other studies[12,13] have observed a dominance of male participants. Among our total participants, the largest proportion were from the middle-class category, with low-income cases accounting for nearly one-third. A separate study[14] revealed that a significant proportion of participants belonged to a low socioeconomic background. In our study, all participants experienced fever. Besides fever 'cough with sputum and anorexia with weight loss was also prevalent among the majority of the cases. Nearly similar frequencies of symptoms were observed in some other previous studies[12,13]. Among our total TB, the majority were diagnosed based on clinical evaluation, while 44% were identified through bacteriological testing. Our study revealed that most of our cases were diagnosed with pulmonary TB. However, extrapulmonary TB was the most common finding in other studies[15,16], even when their study

populations included children under 15 years old. Our study found that TB lymphadenitis was the most common presentation, followed by abdominal TB. In another Indian study[17], TB lymphadenitis was also found to be the prevalent form of extrapulmonary tuberculosis, which aligns with our research findings. Nearly one-fourth of our participants had cervical lymphadenopathy, while 8.76% had both abdomen and axillary lymphadenopathy. A recent study reported that peripheral tuberculous lymphadenitis can occur in the context of a primary infection, typically seen in young children and immunocompromised patients[18].It may also indicate the reactivation of a prior primary infection. Among our participants, 66% completed treatment and were cured; 3.6% completed treatment but weren't cured; and 3.8% died; the treatment success rate was 94.9%. In another study[19], out of 56 children whose treatment outcomes were recorded, 69.6% completed treatment, 28.5% were cured, and 1.7% experienced treatment failure. However, similar to our findings, Siamisang et al. reported a treatment success rate of 93.1% [20] in Botswana from 2008 to 2019. In Ethiopia, Weldegebreal et al. found a treatment success rate of 88.6% [21] from September 1, 2017, to January 30, 2018.

Conclusion:

Pulmonary tuberculosis (TB) is prevalent in pediatric patients, typically presenting with symptoms such as fever and cough. Although some patients may discontinue treatment prematurely, the majority achieve a cure with appropriate anti-TB drugs. The Directly Observed Treatment, Short-course (DOTS) strategy has proven effective, ensuring adherence and successful outcomes, without significant adverse effects from the medications.

Limitations of the study:

This study was conducted in a single center. One major limitation of the study was the smaller sample size, the number of children treated with conventional anti TB drugs was to allow for definitive conclusion about efficacy.

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 Sir Salimullah Medical College Mitford 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

CORRELATION OF THYROID FUNCTION TEST WITH SEVERITY OF LIVER DYSFUNCTION IN CIRRHOSIS OF LIVER

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Abstract

Background: *A normal function of both the thyroid gland and the liver is necessary to maintain normal thyroid hormone levels and action. This study aimed to find out the thyroid abnormalities in patients presenting with liver cirrhosis and also to look for any correlation between thyroid function test (TFT) abnormalities and severity of liver disease.* ***Methods:*** *This cross-sectional observational study was conducted at the department of Gastroenterology and department of Medicine in Sir Salimullah Medical College, Dhaka, for 12-months. A total of 328 patients with liver cirrhosis were included after written informed consent. A detailed history, thorough laboratory and physical examination were carried out in each patient. Severity of liver dysfunction was graded by using Child Pugh Scoring. Thyroid function test was done. Data were collected in separate case record form and analyzed by SPSS 24.0.* ***Results:*** *According to Child Pugh score 31.1% had disease severity score A, 24.1% had B and 44.8% had C. Mean FT3 level (fmol/l) significantly decreases (5.3±1.5 in class-A, 3.5±1.7 in class-B and 3±1.3 in class-C) and TSH level (µIU/ml) significantly increases (3.3±1.3 in class-A, 5.3±2.1 in class-B and 5.5±1.8 in class-C) with increases number of disease severity score ($p<0.05$).* ***Conclusion:*** *There is a negative and inverse correlation between decreasing FT3 with severity of liver cirrhosis as measured by child pugh score and a positive and direct correlation between increasing Serum TSH with severity of liver cirrhosis as measured by child pugh score. This suggests that thyroid function test can be used as a prognostic indicator in cirrhotic patient.*

Key words: *Thyroid function test, Thyroid function abnormalities, Liver dysfunction, Cirrhosis of liver, CTP score.*

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Introduction:

One of the main causes of illness and death worldwide is chronic liver disease (CLD). Alcohol intake, viral hepatitis, and nonalcoholic fatty liver disease are the avoidable causes.[1] The advanced stage of liver disease known as liver cirrhosis is marked by the formation of regenerating nodules, scarring, and histological changes to the hepatic tissue.[2] It accounted for 2.2% of deaths and 1.5% of disability-adjusted life years globally in 2016, ranking as the 11th and 15th main causes of death and morbidity, respectively.[3] Eight million people with chronic hepatitis B virus (HBV) and chronic hepatitis C virus (HCV) infections are estimated to reside in Bangladesh. "Compensated" and "decompensated" cirrhosis are the two forms that exist. Hepatic encephalopathy (HE), bleeding varices, ascites, jaundice, or cirrhosis worsened by one or more of these symptoms is known as decompensation. Hepatorenal syndrome, hyponatremia, and spontaneous bacterial peritonitis - all of which are indicative of decompensation. None of these characteristics apply to compensated cirrhosis patients.[4]

The thyroid gland produces two related hormones called triiodothyronine and thyroxine (T4) (T3). These hormones, which function through the thyroid hormone receptors α and β, are essential for cell differentiation during development and aid in preserving the adult's thermogenic and metabolic homeostasis.[5] Thyroid gland secretes T4 in excess of T3 by a factor of twenty. As the primary organ in the peripheral conversion of tetraiodothyronine (T4) to T3 by Type 1 deiodinase, the liver is involved in the metabolism of thyroid hormones. The primary enzyme, type I deiodinase, is derived from the liver and is responsible for 30–40% of the extrathyroidal synthesis of T3.[1] It can also convert T4 to T3 by both 5'-and 5-deiodination. In addition, the liver is involved in the manufacture of thyroid binding globulin, thyroid hormone conjugation, and thyroid hormone excretion. The THS are metabolized by the liver, which also controls their systemic endocrine effects. The liver is mainly responsible for the transportation, storage, activation, and metabolism of thyroid hormones. Impaired hepatic conversion of T4 to T3 is important in cirrhosis. Catalyzed by type-1 deiodinase, T4 is converted to T3. The liver is where this enzyme is mostly found. A decrease in serum T3 might, therefore, be explained by a presumed deficit of hepatic type 1-deiodinase activity. Impaired cellular absorption and hepatic deiodinization result in decreased T3 and T4 levels.[6]

Both the liver and the thyroid can be affected by thyroid disorders, liver illness affects the metabolism of thyroid hormones, and many systemic diseases impact both organs. Patients with subacute thyroiditis or hyperthyroidism may have abnormal liver function tests.[7] Thyroid hormones influence oxidative processes and the activity of enzymes that control lipogenesis, lipolysis, and other aspects of liver function. As a result, the thyroid and liver have a mutually beneficial interaction that influences other organ function.[8]

A study conducted in India in 2023, found a substantial inverse relationship between the severity of cirrhosis and the serum levels of FT3 and FT4.[6]

According to a different study in 2019, the severity of cirrhosis was significantly inversely correlated with the serum levels of FT3, and FT4.[9]

Another study in 2022, observed that TSH levels were directly correlated with the severity of liver disease.[1]

In a study conducted in Nepal in 2019, it was shown that there was a statistically significant correlation between the mean scores of FT3 and FT4 across the various CPS categories.[7]

A study in India in 2018 revealed that in patients with liver cirrhosis, mean levels of FT3, FT4, and TSH were significantly higher and mean levels of FT3 and FT4 were significantly lower, respectively, and that these levels also correlated with the severity of liver disease.[4] Higher Child Pugh ratings were linked to lower mean free T3 levels in patients in a different study trial, however there was no significant relationship found between free T4 and TSH levels.

According to a different also conducted in India in 2017, more severe liver injury is linked to low free T3 and T4 levels.[10]

The most common reason for low free T3 levels in liver disease is reduced Type I deiodinase, which causes peripheral T4 to T3 conversion to be reduced.[11]

The precise relationship between the degree of liver cirrhosis and thyroid function test has not yet been determined in our population.

Thyroid hormone function test study will help manage chronic liver disease by shedding light on the functional components of the disease and improving understanding of how thyroid function tests relate to chronic liver disease. The objective of our study was to determine the correlation between thyroid function test and severity of liver dysfunction in cirrhosis of liver.

Methods:

A hospital based cross-sectional observational study was conducted in the Department of Gastroenterology and Medicine at Sir Salimullah Medical College Mitford Hospital, Dhaka. Total 328 patients were aged between

18 to 70 years irrespective of sexes with clinical, biochemical, and or diagnostic imaging (ultrasonography, Upper GIT Endoscopy and fibroscan) evidence of liver cirrhosis who attended in both indoor and outdoor facilities of the department of Gastroenterology and Medicine of SSMC MH, also patients who were referred to department of Gastroenterology for endoscopy of upper GIT, EVL procedure and fibroscan between August 2022 to July 2023 were enrolled in this study by purposive sampling method. Patient with sepsis, cardiac failure, renal failure, nephrotic syndrome, any malignancy, any chronic disease(except liver cirrhosis), pregnancy, with prior history of thyroid disease (Any known documented thyroid disease or history suggestive of thyroid disease) or taking medication that may affect the activity and metabolism of thyroid hormones were excluded from this study. After selection of participants according to the inclusion and exclusion criteria, detailed history and physical examination, drug history were taken as per predesigned questionnaire. S.billirubin , prothrombin time with INR, S.Albumin, thyroid function test: TSH, FT3, FT4 were done in each patient. Severity of liver dysfunction was graded by using Child Pugh Scoring. According to Child Pugh Scoring, severity of liver cirrhosis was categorized as A, B, C group. All the data were collected in separate case record form by researcher himself.Prior to beginning analysis, the data were evaluated for accuracy, consistency, and completeness after collection. The data analysis was done with SPSS version 24. (IBM Corp., Armonk, NY). A level of P<0.05 was used to determine statistical significance. An analysis of exploratory data was done in order to characterize the study population. Categorical variables were summarized using frequency tables, while continuous variables were summarized using metrics of central tendency and dispersion such as mean, median, percentiles, and standard deviation. The chi-square method was used to evaluate categorical data. One way ANOVA test was used to compare the TFT level with CPS categories and Post-hoc test was done by Bonfrroni test whenever p-value was <0.05.

Results:

In this study, there were 328 participants who satisfied the selection criteria. Majority (62.2%) of the patients were aged between 41 to 60 years followed by 30.2% were above 60 years and 7.6% were 40 years or below. Mean age of the patients was 52.9±9.6 years.

Among all, 58.8% (n=193) of the patients were male and 41.2% (n=135) were female. According to Child Pugh score 31.1% had disease severity score A, 24.1% had B and 44.8% had C. Among all, 53.4% had Ascites, 25.9%v had Encephalopathy, 11% had Hematemesis, 9.8% had melena and 11% had jaundice which is shown in Table I.

Table-I

Distribution of the patients according to clinical parameter (n=328)

Clinical parameter	Frequency (n)	Percentage (%)
Encephalopathy	85	25.9
Ascites	175	53.4
Hematemesis	36	11
Melena	32	9.8
Jaundice	36	11

Multiple answers considered.

In Class A, 6% had FT3 level <3.5fmol/l and 94% had 3.5 to 8.56 fmol/l, in Class B, 46.8% had <3.5fmol/l and 53.2% 3.5 to 8.56 fmol/l and in Class C, 89.8% had <3.5fmol/l and 10.2% had 3.5 to 8.56 fmol/l. FT3 level significantly decreases with the increasing number of disease severity score which is depicted in Table II.

Table II

Distribution of the patients according to FT3 level in different stage of disease (n=328)

FT3 level (fmol/l)	Class A n(%)	Class B n(%)	Class C n(%)	p-value
<3.5	7 (6)	37 (46.8)	132 (89.8)	<0.001
3.5 to 8.56	95 (94)	42 (53.2)	15 (10.2)	

p-value was determined by* Chi-square test. within parenthesis percentage over column in total.

In Class A, 7% (n=7) had FT3 level <3.5fmol/l and 93% (n=95) had 3.5 to 8.56 fmol/l, in Class B, 46.8% (n=37) had <3.5fmol/l and 53.2% (n=42) 3.5 to 8.56 fmol/l and in Class C 80.8% (n=132) had <3.5fmol/l and 10.2% (n=15) had 3.5 to 8.56 fmol/l. FT3 level significantly decreases with the increasing number of disease severity score.

In Class A, 26.5% had FT4 level <8.5fmol/l and 73.5% had 8.56 to 25.6 fmol/l, in Class B, 25.3% had <8.5fmol/l and 74.7% had 8.56 to 25.6 fmol/l and in Class C, 37.4% had <8.5fmol/l and 62.6%had 8.56 to 25.6 fmol/l. FT4 level decreases with the increasing number of disease severity score but these finding was statistically insignificant (Table III).

Table-III

Distribution of the patients according to FT4 level in different stage of disease (n=328)

FT4 level (fmol/l)	Class A n(%)	Class B n(%)	Class C n(%)	p-value
<8.56	27(26.5)	20(25.3)	55(37.4)	0.083
8.56 to 25.6	75(73.5)	59(74.7)	92(62.6)	

p-value was determined by* Chi-square test. within parenthesis percentage over column in total.

In Class A, 26.5% (n=27) had FT4 level <8.5fmol/l and 73.5% (n=75) had 8.56 to 25.6 fmol/l, in Class B, 25.3% (n=20) had <8.5fmol/l and 74.7% (n=59) had 8.56 to 25.6 fmol/l and in Class C, 37.4% (n=55) had <8.5fmol/l and 62.6% (n=92) had 8.56 to 25.6 fmol/l. FT4 level decreases with the increasing number of disease severity score but these finding was statistically insignificant.

In Class A, 88.2% had TSH level 0.3 to 5 μIU/ml and 11.8% had >5 μIU/ml, in Class B, 59.5% had 0.3 to 5 μIU/ml and 40.5% had >5 μIU/ml and in Class C, 69% had 0.3 to 5 μIU/ml and 53% had >5 μIU/ml. TSH level significantly increases with the increasing number of disease severity score (Table IV).

Table-IV

Distribution of the patients according to TSH level in different stage of disease (n=328)

TSH level (μIU/ml)	Class A n(%)	Class B n(%)	Class C n(%)	p-value
0.3 to 5	90(88.2)	47(59.5)	69(47)	<0.001
>5	12(11.8)	32(40.5)	78(53)	

p-value was determined by* Chi-square test. within parenthesis percentage over column in total.

In Class A, 88.2% (n=90) had TSH level 0.3 to 5 μIU/ml and 11.8% (n=12) had >5 μIU/ml, in Class B, 59.5% (n=47) had 0.3 to 5 μIU/ml and 40.5% (n=32) had >5 μIU/ml and in Class C, 69% (n=47) had 0.3 to 5 μIU/ml and 53% (n=78) had >5 μIU/ml. TSH level significantly increases with the increasing number of disease severity score.

Mean FT3 level significantly decreases and TSH level significantly increases with increases number of disease severity score. (Table V).

Table-V

Association of thyroid function test with severity of liver function test (n=328)

Thyroid function test	Class A Mean±SD	Class B Mean±SD	Class C Mean±SD	p-value
FT3 level (3.5-8.56fmol/l)	5.3±1.5	3.5±1.7$^{\alpha}$	3±1.3$^{\alpha}$	<0.01
FT4 level (8.56-25.6fmol/l)	10±2.2	9.6±-2.1	9.4±2.5	0.192
TSH level (.3-5μIU/ml)	3.3±1.3	5.3±2.1$^{\beta}$	5.5±1.8$^{\beta}$	<0.01

Serum bilirubin level and prothrombin time were significantly increased and albumin level significantly decreases with increasing severity of disease. (Table VI).

Table-VI

Association of Biochemical marker with severity of liver function test (n=328)

Biochemical marker	Class A Mean±SD	Class B Mean±SD	Class C Mean±SD	p-value
Serum bilirubin (mg/dl)	1.4±0.3	1.7±0.2	2.2±1.4$^{\alpha\beta}$	0.006
Serum albumin (mg/dl)	3.5±0.8	3.1±-0.4	2.9±0.6$^{\$\#}$	<0.01
Prothrombin time (sec)	12±2	19±2	22±3$^{\gamma}$	<0.01

p-value was determined by Post-Hoc analysis of Bonferroni by One Way ANOVA test.
$^{\alpha}$denotes significant difference between Class A vs Class C regarding serum bilirubin level.
$^{\beta}$denotes significant difference between Class B vs Class C regarding serum bilirubin level.
$^{\$}$denotes significant difference between Class A vs Class B and Class C regarding serum albumin level.
$^{\#}$denotes significant difference between Class B vs Class C regarding serum albumin level.
$^{\gamma}$denotes significant difference between Class A vs Class C regarding prothrombin time.

Discussion:

A total of 328 patients with cirrhosis of liver was enrolled in our study. In our study, Mean age of the patients was 52.9±9.6 years with 62.2% were aged between 41 to 60 years.

A previous study in India had the mean age of 43 ± 14 years among the patients.[4] Another study also revealed that 63% of the patients were aged between 41 to 60 years.[1]

In our study, Male predominant was observed among the patients with 58.8% which was consistent with the previous study where, 71% were male.

The majority of the patients that were enrolled in the previously mentioned study trial were men. Another study conducted in Bangladesh also revealed that cirrhosis of liver is more common in male than female patient.[10]

In our study, According to Child-Pugh score majority (44.8%) of the patients were in class C followed by 31.1% were in class A and 24.1% were in class B. According to the study most of the patients presented in advanced stage with decompensated liver cirrhosis.

In a study based on the Child Pugh score, class A included 15% patients, class B included 26%, and class C included 59% patients.[10] A study conducted in India revealed that patients were classified according to Child Pugh scoring according to which 24% cases were Child A and 45% cases were Child B and 31% cases were Child C.[1]

In our study, class B was found relatively low due to a smaller number of patients was admitted in the hospital in this stage during the study period.

Among all, 53.4% had Ascites, 25.9% had Encephalopathy, 11% had Hematemesis, 11% had jaundice and 9.8% had Melena.

According to a research in Bangladesh, the majority of patients (49.4%) had ascites, which was followed by peripheral edema (24.7%), gastrointestinal hemorrhage (27%), encephalopathy (21.3%), and jaundice (3.4%).[13] A study conducted in Sweden revealed that out of 1317 patients of cirrhosis, ascites was present in 43% cases followed by variceal bleeding in 6% and overt encephalopathy in 4% cases.[14]

In our study, it was shown that as the severity of liver disease increases from Child Pugh grade A to C, the percentage of patients , having decreased level of serum FT3 and FT4 level increased and raised TSH level also increased . FT3 and TSH level showed statistically significant.

A previously mentioned study conducted in India in 2023, revealed that there was significant inverse correlation between serum level of FT3 and FT4 with severity of cirrhosis is very much similar to our study, where FT3 level decreased in 4% of patients who were categorized in CPS A, 91% in CPS B, 92%% in CPS C. FT4 level decreased in 9.3% of patients who were categorized in CPS A, 33.3% in CPS B, 57.4% in CPS C and S.TSH increased in 10% of patients who were categorized in CPS A,31% in CPS B,58.2% in CPS C.[6]

A study conducted in 2019, revealed that there was significant inverse correlation between serum level of FT3, and FT4 with severity of cirrhosis[9] is similar to our study, where FT3 level decreased in 26% of patients who were categorized in CPS A, 52% in CPS B,84.6% in CPS C .S.TSH increased in 15% of patients who were categorized in CPS A,69% in CPS B,88% in CPS C.

An already mentioned study in India found that TSH levels were inversely correlated with the severity of liver disease, with increased levels of S. TSH seen in 12.5 percent of CPS A cases, 77 percent of CPS B cases, and 83.8 percent of CPS C cases (p-.01). Additionally, FT3 was low in the majority of CPS B (75.5 percent) and CPS C (96.78 percent) cases. There was no statistically significant correlation with FT4.[1] These findings are very much similar to our study.

In our study, we found that, mean FT3 level was significantly decreased and mean S.TSH significantly increased with increases number of diseases severity score from CPS A-C.

In the previously mentioned study conducted in Nepal in 2019, according to Child Pugh score (CPS) 56.36% patients were in Class C, 31.82% patients were in Class B. Correlation between different CPS categories was found to be statistically significant with the mean score of FT3 and mean score of FT4.[7] On the contrary, in our study, mean FT4 level was not significant.

A previous study suggested that mean FT3 and FT4 levels were significantly decreased and mean TSH levels were significantly increased in liver cirrhosis patients and level of FT3, FT4, and TSH also correlate with the severity of liver disease. Most common abnormality seen was low FT3(71%),low FT4(21%),high TSH(20%).[4]

In a different research, higher Child Pugh scores were shown to be associated with lower mean free T3 levels but there was no such statistical correlation between free T4 and TSH levels.[10] On the contrary, in our study we found statistically significant correlation between S.TSH and severity of cirrhosis.

According to a study already mentioned, more severe liver injury is linked to low free T3 and T4 levels. The most prevalent explanation for the low free T3 levels

in liver illness is that there is less Type I deiodinase present, which results in less peripheral T4 to T3 conversion.[15]

Conclusion:

This study assessed the correlation between thyroid function test (TFT) abnormalities and severity of liver disease.FT3 level is inversely correlated with severity of cirrhosis (Low FT3 level is associated with more severe disease), S.TSH level is directly correlated (High TSH is associated with more severe disease). Data from this study depicted that mean FT3 level significantly decreases and TSH significantly increases with the increasing disease severity by Child Pugh score, making it a possible biomarker that is associated with disease severity and help identify patients with worse prognosis.

Limitations of the study:

This study was conducted in a single center study. One major limitation of the study was the smaller sample size.

Ethical Approval:

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Institutional Review Board of the Sir Salimullah Medical College Mitford Hospital (Ref: 59.14.1100.031.18.001.23.135). Written informed consent was taken from all the patients before taking part of the study.

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None.

Conflict of Interest:

No author has any conflict of interest to disclose for this manuscript. The authors themselves are responsible for their ideas and views expressed in this article, which do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated.

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ORIGINAL ARTICLE

CLINICAL PROFILE, ETIOLOGY AND IN-HOSPITAL OUTCOME OF ACUTE PANCREATITIS: EXPERIENCE AT A TERTIARY CARE CENTER, BANGLADESH

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Abstract:

Background: *Acute pancreatitis (AP) is a potentially life-threatening disease with varying clinical presentations influenced by etiology, social factors, cultural habits, and patient characteristics.* ***Aim:*** *To assess the demographic profile, etiology and in-hospital outcomes of Acute pancreatitis patients.* ***Methods:*** *This prospective observational study was conducted in Department of Medicine, Sir Salimullah Medical College Mitford Hospital, Dhaka from January 2023 to December 2023 after obtaining ethical clearance from ethical review board. We enrolled 107 AP patients diagnosed according to the revised Atlanta classification (2012). Demographics, clinical presentations, risk factors, laboratory data, and imaging findings were collected using a structured questionnaire. All the data were compiled and sorted properly and analyzed by using IBM SPSS, Version 26.0. Results: The mean age was 52.09±14.94 years, with male predominance (66.4%). In this study we found common presentations are abdominal pain (100%), nausea/vomiting (91.6%), and abdominal distension (44.9%). Our study revealed, main etiologies were alcohol consumption (35.5%) and gallstones (34.6%). We observed common comorbidities included diabetes mellitus (42.1%) and hypertension (35.5%). The mean hospital stay was 6.77±1.51 days. Most patients (77.6%) achieved good recovery, while 22.4% had partial recovery. Only 3.7% required ICU care, with no mortality reported.* ***Conclusion:*** *In our study, acute pancreatitis predominantly affected middle-aged males, with alcohol and gallstones being the leading causes. Most patients had good outcomes with conservative management, suggesting effective treatment protocols was follows at our center.*

Kew words: *Acute pancreatitis (AP), Clinical Profile, Etiology, In-hospital outcome*

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Introduction:

Acute pancreatitis (AP) is an acute inflammation of the pancreas due to auto digestion of the gland by pancreatic digestive enzymes, leading to morphologic changes and impairment of function. It is a reversible process.[1,2] Men are affected more than women. The incidence of acute pancreatitis varies from 5.4 to 79.8 per 1,00,000 population and it carries an overall mortality rate of 10 – 15%.[3,4]

AP is a potentially life-threatening disease with variable presentation. All patients presented with abdominal pain. Pain is mostly in the epigastrium, severe,

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constant and may radiate to the back. Pain starts at 12-48 hours after a large meal or after a bout of alcohol. Nausea, vomiting, jaundice, tachycardia, epigastric tenderness, hypoactive or absent bowel sounds, raised serum amylase, serum lipase, fever and abdominal distensions are the other features. Grey Turner's sign and Cullen's signs are present in about 1 to 3% patients due to hemorrhage in peripancreatic area and indicate severe episode of acute pancreatitis.[5]

Alcohol, gallstones, hypertriglyceridemia, diabetes, obesity, smoking, post ERCP, pancreatic ductal obstruction, trauma, infectious agents and drugs are the causes of acute pancreatitis in many countries. Gallstones are responsible for 50 to 60%, alcohol 8 to 32%, hypertriglyceridemia and drug induced 2–5% cases of acute pancreatitis. About 10-25% of acute pancreatitis cases appear to have no discernible cause but often turn out to be caused by autoimmunity and genetic mutations.[5-8]

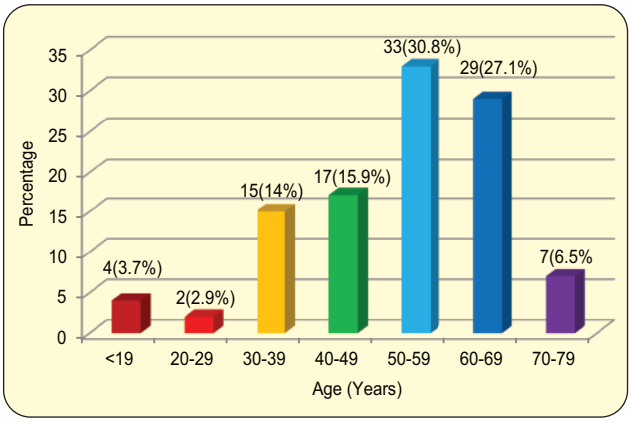
Symptoms of acute pancreatitis vary considerably according to its etiology, social, cultural habit and general physical condition of patients. Early diagnosis of acute pancreatitis has a crucial impact on treatment strategy but the early and effective detection of severe disease is very much challenging. If the cause of the occurrence can be eradicated there will be no further attack and the pancreas will come back to normal[9].In our country, limited data exists regarding the disease pattern, severity trends, and outcomes of AP. This study aims to bridge this knowledge gap by examining the demographic profile, etiology, and in-hospital outcomes of AP patients in a tertiary care setting.

Methods:

We conducted a prospective observational study at the Department of Medicine, Sir Salimullah Medical College Mitford Hospital, Dhaka, from January to December 2023.We enrolled 107 patients diagnosed with AP based on the revised Atlanta classification (2012). Exclusion criteria included chronic pancreatitis, relapsing pancreatitis, pancreatic malignancy, diabetic ketoacidosis, chronic kidney disease, hepatic encephalopathy, and chronic liver disease. After taking ethical clearance and informed consent, we collected data using a structured questionnaire. Information included demographic details, clinical presentations, risk factors, laboratory findings, and imaging results.All the data were compiled and sorted properly. Then data analysis was performed using IBM SPSS Statistics Version 26.0. Quantitative data were presented as mean ± SD, while qualitative data were expressed as frequencies and percentages.

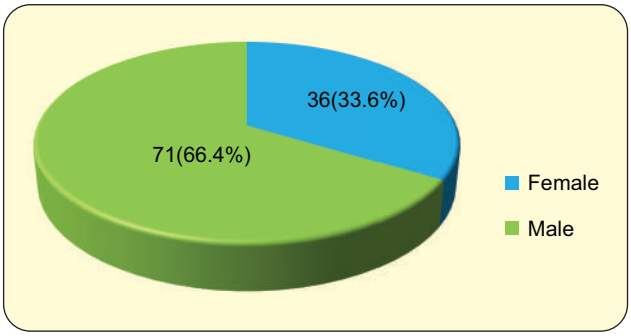
Results:

In this study, the mean age of participants was 52.09±14.94 years, with the majority (30.8%) in the 50-59 age group (Figure-1). About males comprised 66.4% of the study population. (Figure-2). We found Most patients (65.4%) were from urban areas and 37 (34.6%) patients came from rural area. 13 (12.1%) respondents were illiterate, 37 (34.6%) were completed primary education, 18 (16.8%) were completed secondary education, 20 (18.7%) were passed SSC, 18 (16.8%) completed their HSC and only 1 (0.9%) was graduate. They were service holder (26; 24.3%), businessmen (4; 3.7%), house wife (18; 16.8%), driver (33; 30.8%) and others (16; 15.0%) in their occupation. Maximum (54; 50.5%) study subjects belonged to lower income family (Table-I). All patients (100%) presented with abdominal pain, followed by nausea/vomiting (91.6%) and abdominal distention (44.9%) (Table-II). Our study revealed, the predominant causes were alcohol consumption (35.5%) and gallstones (34.6%), followed by dyslipidemia (11.2%) (Table-III). We observe that Common comorbidities included diabetes mellitus (42.1%), hypertension (35.5%), ischemic heart disease (8.4%), and chronic kidney disease (6.5%). (Figure-3). The mean hospital stay was 6.77±1.51 days. Complete recovery was achieved in 77.6% of patients, while 22.4% had partial recovery. Only 3.7% required ICU care, and no mortality was observed (Table-IV).



Data were expressed as frequency and percentage

Fig.-1: *Distribution of study subject according to age (N=107)*



Data were expressed as frequency and percentage

Fig.-2: *Distribution of study subject according to gender (N=107)*

Table-I

Socioeconomic characteristics of study subjects (N=107)

Socioeconomic Characteristics	Frequency	Percentage
Dwelling	37	34.6
Rural		
Urban	70	65.4
Educational status		
Illiterate	13	12.1
Primary	37	34.6
Secondary	18	16.8
SSC	20	18.7
HSC and above	19	17.8
Occupational status		
Unemployed	10	9.4
Service	26	24.3
Business	4	3.7
House wife	18	16.8
Driver	33	30.8
Others	16	15
Socioeconomic status		
Lower income	54	50.5
Lower-middle	47	43.9
Upper-middle	6	5.6

Data were expressed as frequency and percentage

Table II

Distribution of study subject according to presenting complaints (N=107)

Presenting complaints	Frequency	Percentage
Abdominal pain	107	100.0
Nausea/vomiting	98	91.6
Abdominal distention	48	44.9
Others	17	15.9

Data were expressed as frequency and percentage. Multiple response was present

Table III

Distribution of study subject according to etiology (N=107)

Etiology	Frequency	Percentage
Alcohol	38	35.5
Gall stone	37	34.6
Dyslipidemia	12	11.2
Others	20	18.7

Data were expressed as frequency and percentage

Data were expressed as frequency and percentage. Multiple response was present

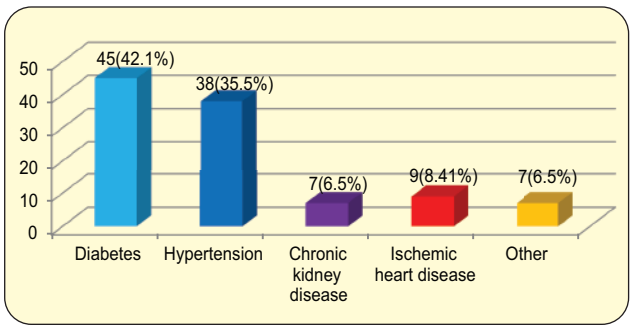


Fig.-3: *Distribution of study subject according to comorbidities (N=107)*

Table IV

Distribution of the study subjects according to in-hospital outcome (N=107)

Outcome	Frequency/ Mean±SD	Percentage
Length of hospital stay (day)	6.77±1.51	
Complete recovery	83	77.6
Partial recovery with complication	24	22.4
Transfer to ICU	4	3.7
Death	0	0

Data were expressed as frequency, percentage, Mean ± SD

Discussion:

Early diagnosis is important goals in the preliminary management of acute pancreatitis. Due to the risk of rapid worsening in severe acute pancreatitis, the assessment of severity becomes crucial to a clinician. Our findings demonstrate that AP predominantly affects middle-aged males in our population, consistent with previous studies by Szakács et al.[11] Baeza-Zapata et al.[12] and Carvalho et al.[13] The male predominance may be attributed to higher alcohol consumption among men, as suggested by Zhang et al.[14] Drake et al.[15] stated that rates of acute pancreatitis were similar in both sexes but chronic pancreatitis is more common in males.

Current study found that 65.4% patients hailing from urban area and 34.6% patients came from rural area. Sardana et al.[16] found similar findings. Fan et al.[17] showed hospitalization was increased annually both in urban and rural areas and the increasing rate in the rural area was much higher might be attributed to the huge floating population in the working age. Most of the floating population reside in the sub-urban area due to the rented accommodation costs and cheaper living.

Socioeconomic factors, including education and income levels, showed significant associations with AP occurrence, supporting observations by Mao et al.[18], Sardana et al.[16] and Roberts et al.[19]

In concurrent study, our respondents were presented with abdominal pain followed by, nausea/vomiting and abdominal distention. The clinical presentation pattern in our study matches previous reports by Manjunath et al.[20] and Karim et al.[21], with abdominal pain being the universal presenting symptom (100%).

In this study, alcohol (35.5%), gall stone (34.6%), dyslipidemia (11.2%) and others (18.7%) were common aetiologies. A comparable finding was observed by Vengadakrishnan and Koushik[22] and Manjunath et al.[20]. Samokhvalov et al.[23] reported that cigarette smoking and alcohol abuse are complicating factors in acute pancreatitis. Roberts et al.[19] described that acute pancreatitis was significantly found more (48%) during the Christmas and New Year weeks.

We observed in our study population, comorbidities played a significant role, with diabetes mellitus being the most prevalent (42.1%), followed by hypertension (35.5%), ischemic heart disease (8.4%), and chronic kidney disease (6.5%). This comorbidity profile aligns with findings from Vengadakrishnan and Koushik[22] and Manjunath et al.[20], though our diabetes prevalence was notably higher. Regular assessment of these comorbid conditions likely contributed to the favorable outcomes observed in our study.

In our study demonstrated generally favorable results, with a mean hospital stay of 6.77±1.51 days, which is notably shorter than previous studies such as Karim et al.[21] who reported 9-13 days for mild pancreatitis and 13.5-18 days for severe cases.

The duration of hospital stay was significantly higher in patients with severe acute pancreatitis probably due to tissue damage by inflammation.[21] Most patients (77.6%) achieved complete recovery, while 22.4% were discharged with partial recovery. Only 3.7% of cases required ICU care, and no mortality was observed. Karim et al. [21] showed that 38.71% patients developed complication and 61.29% patients were discharged with complete recovery. Another study by Manjunath et al.[20] showed 8% died and 10% were discharged against medical advice.

Conclusion

In current study revealed, acute pancreatitis predominantly affected middle-aged males, with alcohol (35.5%) and gallstones (34.6%) as primary etiologies. Despite high comorbidity rates, outcomes were favorable with 77.6% complete recovery, short hospital stays (mean 6.77 days), and no mortality. These findings demonstrate effective management of AP in our setting. Due to demographic similarities, our findings might represent the status of whole communities of our country in general. This will help in formulating a hospital strategy which would be beneficial.

Limitations:

Single-center and the relatively short study duration may limit validity. Future multi-center studies with longer follow-up periods would provide more comprehensive insights.

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 Sir Salimullah Medical College Mitford Hospital (SSMCMH) 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

GASTROINTESTINAL MANIFESTATIONS AND LABORATORY PARAMETERS OF DENGUE PATIENT IN A DENGUE CORNER AT A SPECIALIZED HOSPITAL, BANGLADESH

PARASH ULLAH[1], SHAMIM ARA KEYA[2], FAZLE RABBI CHOWDHURY[3], FARHANA SALAM[4]

Abstract:

Background: *Dengue is an important tropical infection caused by Dengue virus and its epidemics are becoming more frequent over the time. Gastrointestinal (GI) manifestation is one of the most common manifestations and mostly missed due to lack of awareness and knowledge. This study was conducted to find out the gastrointestinal manifestations, laboratory parameters and its correlation with the severity of dengue fever.* ***Methods:*** *It was a cross-sectional observational study, conducted on 100 serologically confirmed dengue virus infected patients admitted in DNCC Dedicated Covid-19 Hospital. Patients were examined clinically, and laboratory data was collected in respect of GI manifestations. Statistical analysis was done using SPSS software version 25.* ***Results:*** *The study participants were 100 consecutive cases of dengue syndrome, out of which 38% cases were dengue fever (DF), 12% were Dengue haemorrhagic fever (DHF), 22% were Dengue Shock syndrome (DSS) and 28% were Dengue expanded syndrome (DES). Mean age was 29.66 ± 19.69 years and age range were from 03 to 85 years, 62% were males and 38% were females, male to female ratio was1.6:1, and 44% patients were from Dhaka city. Gastrointestinal manifestations were anorexia 92%, nausea 90% & abdominal pain and vomiting were 84% followed by diarrhoea 56%. GI bleeding manifesting were 38%, among them, hematemesis, melena and gum bleeding were found 14%, 26% and 16% respectively. Others manifestations like ascites, hepatomegaly, acalculous cholecystitis and jaundice were found 52%, 26%, 42% and 10% respectively. Of these, GI manifestations diarrhoea correlated with severity of Dengue fever.* ***Conclusion:*** *Gastrointestinal manifestations are very common in Dengue fever. Atypical Gastrointestinal manifestations should be handled very cautiously.*

Keywords: *Dengue fever, Gastrointestinal Manifestations, Liver Enzymes, Hepatomegaly, Dengue severity.*

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Introduction:

The origin of the word dengue is not exactly clear, but there is a theory that it derived from the Swahili phrase "Ka-dinga pepo", meaning "cramp-like seizure caused by an evil spirit". The Swahili word "dinga" may possibly origin in the Spanish word "dengue" meaning fastidious or careful, which would describe the gait of a person suffering the bone pain of dengue fever.[1]

The first record of a case of probable dengue fever is in a Chinese medical encyclopaedia from the Jin Dynasty (265–420 AD). The first recognized Dengue epidemics

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occurred almost simultaneously in Asia, Africa, and North America in the 1780s. The first confirmed case report dates from 1789 and is by Benjamin Rush, who coined the term "breakbone fever" because of the symptoms of myalgia and arthralgia.[1]

Dengue is one of the most common and widespread arthropod mediated viral infection. It is caused by flavivirus and spread by the Aedes aegypti mosquito. More than 2.5 billion people reside in the risky areas for dengue infection in the world.[2] In Asia, Dengue has appeared as an important public health issue since 1950. Worldwide South East Asian countries contribute more than half of dengue global risk. Bangladesh, India, Pakistan, and Sri Lanka are the most vulnerable counties among them.[3,4]

Bangladesh is situated in the tropical and sub-tropical areas have become a suitable habitat for the dengue infections. Dengue occurs in sporadically at Dhaka and other parts of the country before 2000.[2] Dengue outbreaks from 2000-2017, both types of the vectors (*Aedes aegypti* and *Aedes albopictus*) were identified in Bangladesh.[5]

Dengue fever has a wide range of clinical manifestations and range from an asymptomatic or mild febrile illness (viral syndrome), dengue fever (DF), dengue haemorrhagic fever (DHF) to dengue shock syndrome (DSS) and atypical manifestations or Expanded Dengue Syndrome (EDS) like hepatitis and gastrointestinal involvement which could be challenging for clinicians.[6,7] Atypical gastrointestinal manifestations like hepatitis, acute pancreatitis, acute cholecystitis etc. are increased with rising disease burden due to rapid urbanization, growing population and inappropriate sanitary measures.[7,8,9]

Hasan et al. (2021), in a study found the gastrointestinal (GIT) features as abdominal pain (86.5%), anorexia and/or vomiting (69.6%), and Diarrhoea (26.2%) and these findings were more frequent than typical rash and other pain symptoms. Compared to outbreaks of 2008, 2016, and 2018, increasing trends in GIT symptoms e.g. anorexia, abdominal pain, and diarrhoea were observed. While a negative trend in haemorrhagic manifestations (skin rash, melena, and conjunctival haemorrhage/ haemorrhagic sclera) and arthralgia/ joint pain were found.[10] So, this study is aimed to identify the recent spectrum of gastrointestinal symptoms, signs and laboratory parameters of dengue patients in our settings.

Methods:

This was a descriptive cross-sectional study conducted in DNCC Dedicated Covid-19 Hospital (Dengue corner), Mohakhali, Dhaka, Bangladesh during the period from August 2023 to January, 2024. All the patients presented with serologically positive dengue cases and fulfilling the inclusion criteria were selected as the study population. In this study, we enrolled around 100 cases within speculated time. Non-randomized purposive sampling was employed as sampling technique and a predesigned structured questionnaire was used for data collection. Patients of any age irrespective of sex and patients with dengue syndrome, NS1 or IgM positive with or without IgG positive. Patients with Malaria. meningitis and Enteric fever and other causes of fever except dengue, decompensated chronic liver disease, acute pancreatitis or cholangitis, cholelithiasis or cholecystectomy, previously diagnosed bleeding disorder were excluded

Following admission in the DNCC Dedicated Covid-19 Hospital (dengue corner), patients was sort out according to inclusion and exclusion criteria. All the patients were counselled regarding the study aim, objectives, and usefulness of the study. Written informed consent was collected from each patient and interviews were taken by the researcher himself with a structured questionnaire. History regarding demographic profile, co-morbid disease and clinical presentation, gastrointestinal manifestations were taken. Patients were followed up daily during their hospital stay and their clinical and laboratory parameters were collected. The most extreme (highest or lowest) laboratory parameters were taken for analysis.

During data collection, highest standard ethical measures were ensured and maintained throughout the study. Following data collection, it was checked and verified. Collected data were encoded and analysed in SPSS software 25 for windows 7. It was described and presented as mean ± standard deviation. Frequencies and percentages were calculated for gender, disease nature (DF, DHF, DSS, EDS), dengue serology, gastrointestinal symptoms, and atypical GI manifestations. Test of significance was applied for GI manifestations to find out any relationship with the severity of dengue infection. A P value of <0.05 was considered as statistically significant.

Results:

Table I

Demographic profile of study population (n=100)

Variables	n (%)	
Age	Range (years)	03-85 (years)
	Mean ± SD	29.66 ± 19.69
Sex	Male	62 (62%)
	Female	38 (38%)
Residence	Dhaka city	44 (44%)
	Outside of Dhaka City	56 (56%)
Clinical manifestations	Dengue fever (DF)	38 (38%)
	Dengue haemorrhagic fever (DHF)	12 (12%)
	Dengue Shock syndrome (DSS)	22 (22%)
	Dengue expanded syndrome (DES).	28 (28%)
Severity of Dengue syndrome	Non severe dengue	38 (38%)
	Severe dengue	62 (62%)

Table I shows the demographic profile of study population. The mean age was 29.66 ± 19.69 years. 62% were males and male to female ratio was 1.6:1. 44% patients were from Dhaka city and 56% came from outside of Dhaka city. Severe Dengue was 62%, among them, 12(12%) were Dengue Haemorrhagic Fever (DHF) and 22(22%) were Dengue Shock Syndrome (DSS) and the rest 28 (28%) were Dengue Expanded Syndrome (DES).

Table II

Diagnosis of dengue cases (n=100)

Test	Positive	Negative	Not detected
NS1	86	8	6
IgM	20	54	26
IgG	10	64	26
IgM +IgG	10		

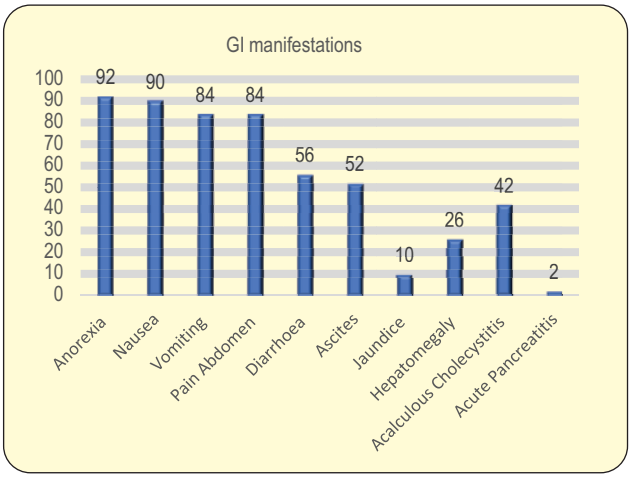

Fig.- 1: *Distribution of various GI manifestations in Dengue fever (n=100)*

Table II shows the diagnostic tools for Dengue patients. Most of the patients were NS1 (86%) positive, followed by anti-dengue IgM antibody positive 20%. 10% patients had both IgM and IgG positive.

Most common gastrointestinal presentation were anorexia 92%, nausea 90%, Vomiting and abdominal pain were 84%, followed by diarrhoea 56%. Ascites, jaundice, hepatomegaly and acalculus cholecystitis were noted in 52%, 10%, 263% and 42% respectively. Acute Pancreatitis was found in 02 cases.

Table III

Gastrointestinal bleeding manifesting among the study population

Manifestations		Percentage
GI bleeding	Hematemesis	14 (14%)
manifesting	Melena	20(20%)
38 (38%)	Gum Bleeding	16 (16%)
	Per Rectal bleeding	12 (12%)

GI bleeding was found in 38% cases. Among bleeding manifesting, hematemesis, melena, gum bleeding and per rectal bleeding were found in 14%, 20%, 16% and 12% patients respectively. Most of the bleeding manifestations were overlapped with each other.

Table IV

GI manifestations and laboratory parameters with severity of dengue (n=100).

GI manifestation	Non severe dengue DF, (n=38)	Severe dengue (n=62)			P value
		DHF, n=12	DSS, n=22E	DES, n=28	Total, n=62	
Anorexia	34	10	22	26	58	0.465
Nausea	34	10	20	26	56	0.890
Vomiting	30	8	20	26	54	0.280
Pain abdomen	30	8	20	26	54	0.280
Diarrhoea	12	8	16	20	44	0.0001*
Ascites	18	6	12	16	34	0.467
Jaundice	2	0	0	8	8	0.216
Hepatomegaly	12	4	0	10	14	0.319
Acalculous cholecystitis	18	6	4	14	24	0.394
GI Bleeding	12	8	6	12	26	0.300
SGPT	30	10	14	28	54	0.280
SGOT	38	12	20	28	60	0.613

* Statistically Significant, P value <0.05, Chi-Square test was applied

Table IV denotes the Gastrointestinal and related biochemical parameters in both severe and non-severe dengue cases. In this study only diarrhoea is statistically significant (p <0.05) among severe dengue patients.

Discussion:

In this study, 100 serologically confirmed dengue patient were enrolled and the clinical and laboratory profile related to gastrointestinal involvements during the period of august 2023 to January 2024 at DNCC dedicated Covid-19 Hospital in Dhaka, Bangladesh were observed.

The study population in this study were in between 3-85 year and the mean age 29.66±19.69. Prashanth VN et al, conducted a study on 100 patients in Bangalore, India and they found the age distribution between 18-70 years and mean age 32.98±12.4 years.[8] Tanveer Hussain et al, also conducted a study in Pakistan on 100 patients and they found the study populations in between 13-72 years.[11] So, these findings are consistent with other related studies.

In the present study, male was 62%, female was 38% and male to female ratio was 1.6:1. These findings are matched with the study of Tanveer Hussain et al, where they found 58% male and 42% female.[11] Male predominant may be due to the more exposure of male to mosquito bite during outdoor activities and female has relatively less infection may be due to the traditional wearing of full slip cloth as well as less time spending at outside.[12]

Dengue is a widely spread infectious disease. In our study, it was found that 44% patients were from Dhaka city and 56% admitted from outside of Dhaka city. Recent study revealed that 56% patients from urban areas and 44% from rural areas.[8] According to WHO, dengue virus infection gradually shifted to rural areas.[13] DGHS reported that, more than 100,000 cases were hospitalized due to dengue, and among them, about 50% were from Dhaka City in 2019.[14]

The participants of this study, categorized into DF, DHF and DSS and EDS according to WHO guidelines 2009 and national guidelines for clinical management of dengue fever of Bangladesh.[2,7,13,14] Non severe dengue were 38% and Severe Dengue was 62%, among them, 12(12%) were Dengue Haemorrhagic Fever (DHF) and 22(22%) were Dengue Shock Syndrome (DSS) and the rest 28 (28%) were Dengue Expanded Syndrome (DES). In another study, 35% patients have DF, 54% DHF and 11% DSS.[11] In a study by Mazumder et al, they found 57% classical DF, 26% DHF and 17% DSS.[12] In this study severe dengue cases were found more which may be due to the DNCC centre, as because this centre was dedicated as dengue hospital and critical cases were referred here.

The gold standard investigation for the diagnosis of dengue is the detection, isolation and identification of virus by the RT- PCR method.[15] But due to economical constraints, low cost and easy serological test is an alternative way to diagnosis dengue for developing countries. For this perspective, ELISA test for NS1 antigen or specific IgM and IgG detection is an important diagnostic tool compared to RT-PCR.[16] In the present study, most of the patients were NS1 (86%) positive, followed by anti-dengue IgM antibody (20%) positive. 10% patients had both IgM and IgG positive. R. Mahmood et al. conducted a study where they found NS1 Positive in 93%. So, the observations are in line with the study conducted by R. Mahmood et al.[17]

Dengue has wide spread presentation. In this current study predominantly, gastrointestinal features had been studied. Most common gastrointestinal presentation was anorexia (92%), nausea (90%). Vomiting and abdominal pain were 84%, followed by diarrhoea 56%. Ascites, jaundice, hepatomegaly and acalculus cholecystitis were noted in 52%, 10%, 263% and 42% respectively. Acute pancreatitis was found in 02 cases. A current study *found that gastrointestinal* manifestations in 96% cases. They observed nausea 71%, vomiting 59%, pain abdomen 33 %, diarrhoea 13%. Ascites was present in 24%, acalculous cholecystitis in 13%, hepatomegaly 14%, splenomegaly 16%. Acute pancreatitis was found in 4% of patients.[8] Another study by Tanveer Hussain et al., found nausea 89%, vomiting 55%, abdominal pain 59%, diarrhoea 18%, ascites 44%, hepatomegaly 14%, acalculous cholecystitis 22%, acute severe liver injury in 5% and acute pancreatitis in 2%.[11] So, the clinical findings of our study are consistent with the other various study.

GI bleeding was found in 38% cases. Among bleeding manifesting, hematemesis, melena, gum bleeding and per rectal bleeding were found in 14%, 20%, 16% and 12% patients respectively. Most of the bleeding manifestations were overlapped with each other. Recent studies found GI bleeding in 9% and 6% respectively.[8,11]

Bleeding manifestation is a common presentation in Dengue. Petechiae, purpura, ecchymosis, and GI bleeding may occur in critical cases. Among gastrointestinal bleeding manifesting, hematemesis, melena, gum bleeding and per rectal bleeding were found.[18,19] Bleeding manifestation in Dengue has multifactorial causes, it may be due to decreased platelet function. The other causes are fibrinogen consumption, prolongation of PT/aPTT, and vasculopathy.[20]

In this present study, there are many gastrointestinal presentations, among them, only diarrhoea is statistically significant ($p < 0.05$) in severe dengue patients. Prashanth VN observed that nausea, vomiting, abdominal pain, jaundice, GI bleeding, ascites, elevation of transaminases, acute fulminant hepatitis and acute pancreatitis correlated with severity of Dengue fever. Other studies found that GI bleedings (hematemesis & melena), ascites, hepatomegaly were significant with dengue severity.[8,12]

Conclusion:

Dengue fever is very common infection in our country with vast of presentation and complications. Preventive measures, prompt diagnosis and proper management can bring down its mortality. Patients present with atypical GI manifestations should be handle very cautiously.

Ethical Approval:

The study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Institutional Review Board of Shaheed Suhrawardy Medical College (Memo no/ShSMC/Ethical/2023/02). Written informed consent was taken from all the patients before taking part of the study.

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No author has any conflict of interest to disclose for this manuscript.

Author Contributions:

Conception and design of the study: PU. Acquisition, analysis and interpretation of data: PU, FRC, Manuscript drafting and revising it critically: PU, SAK, FRC, FS, Approval of the final version of the manuscript: PU, SAK, FRC and Guarantor accuracy and integrity of the work: PU

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ORIGINAL ARTICLE

ABO BLOOD GROUP DISCREPANCIES AMONG THE RECIPIENTS IN A TERTIARY CARE CENTRE

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Abstract:

Background: *ABO Blood Group discrepancy means the difference between forward and reverse grouping due to an unexpected extra reaction or a missing reaction. This is one of the major reasons for a transfusion reaction. The aim of this study was to analyze ABO blood group discrepancies in an algorithmic manner and find out the risk factors among the recipients.* ***Methods:*** *This cross-sectional observational study was carried out among 200 patients in the Department of Transfusion Medicine, BSMMU, Dhaka, for a period of 6 months. Both forward and reverse blood grouping were done among the recipients' sample and risk factors related to ABO grouping discrepancies was evaluated.* ***Results:*** *Presence of ABO discrepancies were found in 5.5% blood recipients (n=11). Among them the major risk factors were transfusion dependent thalassemia (TDT), mismatched transfusion, autoimmune hemolytic anemia (AIHA) and multiple myeloma (2 patients in each category, 1% each). Furthermore, 83.0% recipients were having blood transfusion d"5 times.* ***Conclusion:*** *Despite all precautions ABO discrepancies still exist in transfusion sectors. Conditions where chance of ABO discrepancy is high needs extra precautions before ABO grouping to ensure safe blood transfusion.*

Key words: *Blood Group Discrepancy, ABO Incompatibility, Forward and Reverse Blood Grouping, Pre-transfusion testing.*

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Introduction:

The ABO system, discovered by Landsteiner (1900), is crucial among all blood group systems as far as the blood transfusion is concerned. The basic of ABO grouping system depends upon the presence of antibodies in their serum against the antigen that are absent from their red blood cell. In the ABO system there are three major alleles, A, B and O, any one of which may occupy the ABO locus on each of the paired chromosomes. The O gene does not produce any demonstrable red cell antigen.[1] Antigenic determinants of ABO blood groups are oligosaccharides located on glycoproteins and glycolipids expressed on erythrocytes and tissue cells and occur in various body fluids and secretions. Depending on an individual's ABO blood type, immunoglobulin M (IgM) antibodies directed against the missing A and/or B antigens are regularly present in serum; that constitute an immunologic barrier against incompatible blood transfusion and organ transplantation. The ABO gene codes for the glycosyltransferases that transfer specific sugar residues to H substance, resulting in the formation of

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blood group A and B antigens.[2] Transfusion of ABO-incompatible blood potentiates a greater risk for the recipients. ABO incompatibility accounts 37% of all reported transfusion-associated fatalities in the United States. Published reports cite an incidence of ABO discrepancy due to inappropriately identified specimens ranging from 1 in 517 to 1 in 3,400 samples.[3,4,5] The true incidence of transfusion errors has been estimated to be as high as 5 times the number of detected errors, so the risk of mistransfusion may be severely underestimated.[6]

ABO discrepancies occur when unexpected reactions occur in the forward and reverse grouping. These can be due to problems with the patient's serum (reverse grouping), problems with the patient's red cells (forward grouping), or problems with both the serum and cells. The unexpected reaction can be due to an extra positive reaction or a weak or missing reaction in the forward and reverse grouping. Technical errors can also cause ABO discrepancies.[7] Common Sources of Technical Errors Resulting in ABO Discrepancies are as follows: 1. Incorrect or inadequate identification of blood specimens, test tubes, or slides 2. Cell suspension either too heavy or too light 3. Clerical errors or incorrect recording of results 4. A mix-up in samples or Contaminated reagents 5. Missed observation of hemolysis 6. Failure to add reagents or sample 7. Failure to follow manufacturer's instructions 8. Uncalibrated centrifuge 9. Over or under centrifugation, Warming during centrifugation. If the initial test was performed using RBCs suspended in serum or plasma, repeat testing of the same sample using a saline suspension of RBCs can usually resolve the ABO discrepancy.[8] Categories of ABO Discrepancies: ABO discrepancies may be arbitrarily divided into four major categories: group I, group II, group III, and group IV discrepancies.[9]

Group I Discrepancies: Group I discrepancies are associated with unexpected reactions in the reverse grouping due to weakly reacting or missing antibodies. These discrepancies are more common than those in the other groups listed. Common populations with discrepancies in this group are newborns, elderly patients, patients with leukemia, patients using immunosuppressive drugs that yield hypogammaglobulinemia or immunodeficiency diseases and patients with bone marrow or stem cell transplantations.

Group II discrepancies are associated with unexpected reactions in the forward grouping due to weakly reacting or missing antigens. This group of discrepancies is probably the least frequently encountered. Some of the causes of discrepancies in this group include subgroups of A (or B), leukemia's may yield weakened A or B antigens, and Hodgkin's disease, weak reactions with anti-B antisera and is most often associated with diseases of the digestive tract (e.g., cancer of the colon). Rare Group II discrepancies: Weakly reactive or missing reactions in RBC grouping may be due to excess amounts of blood group–specific soluble (BGSS) substances present in the plasma, which sometimes occurs with certain diseases, such as carcinoma of the stomach and pancreas.

Group III discrepancies between forward and reverse groupings are caused by protein or plasma abnormalities and result in rouleaux formation or pseudo agglutination. Examples are elevated levels of globulin from certain disease states, such as multiple myeloma, Waldenström's macroglobulinemia or other plasma cell dyscrasias, elevated levels of fibrinogen, raised ESR, Wharton's jelly in cord blood sample and plasma expanders, such as dextran and poly vinyl pyrrolidone

Group IV discrepancies between forward and reverse groupings are due to miscellaneous problems and have the following causes: Cold reactive autoantibodies in which RBCs are so heavily coated with antibody that spontaneously agglutinate, independent of the specificity of the reagent antibody. Patient has circulating RBCs of more than one ABO group due to RBC transfusion or marrow/stem cell transplant. Unexpected ABO iso-agglutinins and non-ABO alloantibodies are also denoted in group IV discrepancies.

The delivery of this vital product 'blood' involves many people at different levels and different areas of the hospital. Errors can occur at any point. The first step in preventing mismatch is obtaining blood for pre-transfusion testing from the right patient and ensuring that all labeling is correct. Errors in these critical steps are recognized as the primary source of mismatching. It is imperative to recognize discrepant results and resolve them. Correct blood typing and labeling of an individual are essential to prevent ABO incompatibility. Different methods are available for determining ABO types of blood donors and recipients. Despite all the modern technologies and reagents availability, blood group discrepancies still occur. This study investigated the incidences ABO blood group discrepancy between red cells (forward blood grouping) and serum (reverse blood grouping) grouping of blood samples and tried to evaluate the risk factors. Therefore, the observations of this study will enrich our experiences in future as there are very few documents or data currently available to notify ABO discrepancies of our

country.That is why this study will help us to avoid single serious mismatched transfusion.

Methods:

This is a Cross sectional observational study done at Department of Transfusion Medicine of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. This study was conducted from November 2015 to April 2016 where two hundred recipient's blood samples were observed. All participants of this study were between the ages of 8 to 60 years except known cases of auto immune hemolytic anemia. The preliminary screening panel for each sample was included the age, sex, pregnancy, medication, lab tests and previous blood transfusion history. For identification of ABO blood group discrepancy, the following flow chart was executed:

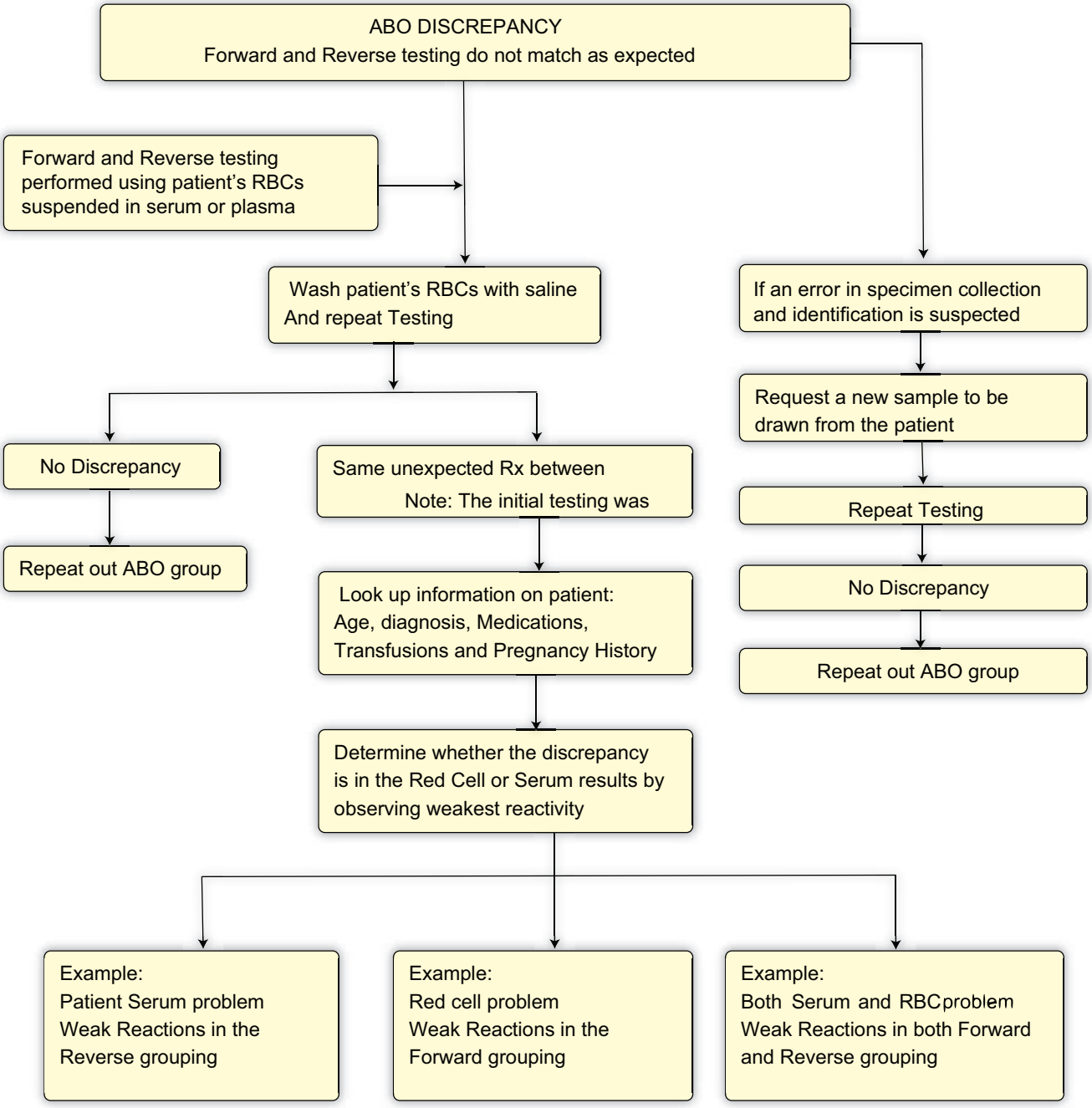

Fig.-1: *Algorithm for identifying ABO discrepancies*[8].

Blood sample was collected in two pilot tubes from each recipient for cell and serum grouping. Seven to eight ml of EDTA blood was used for forward grouping and adsorption and elution techniques. Serum grouping was performed on clotted sample. ABO blood grouping was carried out by standard tube technique after washing the donor and reagent RBC's thrice with 0.9% normal saline. Cell grouping was performed using commercially available monoclonal anti-A and anti-B, anti-AB, antisera from two manufacturers (Tulip diagnostics and Span diagnostics) as per standard operating procedures and monoclonal anti-A, B sera (Tulip diagnostics) was used to confirm the routine findings. Serum grouping was performed using in-house pooled A cells, B cells, and screening O cells. Results of cell grouping, and serum grouping were matched. If there was any discrepancy, test was repeated with the same sample to rule out the possibility of technical errors. If it remained the same, then the possibility of a problem related to the sample was considered. Sample-related problem was divided further into two groups: ABO discrepancies that affected the ABO red-cell testing and those that affected the ABO serum testing. Those ABO discrepancies that affect either red-cell or serum testing was classified into whether an extra reaction was present or expected reaction was missing. Additional information pertaining to age, sex, pregnancy, history of previous blood transfusion, and medication was also obtained. Test was repeated on the fresh sample also. Supplementary reagents such as anti–A_1 (Tulip diagnostics) and anti-H (Tulip diagnostics) were also used. We also performed extended incubation at 4°C along with auto control and 'O' cells as a part of routine detailed serological workup for all samples where cell and serum grouping showed discrepant results. Polyclonal antisera of human origin from group B, group A, and group O individuals were used for adsorption to determine these subgroups. Heat elution technique using 6% bovine serum albumin was carried out at 56°C for 10 min and elute was tested against three un pooled reagent cells (A, B and O). In some tubes, agglutination was present after immediate spin, whereas tubes showing no agglutination in the above step were incubated at 37 °C for 60 min. In these tubes, agglutination was observed after adding anti-human globulin reagent.[9]

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The quantitative observations were indicated by frequencies and percentages.

Results:

Table I

Distribution of the study patients (blood recipient) by age groups (n=200).

Age (years)	Number of patients	Percentage (%)
≤10	8	4.0
11-20	34	17.0
21-30	54	27.0
31-40	34	17.0
41-50	32	16.0
51-60	26	13.0
>60	12	6.0

Table I shows age distribution of the study patients (blood recipient). It was observed that majority 54 (27.0 %) of patients (blood recipient) belonged to age 21-30 years.

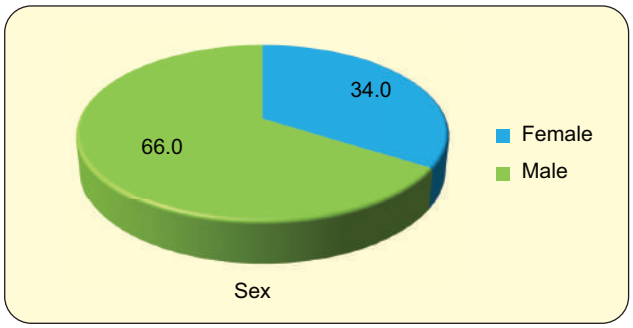

Figure 2: *Pie chart shows sex distribution of the study patients.*

Table II

Distribution of the study patients by ABO blood groups (n=200).

ABO blood groups		A	B	O	AB	A_2B
Forward blood group	Number of patients	40	80	55	24	1
	Percentage (%)	20.0	40.0	27.5	12.0	0.5
Reverse blood group	Number of patients	40	80	55	24	1
	Percentage (%)	20.0	40.0	27.5	12.0	0.5

Table II shows ABO blood groups of the study patients (blood recipient). It was observed that forward blood group was found to have 40(20.0%) patients in blood group A, 80(40.0%) in B, 55(27.5%) in O, 24(12.0%) in AB and 1(0.5%) in blood group A_2B. Reverse blood group was found to have 40(20.0%) patients in blood group A, 80(40.0%) in B, 55(27.5%) in O, 24(12.0%) in AB and 1(0.5%) in blood group A_2B.

Table III

Distribution of blood recipients by the presence of ABO discrepancies (n=200).

Presence ABO discrepancies	Number of patients	Percentage (%)
Present	11	5.5
Absent	189	94.5

Table III shows presence ABO discrepancies of the study patients (blood recipient). It was observed that presence ABO discrepancies were 11(5.5%) patients (blood recipient).

Table IV

Conditions with ABO discrepancies (n=200)

Causes of ABO discrepancies	Number of patients (blood recipient)	Percentage (%)
Transfusion Dependent Thalassemia	2	1.0
Mismatched transfusion	2	1.0
Autoimmune hemolytic anaemia	2	1.0
Multiple myeloma	2	1.0
Nonhematological malignancy (ovarian tumour)	1	0.5
ABO subgroup (A_2B)	1	0.5
Hematological malignancy (ALL)	1	0.5

Table IV shows risk factors of ABO discrepancies of the study patients (blood recipient). It was observed that 2(1.0%) patients (blood recipient) had TDT followed by 2(1.0%) had mismatched transfusion, 2(1.0%) had autoimmune hemolytic anaemia, 2(1.0%) had multiple myeloma, 1(0.5%) had non hematological malignancy ovarian tumour), 1(0.5%) had ABO subgroup (A_2B) and 1(0.5%) had ALL.

Discussion:

In this present study it was observed that majority 54 (27.0 %) of patients (blood recipient) were in 20-30 years age group. Similarly, Das et al.[10] found a total of 14 patients aged between 18 and 64 years, which are comparable with this current study. This current study observed that 132(66.0%) patients (blood recipient) were male and 68 (34.0%) were female. Male female ratio was 1.9:1. Similarly, male predominant also found by Giri et al.[11] where the authors observed 11554 subjects, among them 95.75% were male and 4.25% were female subjects which is opposite to the findings of Das et al.[10] where male to female ratio was 1:2.5.

In this series of observation forward blood group was found to have 20.0% patients in blood group A, 40.0% in B, 27.5% in O and 12.0% in AB. On the other hand, reverse blood group was found to have 20.0% patients in blood group A, 40.0% in B, 27.5% in O, 12.0% in AB and 0.5% in blood group A_2B. Likewise, Maatoghi et al.[12] reported that the frequency of A and O phenotypes in white populations is 45.0% and 40.0%, respectively.

The distribution of ABO blood group varies regionally, ethically and from one population to another. In the study of Giri et al.[11], the ABO blood group typing in the total sample showed the same trend of prevalence as in the general Indian subcontinent (B ≥O > A > AB). In ABO system, their study showed the highest frequency of blood group B 31.89%, followed by O (30.99%), A (28.38%) and AB (8.72%). The investigators compared their result with other studies carried out in different countries of the world like Britain, USA, Nepal, Nigeria, Pakistan, Guinea, Saudi Arabia etc. Frequency of O blood group is highest in Britain 47.0%, USA 46.0%, Nigeria 54.2%, Guinea 48.9% and Saudi Arabia 52.0% and there is no marked difference in incidence of O blood group in these countries. In different part of India Warghat et al.[13] and Rai et al. [14] revealed that the frequency of blood group B (33.06%), followed by O (31.04%), A (27.02%) and AB (8.33%); and blood group B (42.0%), followed by O (30.04%), A (23.5%) and AB (4.0%) respectively.

In this study it was observed that presence of ABO discrepancies was 5.5% (11blood recipients out of 200 samples). Besides this, it was observed that 1.0% patients (2 recipients) had TDT, 1.0% had mismatched transfusion, 1.0% had AIHA, 1.0% had multiple myeloma, 0.5% (1 recipient) had non-hematological malignancy (ovarian tumor), 0.5% had ABO subgroup (A_2B) and 0.5% had hematological malignancy (ALL). Similarly, Zhang et al.[15] obtained, three conditions were related with the ABO blood type discrepancy, which included weaken antigen (2 cases), weakened antibody (3 cases) and ABO subtype (1 case). The satisfactory effect of transfusion was achieved in all patients with the principle of the same blood type or the compatible cross match.[16]

Decision to transfuse in autoimmune hemolytic anemia (AIHA) should be based on the pre-clinical condition of the patient rather than correcting the laboratory values. Moreover, delay in blood transfusion due to incompatible crossmatch, lack of adequate blood bank infrastructure, series of immune-hematological tests, lack of skilled person and critical patient condition make the transfusion management more challenging. More delay has been observed in patients with blood group discrepancy or patients suspected to carry underlying alloantibody due to previous blood transfusion or pregnancy.[17] Blood group discrepancy in one patient was resolved using eluted red cells and adsorbed serum. Therefore, Das et al.[10] concluded that decision to transfuse in AIHA should be based on the clinical condition of the patient. No critical patient should be denied blood transfusion due to serological incompatibility. All transfusion services should be capable of performing the minimum test required to issue "best match" PRBCs in AIHA. Specialized techniques such as elution and adsorption which are very much helpful in enhancing blood safety in AIHA should be established in all blood banks.

Furthermore, Gude et al.[18] reported that discrepancies in ABO blood grouping can be catastrophic and even fatal. There are a few reasons that may contribute to ABO discrepancies other than clerical errors. Medical disorders such as liver disease and multiple myeloma may also contribute to such discrepancies. In acute leukemia, the A antigen may be weakened. Sometimes the blood appears to contain a mixture of group A and group O cells. In other cases, the red cells react weakly with anti-A. In a patient with erythroleukemia, of group B, 60% of the cells were not agglutinated by anti-B and appeared to be group O, but were very weak B, when separated from the normal B cells they would absorb anti-B.[19]

Conclusion:

For minimizing the event of hemolytic transfusion reaction, it is crucial to perform proper blood grouping both forward and reverse groups. These discrepancies can be avoided through detailed analysis of blood group typing. It will be beneficial not only for the patient but also the donor and will ensure the safety and efficacy of blood transfusion.

Limitations:

The study population was selected from one hospital in Dhaka city, so that the results of the study may not reflect the exact picture of the country. The present study was conducted at a very short period of time. Small sample size was also a limitation of the present study. Therefore, further study may be undertaken with large sample size.

Data availability:

The datasets of this study were not publicly available due to the continuation of analyses but will be available from the corresponding author on reasonable request.

Conflicts of interest:

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

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This research did not receive any fund.

Ethical Consideration:

Ethical approval has been taken before starting the study from the Ethical Review Committee of Bangabandhu Sheikh Mujib Medical University, Ref No: BSMMU/2016/2799.

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ORIGINAL ARTICLE

PERADENIYA ORGANOPHOSPHORUS COMPOUND POISONING SCORE, GLYCEMIC STATUS AND ELECTROCARDIOGRAPHIC CHANGES AT THE TIME OF ADMISSION IN ORGANOPHOSPHORUS COMPOUND POISONING AND THEIR CORRELATION WITH SEVERITY AND CLINICAL OUTCOME

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Abstract

Background: *Acute organophosphorus compound (OPC) poisoning is a serious public health issue, especially in the rural areas. Peradeniya organophosphorus poisoning (POP) scale was developed to assess the severity of OPC poisoning. Although degree of choline- esterase inhibition plays a key role in the severity of OPC poisoning, some other metabolic factors like dysglycemia also has an association. Cardiovascular effects of acute OPC poisoning are also common.* ***Methods:*** *This hospital based prospective observational study was conducted at indoor of Department of Medicine, Chattogram Medical College Hospital for six months period, from January 2020 to June 2020. Fifty patients above 12 years of age with acute OPC poisoning who fulfilled the selection criteria were selected consecutively for the study. After initial resuscitation severity of poisoning was assessed by POP scale, Random blood glucose (RBS) and 12 lead ECG was documented at the time of admission. Patients were followed up till their hospital stay to observe the outcome in terms of death, need for Intensive care unit support, and length of hospital stay.* ***Results:*** *The mean age was 33.33 (±11.73) (Range: 15-65) years. Male to female ratio was 1.77:1. As per the POP score 24% had mild, 54% had moderate and 22% had severe grade of poisoning. The mean Random blood glucose level was 186.05±51.44 mg/dl (range 90-288 mg/ dl) with 21 (42 %) cases having blood glucose value above 200 mg/ dl. ECG finding was abnormal in 56% of case with ST-T changes as the most common abnormality. Mortality rate was 24%. Most of the death occur in an average of 4th day of admission. POP score at the time of admission 7.5 or more had 91.7% sensitivity and 100% specificity to predict in hospital mortality. Admission Random blood glucose level of 207.9 mg/dl had 75% sensitivity and 68.4% specificity to predict in hospital mortality and morbidity.* ***Conclusion:*** *POP scale, glycemic changes and ECG are good markers for predicting morbidity and mortality and can be used as assessment tools for severity of poisoning and also to assess the prognosis of OPC poisoning cases.*

Keywords: *Organophosphate compound poisoning, Peradeniya organophosphorus poisoning score, Random blood glucose, Electrocardiography.*

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Introduction:

Organophosphorus compounds (OPC) are pesticide that can bind and inhibit, cholinesterase enzyme making it unable to breakdown acetylcholine.[1] Acute OPC poisoning is a major clinical and public health concern across rural part of Asia.[2] Unfortunately, in most rural hospitals there is insufficient staff or inadequate equipment available to deal with patients with severe poisoning.[3] Acute OPC poisoning remains a serious problem in Bangladesh.[4] In a review Dewan et al. identified that pesticide poisoning is a cause for greater number of admission and death in Bangladesh. In his review 89.8% are due to OPC.[5] Pesticide poisoning was responsible for 72.6% of total poisoning related deaths. Approximately 0.7 deaths per 100,000 population was due to pesticide poisoning.[5] OPC poisoning are one of commonly encountered emergency situations and accounts for more than 75% of all cases of acute poisoning in hospital practice in Bangladesh and mortality rate is about 16%.[6]

As mentioned earlier, OPs compounds mainly work by inhibiting acetyl cholinesterase (AChE) enzyme. AChE is a neurotransmitter found both in central and peripheral nervous system and its normal physiological action is breakdown of acetylcholine (ACh). OPC inactivate AChE by phosphorylating the hydroxyl group located at the active site of AChE. Once AChE has been inactivated acetylcholine accumulates in the autonomic nervous system, PNS and CNS resulting in overstimulation of muscarinic and nicotinic receptors. Accumulation of acetylcholine at nerve endings has played a major part in providing a rationle for specific antidote treatment using atropine and oximes.[7]

Although more than 1000 organophosphorus insecticides exist, three most common type used for self-poisoning in Sri Lanka. These three types differs in clinical features and severity.[8] The preliminary assessment of patients is mainly based on the clinical presentation of the patients.[9] However, it is complex to evaluate the severity of toxicity and the prognosis of patients with acute OPC poisoning in hospitals. A practical bed side scoring system was developed for severity assessment of OPC poisoning patients. Routine use of this scoring system could rapidly assist in identifying patients at higher risk who require more intensive care or Transfer for better management.[10]

OPC poisoning is associated with a high case fatality rate with more preventable deaths occurring in developing countries than in developed countries and yet there are no clear-cut evidence-based guidelines for the management of OPC poisoning.[11,12] Till date, many studies have been carried out to assess factors determining the severity of OPC poisoning and to predict morbidity and mortality. These include Glasgow coma scale score, Acute Physiology and Chronic Health Evaluation II score, pseudo cholinesterase level, lactate dehydrogenase level, serum immunoglobulin, circulating complements, various scoring systems, and creatinine phosphokinase.[13,14] However, there is no consensus regarding contribution of these factors and score to determine severity and also to predict morbidity and mortality. The clinical relevance of these changes to prognosis is not yet clear.[15]

As expected, the higher the level of toxins in the tissue more should be symptoms. Based on this hypothesis, a scoring system known as Peradeniya Organophosphorus poisoning (POP) scale was put forth by Senanayake et al. [16] This scale uses 6 clinical parameters to assess the severity of poisoning and graded as mild (score 0-3), moderate (score 4-7) and severe (score 8-11).[16]

POP scale has not been studied much in Bangladeshi scenario. It could be a simple and effective tool to determine the need for ventilatory support early in the course. In a recent Indian study, the POP scale showed a significant association in predicting the poor prognosis group (Intermediate syndrome, ventilatory support and mortality). Lower grade of poisoning had a better outcome whereas higher had a poorer outcome.[17]

All varieties of glycemic changes ranging from hypoglycemia to hyperglycemia and ketoacidosis have been reported in OPCs poisoning cases.[18,19] A recent prospective analytical study of 100 patients with diagnosed acute OPCs poisoning conclude that the glycemic status at the time of presentation in acute OPCs poisoning patients is a simple, cheap, reliable marker to asses the clinical severity and outcome when considered with clinical severity scores.[20]

Electrocardiographic changes in OPC poisoning have been reported along with the associated structural myocardial damage. Abnormal ST-T changes and progressive fall in voltage and or low voltage were the commonest ECG changes encountered in patients with OPC poisoning. These occurred significantly more often in patients with moderate or severe poisoning. The patients with a combination of these ECG abnormalities required higher doses of atropine and those who survived it takes longer time to normalize the ECG despite normal clinical recovery rate as compared to other cases. Other ECG abnormalities like prolongation of the QT interval, ectopic beats, conduction defects and peaked P wave were seen less frequently and had returned to normal with clinical recovery and did not correlate with prognosis.[21]

Contemplating this background this study was intended to observe the morbidity and mortality in terms of requirement of ventilation and hospital stay and time of death from admission which can be accessed from POP score, ECG findings and glycemic status at presentation. The study also tried to identify the levels of these parameters at which they indicate chances of significant morbidity and mortality.

Methods:

A hospital based prospective observational study was performed in indoor patients of documented OPC poisoning admitted in different Medicine Units of Chattogram Medical College Hospital between January 2020 to June 2020. Patients of 12 years and older irrespective of sexes who volunteered history of ingestion of OPC (irrespective of the nature of poisoning—deliberate self-harm, homicidal or otherwise and regardless of brand of OPC and whether or not a sample was provided for identification were included in this study by consecutive sampling technique. Patients who were already treated at other centers and referred to our center for further management with no details available at the time of first presentation or had consumed alcohol, drugs, mixed poisoning that could affect the glycemic status of the patients were excluded from this study. Pregnant patients or patients with Diabetes Mellitus or any cardiac co-morbidity were not included in this study. After arrival of the patients initial treatment and resuscitation was done by the ward staff. Following resuscitation the patients were assessed for eligibility in the study. When the inclusion and exclusion criteria were fulfilled, patient's attendants were invited to voluntarily participate in the study and to read and sign an informed consent statement. The data were collected by interview, and examination. Identification of the type of chemical was determined by the labels or the names of chemicals the patient was exposed. POP score, Blood sugar and bed side 12 lead ECG was done along with the initiation of appropriate treatment. Appropriate treatment of the patients was started along with atropine and pralidoxime. Atropine was given in the doses of 0.5 to 2mg atropine intravenously and double dose every 3-5 minutes interval till the signs of atropinisation appeared. Patients received the standard treatment as per hospital protocol. However, for convenience and resource limitation, finally it was possible to include 50 patients in the study within study period.

Severity of OPC poisoning was assessed by Peradeniya organophosphorus poisoning (POP) scale which is based on six cardinal manifestations of OPC poisoning (miosis, fasciculation, respiratory difficulty, bradycardia and impairment of consciousness, any history of convulsion).

The scoring system is given below-

Table I

POP scale for severity assessment of OPC poisoning

	Score
Miosis	
Pupil size >2 mm	0
Pupil size <2 mm	1
Pupil size: pin point	2
Fasciculation	
None	0
Present but not continuous	1
Genarlized and continuous	2
Respiration	
Respiratory rate d"20 min	0
Respiratory rate>20 min	1
Respiratory rate>20 min with central cyanosis	2
Bradycardia	
Pulse rate >60 min	0
Pulse rate 41-60 min	1
Pulse rate <40 min	2
Level of consciousness	
Conscious and rational	0
Impaired, respond to verbal command	1
Impaired, no respond to verbal command	2
If convulsion present, add 1	
Total:11; Mild: 0-3; Moderate: 4-7; Severe: 8-11	

A pre designed semi-structured case record form was used as a data collection tool.

After collection data were compiled in a Microsoft Office Excel Worksheet. Then they were fed into SPSS (Statistical Package for Social Science) for Windows version 23 software to process and analyze the data. Continuous variables were reported as mean values ± standard deviation (SD) while categorical variables were expressed as count and percentage. The statistical significance of intergroup differences was compared through unpaired Student's 't'-test for continuous variables and through Pearson's Chi-square test for categorical variables. The ability of the variables (POP score and CBG level) to discriminate survivors from non survivors were determined using receiver operating characteristic (ROC) curves. Correlation between CBG and POP score was assessed by correlation coefficients. Two-sided p value < 0.05 were considered to represent a statistically significant difference.

Results:

In this study, there were 50 participants who selected consecutively fulfilling the inclusion criteria. Out of them 32(64%) were male with a male to female ratio of 1.78:1. 30% of patients fall in age group of 21-30 years with mean age 33.33 ± 11.73 years. Most of the patients had educational qualification below(22%) or up to(46%) secondary level and reside in rural area(56%). Regarding occupation majority of them were either housewife(22%) or involved in business(22%).

In most of the cases nature of poisoning was suicidal and reason was domestic issues. The entire group reported to have oral exposure. Median interval for admission from exposure was 2 hours and only 14% patients received pre-hospital management (Table II).

Table II

Distribution of the patients by exposure related variables (n=50)

Poison related variable	No. of patients	Percent (%)
Nature of poisoning		
Suicidal	42	84.0
Homicidal	2	4.0
Accidental	5	10.0
Reason for poisoning		
Domestic issue	20	40.0
Financial loss	5	10.0
Marital issue	9	18.0
Educational failure	9	18.0
Not specified	7	14.0
Route of poisoning		
Oral	50	100.0
Interval between exposure to admission		
Mean ±SD, hours	2.54±1.55	
Received pre-hospital management		
Yes	7	14.0
No	43	86.0

The severity of the OPC poisoning was assessed by POP scale. The individual parameter those are used to compute POP score are described in Table III.

Table III

Distribution of POP scale parameters of the patients (n=50))

Parameters	No of patients	Percent (%)
Pupil size		
>2 mm	5	10.0
<2 mm	23	46.0
Pin point	22	44.0
Fasciculation		
None	19	38.0
Present but not continuous	25	50.0
Generalized and continuous	6	12.0
Respiratory rate		
Respiratory rate d”20 min	11	22.0
Respiratory rate>20 min	31	62.0
Respiratory rate>20 min with central cyanosis	8	16.0
Hear rate		
Pulse rate >60 min	15	30.0
Pulse rate 41-60 min	26	52.0
Pulse rate <40 min	9	18.0
Level of consciousness		
Conscious and rational	14	28.0
Impaired, respond to verbal command	24	48.0
Impaired, no respond to verbal command	12	24.0
Convulsion		
None	44	88.0
Present	6	12.0

Based on POP score the severity form was classified as mild: score 0-3; moderate: score 4-7 and severe: score 8-11 which is shown in Figure 1.

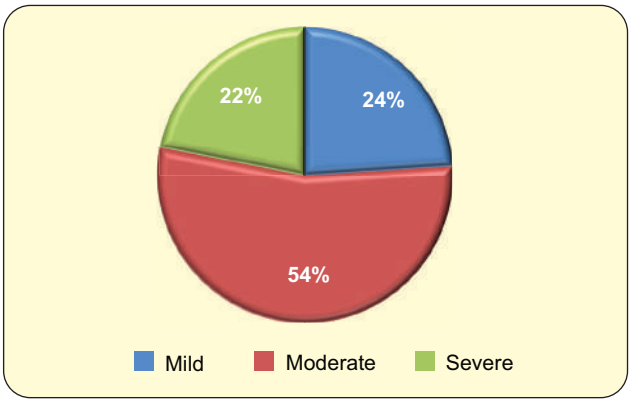

Fig.-1: *Distribution of the study population based on the severity of OPC poisoning by using the POP scale*

The present study group comprised of non-diabetic patients. At the time of admission of a OPC poisoning patient average blood sugar level was 186.05±51.44 mg/dl mg/dl (range 90-288 mg/). 21 (42 %) patients having RBS value above 200 mg/ dl.

ECG finding was normal in 44% cases. The most common ECG abnormality was ST-T change (ST elevation/depression and isolated T inversion) observed in 30% patients followed by QT prolongation (12%) and conduction defect (4%).

In- hospital outcome of the patients is shown in Table IV.

Table IV

In-hospital outcome of the patients (n=50)

Outcome parameters	Frequency	Percent (%)
Develop IMS	4	8.0
Death	12	24.0
ICU referral	11	22.0
Length of hospital stay (days)		
Mean ± SD	5.58±1.42	
Range	2-8	

IMS: Intermediate syndrome

Figure 2 shows that, earliest death was recorded in 2nd day after admission and last death at 8th day after admission. Most of the death (33.33%) was recorded on day 4.

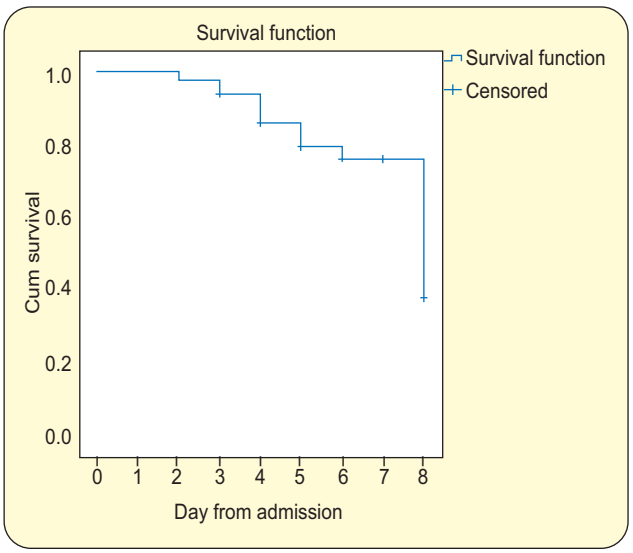

Fig.-2: *In-hospital survival analysis among OPC poisoning patients*

In the present study, 12 (24%) patients died out of 50 included patients. All patients with severe poisoning as per POP score at admission died in hospital. Regarding admission RBS glucose level >200 mg/dl were associated with mortality and morbidity in the study. Admission ECG finding had no significant association with the in-hospital mortality in the study. All these associations are shown in Table 5 and Figure 3.

Table V

Association between baseline POP score, ECG findings and glycemic status with outcome of the patients

Parameters	Level	Outcome of the patients		P value*
		Survived (n=38)	Died (n=12)	
	Mild (0-3)	11 (28.9)	1 (8.3)	
POP	Moderate (4-7)	27 (71.1)	0 (0)	<0.001
	Severe (8-11)	0 (0)	11 (91.7)	
RBS level	<140 mg/dl	7 (18.4)	2 (16.7)	
	140-200 mg/dl	19 (50.0)	1 (8.3)	0.001
	>200 mg/dl	12 (31.6)	9 (75.0)	
ECG	Normal	19 (50.0)	3 (25.0)	0.128
	Abnormal	19 (50.0)	9 (75.0)	

*P values are derived from Fishers exact test.

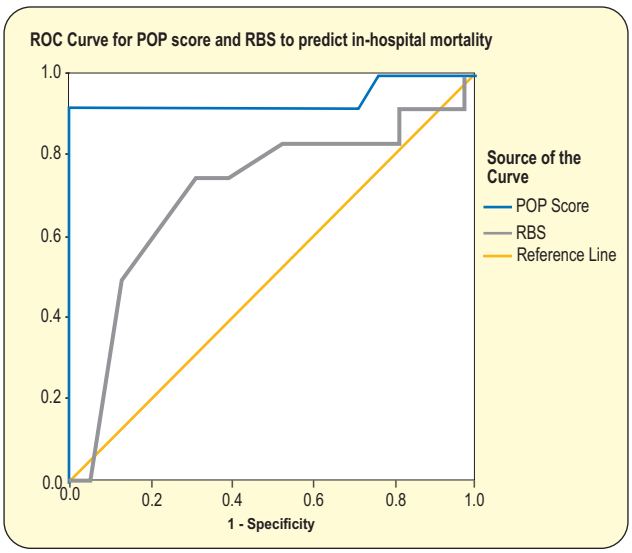

Fig.-3: *Receiver operating characteristic curve showing discrimination of the POP score and admission RBS for the prediction of in-hospital mortality*

Correlation between POP score and admission RBS levels of the patients were assess by Pearson correlation coefficient and presented as a scatter diagram in Figure 4.

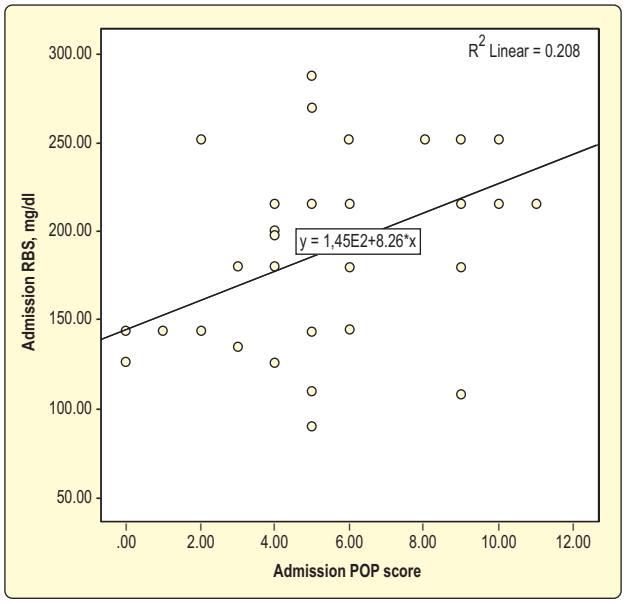

Fig.-4: *Scatter diagram showing correlation of POP score with admission RBS.*

Discussion:

OPC poisoning has been diagnosed as a prime problem in developing countries like Bangladesh because of its predominant use in pest control and crop protection. The diagnosis of OPC poisoning is mainly based on the history of ingestion or exposure, clinical features, low serum cholinesterase levels and therapeutic response to atropine.[9] Present study was conducted to determine and correlate the outcome with the severity of acute OPC poisoning assessed by POP score, admission RBS and ECG findings. Fifty OPC poisoning cases admitted in the medicine ward of CMCH were enrolled for this purpose.

OPC poisoning is mostly common in young, affecting both genders equally.[22-35] which correlates with the current study. The mean age of the patients was 33.26 (±13.13) years. Half of the patients were younger than 30 years. The most predominant age was 21-30 years with 30% cases. Of the entire study subjects males were more in numbers than the females. In the present study majority of patients were housewives or engaged in business. Majority of the patients were from rural area and had education up to or below SSC. This finding was expected because our hospital is a Government level tertiary care hospital usually provides health services mostly to lower to lower middle class patients. These observations with respect to demographic data were in line with observations of other studies conducted in and around our country.[22-37]

Majority of the patients in the present study were in the second or third decade who could contribute to the economic status of the family. Most common reasons identified for consuming the poison was suicidal and reason was domestic issues. Other reasons for suicidal attempt were financial loss, and stress and a similar type of result was quoted by a study done by Mundhe et al.[30] Moreover, individuals in this age group are active physically, mentally and socially and thus more prone to various stresses.

In the present study, out of 50 OPC poisoning cases, 11 patients required ventilation support for respiratory failure. Unfortunately all of them were expired with an overall mortality of 12 (24%). The mortality rates of the current study compares well with another recent study from India where the overall mortality rate was 22%.[38] However, reported mortality rates in OPC poisoning patients widely varied among studies from 61.9% to 11.5%.[39,40] It should be noted that all of the mentioned studies including the current one were single center study with small sample size, which might be attributable for these wide variation in the mortality rate.

The initial evaluation of the severity of acute OPC poisoning remains critical, and this is because severe cases usually need intensive care and ventilator support, which are not available in rural areas. Currently, no widely accepted criteria are present for classifying the severity of such poisoning cases. The

preliminary evaluation is mainly based on the presentation of clinical symptoms.[9] In the current study admission POP score, admission RBS and ECG parameters were evaluated and correlated with the mortality.

The present study demonstrated that, glycemic variability was a marker of poor prognosis. Out of 12 expired patients 9 (75%) had admission RBS level >200 mg/dl. This finding indicated that, hyperglycemia at the time of presentation may be a harbinger of greater in-hospital mortality. Excess activation of nicotinic-N receptors resulting in excess catecholamine release (from sympathetic ganglia) and ACTH (from anterior pituitary)which causes stress hyperglycemia and reduction in glucose induced insulin secretion by beta cells of Langerhans that might be attributable for this association between glucose level and mortality.[33] Raveendra et al.[33] reported a overall mortality of 9%, with highest percentage of deaths occurred among hyperglycemic [3 out of 15(20%)] and a similar trends was also observed in the study conducted by Raghapriya et al.[20] Mir et al.[24] .In this study the patient whose blood glucose levels were 216±61 mg/dl had increased mortality as compared to patients who survived in whom blood glucose levels were 136±88 mg/dl.

In the current study glycemic status as measured by RBS at admission significantly correlated with the severity of the patients as assessed by POP score. In the study of Raveendra et al.[33] observed that, 16% of euglycemic, 30% of hypoglycemic and 60% of hyperglycemic had severe grade of poisoning based on POP scoring and which was statistically significant. Sudhir et al.[22] also assessed glycemic changes in acute anticholinesterase insecticide poisoning and correlate with the severity of poisoning. Similar to our results they concluded that a positive correlation exists between the glycemic changes and the severity of OPC poisoning.

Regarding ECG changes in most of the cases (44%) ECG finding was normal. The most common ECG abnormality was ST-T change (ST elevation/depression and isolated T inversion) observed in 30% patients followed by QT prolongation (12%) and conduction defect (4%). Cha et al.[26] observed that, sinus tachycardia was the most common ECG abnormality and 11.1% had ST change. Some investigators have described a polymorphic ventricular tachycardia of the torsade de pointes type attributed to a prolongation of the Q-Tc interval associated with OPC poisoning.[41-43] In spite of the presence of a prolonged Q-Tc interval in 12% patients in the current study none of them had this type of arrhythmia. For the absences of such grave ECG changes present study failed to determine any association between ECG changes and mortality. Small sample size might be the limited factor for the absence of different ECG changes and their association with mortality in the current study.

In present study, according to POP scale, out of 50 patients, 24% were in mild category, 54% in moderate category and 22% patients fell in severe category. A total of 24% of the patients died, of which none patients belonged to moderate and 11 out of 12 patients belonged to severe group. So, POP scale correlated, directly and significantly, with mortality. Other studies also showed increased mortality and need of ventilator support was more in patients with high POP scale.[28,30]

The clinical significance of the present study was that, POP scale was found to be valid for our patients for prediction of adverse outcome following OPC poisoning. The POP applied at admission was able to predict the outcome of the subjects in terms of mortality and morbidity. The results of the present study agreed with other study done, which had similar results and hence it is safe to assume that POP score which is an easy, quick and inexpensive method can be used on all patients presenting with OP poisoning as a predictor of outcome. The routine use of this scoring system and also the assessment of blood sugar could rapidly assist in identifying patients at higher risk who require more intensive care or transfer to a larger better-equipped hospital. The patients with evidence of moderate and severe degrees of poisoning and high blood sugar need close monitoring, as respiratory failure is the prime cause. However the studies to understand the OPC induced glycemic variability and its role on the severity and outcomes are very few. Prospective studies regarding the same in a large cohort are desirable with focus on mechanistic association between the glycemic status and outcomes. Also the importance of continuous glucose monitoring and the management of the fluctuations in critical care settings need to be investigated and emphasized.

Though from the findings of the present study it can be concluded that initial assessment by POP scale and blood sugar level at presentation in OPC poisoning cases is useful in assessing the severity and at the same time being important indicators of mortality, the methodological limitations specially the small sample size need to be considered during generalizing the study results.

Conclusion:

In conclusion, 22% of the patients had severe grade of poisoning as per POP score, 42% of the patients had blood glucose value above 200 mg/ dl, and ECG finding

was abnormal in 56% of case with ST-T changes as the most common abnormality. POP score at the time of admission 7.5 or more had 91.7% sensitivity and 100% specificity to predict in hospital mortality. Admission Random blood glucose level of 207.9 mg/dl had 75% sensitivity and 68.4% specificity to predict in hospital mortality and morbidity.

Limitations:

This study has some methodological limitations which must be considered in the analysis of the results. Due to the COVID-19 situation and limited resource sample size was relatively small. Moreover, it was a single center study and the samples were collected conveniently which might limit its ability to generalize the results. Toxicological analysis was not possible. The study did not record or analyze the dose of the ingested OPC. Patient follow-up period was short. Admission RBS > 208 mg/dl along with POP score >7 can be considered as a useful factor in predicting the need for ventilator support and as well as mortality of OPC poisoning. Further prospective studies with greater number of patients are needed taking into consideration of various aspects of poisoning like intake of different OPC compounds, the amount of exposure, the type and dose of the drug, time lag between the intake of poison and initiation of treatment as well as the type of treatment to support the current observation as the current study was conducted with a relatively small number of patients, and in only one center of Bangladesh.

Conflicts of interest:

The authors report no conflict of interest.

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Ethical consideration:

The study was approved by the Ethical Review Committee of Sir Salimullah Medical College Mitford Hospital (SSMCMH) Dhaka, Bangladesh. Informed consent was obtained from each participant or caregivers of the patients.

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CASE REPORT

PERITONEAL INCLUSION CYST IN A YOUNG PATIENT WITH A LONG CLINICAL COURSE DEALT AS ASCITES

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Abstract:

Peritoneal inclusion cysts are reactive, fluid filled lesions of the peritoneal lining, mostly affecting women of reproductive age. It commonly occurs with history of previous abdominal surgeries. Para-ovarian cysts, hydrosalpinx, cystic mesothelioma, giant intra-abdominal cysts with uncertain origin are usually considered in the differential but 'may mimic ascites' when it becomes hugely enlarged. In this case report, we present a 23 -year-old female with no known co-morbidities presented to us with progressive abdominal distention. During excluding causes of abdominal distention, peritoneal cyst was suggested on computed tomography and laparoscopic excision was done. Peritoneal inclusion cyst is a rare entity and quite difficult to diagnose and choose appropriate treatment for individual patient.

Key words: *Peritoneal inclusion cyst, giant intra-abdominal cyst, laparoscopic surgery*

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Introduction:

Peritoneal inclusion cysts (PICs) are uncommon mesothelium-lined abdominopelvic cysts, mostly they are reactive.[1] Giant intra-abdominal cystic lesions are seldom encountered and hard to diagnose pre operatively. Intra-abdominal cysts may remain asymptomatic or may encounter non-specific symptoms like abdominal fullness, bloating and pressure symptoms from hugely enlarged cyst.[2] PICs usually affects women of reproductive age, especially who has a history of previous abdominal surgeries, inflammation, or infection.[1] Due to lack of specific symptom, they are often diagnosed incidentally during imaging or surgery for other cause. PICs have no malignant potentiality and fluid re-accumulation may eventually occur even after surgery, so conservative approach can be preferred as an alternative to surgery.[1] Oral contraceptives with combination of image guided aspiration are an effective method. Here, we present a giant peritoneal inclusion cyst in a 23-year-old female with long history of abdominal distention. This case demonstrates the unique challenges of diagnosing and managing a giant PIC in a young patient.

Case Report:

A 23-year-old female presented with the complaints of abdominal distension for last 10 years. Her symptom was gradual increase in size of abdomen. Once she was diagnosed as a case of ascites due to intestinal TB on the basis of exudative ascitic fluid and was given a trial of anti-tubercular therapy. After 14 days of therapy, she developed antitubercular drug induced hepatitis and stopped taking antitubercular drugs. After proper management, hepatitis was subsided but her abdominal distension was not improved. Thereafter she was thoroughly examined for abdominal distension and diagnostic laparoscopy was done. Tissue was taken from abdominal wall which revealed fibro-collagenous tissue with infiltration of chronic inflammatory cells. On this basis, she was advised antitubercular therapy

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for 9 months. After completion of therapy, she was relatively well for 7 years but abdominal distension was not cured completely. Again, for last 3 years her abdominal distension is gradually increasing & causing abdominal fullness. She has no history of abdominal pain, alteration of bowel habit, fever, chronic constipation, stigmata of CLD, weight loss, hematemesis, malaena, loss of consciousness, puffiness of face, reduced urine output, leg swelling or shortness of breath. She denied any co morbid condition & genetic disorder in the family. She was not on any medication.

Upon physical examination, abdomen was distended, flanks were full, umbilicus centrally placed and inverted, fluid thrill was positive & dullness present all over the abdomen with no shifting dullness. There was no tenderness, rigidity or muscle guarding.

Her routine blood & biochemical examinations revealed no abnormality. An abdominal ultrasound revealed anechoic area covering almost all quadrant of abdominal cavity which pushed the solid organ and bowel loops peripherally.

Abdominopelvic computed tomography scan illustrated a huge cystic mass noted in abdomen arising from pelvic cavity. The cyst cannot be separated from left adnexa. Multiple enhancing nodules noted within cyst. It has displaced bowel loops superiorly.

After discussing with patient, a multidisciplinary board meeting was done and decision to do laparoscopy with excision of cyst was taken. Intraoperatively near about 4.5 L turbid, straw color fluid was drained. No specific attachment of the cyst wall was found. Fluid was sent for study and it was negative for tuberculosis and malignant cell. Histopathology of cyst wall revealed fibro-collagenous tissue lined by single layer of bland, flat to cuboidal epithelium in favor of peritoneal inclusion cyst.

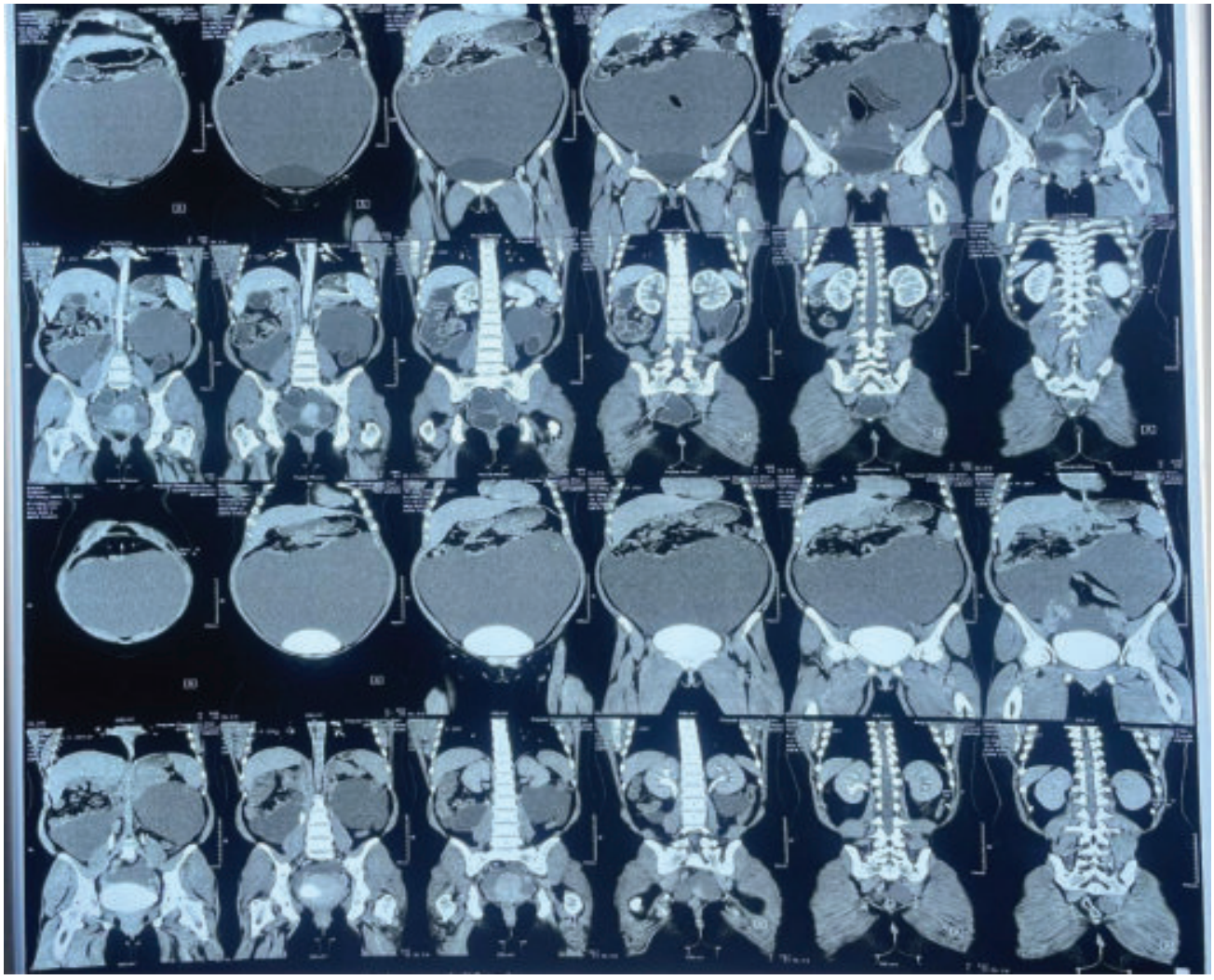

Fig.-1: *CT scan of abdomen showing giant intra-abdominal cyst displacing the bowel loops superiorly.*

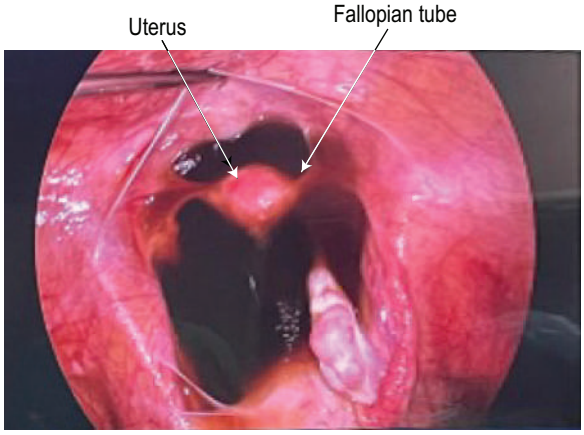

Fig.-2: *Per-operative image from monitor that both fallopian tube and ovaries are free.*

Discussion:

The exact cause of PICs is not clear at all. Although it is thought to be the result of benign inflammatory proliferation or reaction to various factors like prior abdominopelvic surgeries, gastrointestinal inflammation, or pelvic inflammation.[3] In regard to our case, the causes behind her PIC development are peritoneal disruption by prior surgery (diagnostic laparoscopy) or inflammation like history of tuberculosis, even though biochemical and microbiological findings of ascites was not suggestive of tuberculosis.

Though giant intra-abdominal cysts are seldom encountered in recent times due to availability of imaging as they are often picked up at a smaller size. In our case unfortunately ultrasonogram of whole abdomen was done multiple times but cysts could not be identified at early stage rather it was misdiagnosed as ascites. Since the patient has history of abdominal surgery and taking anti tubercular therapy, we had a suspicion of cyst in our mind so we did a CT scan of abdomen, which revealed giant intra-abdominal cyst. So whenever, we noticed a gradual intra-abdominal distention of uncertain etiology, we should emphasize to find out the etiology to minimize our pitfalls of diagnosis.

Various treatment options are available to treat PICs like hormonal management, image guided aspiration, image guided sclerotherapy, potassium-titanyl-phosphate laser ablation and surgical excision.[3] Elective surgeries, including laparotomy followed by excision of cyst or laparoscopy following cyst excision are available. Surgical treatment is usually the most common treatment option due to persistent pressure symptoms for definitive management. Both laparotomic and laparoscopic approaches are valid for excision of PCIs, however laparoscopic surgery is the preferred method because it offers shorter hospital stay, less blood loss, and minimal incision.[4] In spite of low malignant potentiality, PICs have high recurrence rate irrespective of procedures, around 30-50%.[3]

The variation of presentation and subsequent treatment of peritoneal inclusion cysts is evident in the literature. Singh et al. reported a multiparous women with a history of bilateral tubal ligation who presented with gradual lower abdominal pain.[1] Her imaging showed fibroids and numerous, undefined cysts, mimicking ovarian tumor. Ultimately she underwent staging laparotomy only to find healthy ovaries and multiple inclusion cysts, confirmed by histopathology.[1] In a case report by Tamai et al., a middle aged women with a history of left ovarian cystectomy presented with progressive lower abdominal pain.[6] On ultrasonography, intramural myoma was noted but MRI revealed peritoneal inclusion cysts.[6] The similarity in these cases and our case is that, they presented with abdominal distention and history of abdominal surgery, however, the technique of surgery was different, which was laparotomy in their case but diagnostic laparoscopy in our case. Our patient was treated by laparoscopic cyst excision, while Tamai et al. preferred conservative hormonal therapy.[6]

Conclusion:

Although PICs are not commonly encountered, the rising evidence alongside with our case reports emphasizes the significance of considering such a diagnosis in patients with abdominal distention with relevant risk factors. Despite it has low malignant potentiality, prompt diagnosis followed by definite management can aid in decreasing patients' sufferings. Management should be tailored according to individuals' need and presentation. The exact pathogenesis is unclear and recurrence rate is high. Therefore, we need to improve the diagnostic algorithms and more study is needed on management outcomes.

Consent for publication:

Informed written consent was taken from patient to publish details relevant to the disease and management.

Conflict interest:

None

Authors contribution:

All authors were involved in the management of the patient.

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CASE REPORT

DENGUE WITH SCROTAL SWELLING: RARE CASE REPORT

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Abstract:
Dengue fever is a mosquito-borne illness that occurs in tropical and subtropical areas of the world. Dengue fever (DF) is transmitted by Aedes aegypti mosquitoes. With rising disease burden, atypical manifestations have increased as well. We report a case of Dengue fever with acute scrotal swelling. Through detailed history, examinations, investigations including imaging, we confirmed the diagnosis and effectively excluded other possible reasons. Ultimately the swelling got resolved and patient was discharged uneventfully. By examining these cases, we aim to improve awareness of this under-recognized complication and guide healthcare professionals in its diagnosis and treatment.

Keywords: *Dengue, Scrotal oedema, AISE, Unusual Presentation*

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Introduction:

Dengue Fever is the matter of public health concern in Bangladesh as day by day the rate of infection is increasing and also the unusual presentation of dengue also frequently seen. It is transmitted by Aedes aegypti mosquitoes which is caused by a Flavivirus with four serotypes (DEN-1, DEN-2, DEN-3, and DEN-4).[1] While one serotype offers lifelong immunity to itself and temporary protection against others, secondary infections and those involving multiple serotypes can be more severe than primary infections.[1]

Dengue now-a-days became unpredictable with its widespread of clinical features and diverse presentation. [2] Dengue fever typically manifests with fever, muscle aches, and a rash, but it can also present with less common but significant atypical symptoms[1]. These may include hepatitis, diarrhea, renal failure, acalculous cholecystitis, and cardiac conduction abnormalities.[1] Among these, acute scrotal swelling is a relatively rare finding in dengue patients, with more frequent occurrences seen in conditions like epididymo-orchitis, hydrocele, filariasis, nephrotic syndrome, and heart conduction abnormalities[3]. This case underscores the importance of recognizing such unusual presentations to enhance awareness and facilitate accurate diagnosis in clinical practice.

Case Report:

A 25-year-old male came with fever for 4 days, which was high grade continued t in nature, not associated with chills and rigor but associated with nausea, highest recorded temperature was 103°F and which subsided on taking antipyretics. He also complained of generalized body ache for same duration and scrotal swelling for 2 days, which gradually increased in size, and it was painless, initially involved only left side and eventually involved bilaterally.

On examination, he was afebrile, vitals were stable, scrotal swelling was present in both sides without tenderness. Transillumination test was negative. Urine Dipstick test was negative. There were no other remarkable findings on general and systemic examination.

Investigations revealed hemoglobin 16 g/dL, Total WBC Count 8680/Cu mm (Neutrophil-47%, Lymphocytes-41%, Monocytes-11%, Eosinophils- 01%), hematocrit was 48% and platelet count 24000/ Cu mm >45000/ Cu mm >70000/ Cu mm >150000/ Cu mm. Urine

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RME revealed no abnormalities. Dengue IgG and IgM was positive.

ICT for Filariasis was negative. Ultrasonography of scrotum revealed thick edematous scrotal wall. Scrotal swelling subsided within 4 days and platelet count became normal and patient was discharged.

Fig.-1: *Swelling of the scrotum*

Discussion:

The differential diagnosis of scrotal swellings includes epididymoorchitis, Testicular torsion, Filariasis, Nephrotic syndrome, acute idiopathic scrotal edema (AISE). In case of testicular torsion, that requires emergency surgical intervention. Acute scrotal swelling associated with dengue fever is a rare and self-limiting condition. Diagnosis is primarily clinical but can be supported by ultrasonography (US), which helps visualize anatomical features and rule out other causes of acute scrotum. In cases of acute infectious scrotal edema (AISE), vital signs, urinalysis, urine, tissue cultures, and white blood cell counts are typically normal. Characteristic US findings in AISE include scrotal wall edema with increased blood flow, as well as enlargement and hypervascularity of the inguinal lymph nodes.[4] We also found scrotal wall edema as in AISE but did not detect any lymphadenopathy on ultrasonography. Although the exact cause of AISE is not well understood, it is believed to be a variant of angioneurotic edema.[5] In dengue fever (DF), the etiology of acute scrotal edema (ASE) involves an inflammatory response triggered by inflammatory mediators reacting to dengue viral antigens. This response includes antibody-dependent enhancement, increased dengue virus replication, and the release of TNF, IL-4, and interferon. These factors activate endothelial cells, monocytes, and T-cells, leading to coagulation disruption and vascular leakage, which results in pleural effusion, ascites, and localized or generalized edema.[3] The treatment for AISE is conservative and includes scrotal elevation and support, reassurance, and the empirical use of antibiotics and antihistamines.[6]

Our patient is a case of AISE, who developed acute scrotal swelling during the course of dengue hemorrhagic fever and resolved without sequelae in 3 days. To conclude, even though Scrotal edema is rare in dengue infection, detailed clinical examination and Investigation and clinical co-relation should be done to avoid unnecessary surgical exploration.

Our patient experienced acute scrotal swelling as a case of AISE during dengue hemorrhagic fever, which resolved without complications in three days. The patient was managed conservatively with antipyretics, fluid replacement, and scrotal support. The edema fully resolved within three days.

Conclusion:

Scrotal edema is uncommon in dengue infection, thorough clinical examination and investigation, along with careful clinical correlation, are essential to avoid unnecessary surgical exploration.

Consent for publication:

Informed written consent was taken from patient to publish details relevant to the disease and management.

Conflict interest:

None

Authors contribution:

All authors were involved in the management of the patient.

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CASE REPORT

CHALLENGES IN DIAGNOSIS AND MANAGEMENT OF NON- TUBERCULOUS MYCOBACTERIAL INFECTION: REPORTED THREE CASES

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Abstract:

Non-tuberculous mycobacteria (NTM) can cause a wide range of infections, from affecting the lungs (pulmonary) to the other parts of the body (extrapulmonary) like skin, soft tissue, surgical wounds, and areas around catheters and implants. A significant challenge is that NTM infections are often misdiagnosed as tuberculosis. This case series highlights these difficulties by exploring three patient experiences. The first case involves a 48-year-old man who developed a prolonged fever following coronary artery bypass grafting (CABG) surgery. He also presented with enlarged liver and spleen (hepatosplenomegaly). Imaging studies revealed a large saccular aortic ascending aneurysm. While surgery (ascending aortic and proximal arch replacement) addressed the aneurysm, the definitive diagnosis came later. Histopathological and microbiological examinations ultimately revealed the culprit to be NTM. In second case, a 56-year-old male underwent a laparoscopic bilateral total extraperitoneal inguinal hernia repair. However, he experienced persistent serous drainage from the incision site post-surgery. To investigate the cause, discharge was collected and subjected to various tests. Therefore, a PCR test for Non-tuberculous Mycobacteria (NTM) was performed. This test returned positive, confirming the diagnosis of NTM infection rather than tuberculosis. And our third case was post operative endophthalmitis following cataract surgery due to NMT. Through these case reports, our Aim is to raise awareness among healthcare professionals.

Keywords: *Challenges in Diagnosis, Non- Tuberculous Mycobacterial infection*

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Introduction:

Non-tuberculous mycobacteria (NTM) are increasingly recognized as human pathogens globally.[1] Of NTMs isolated, *Mycobacterium abscessus* is associated with the most severe infections including progressive pulmonary disease, skin and soft tissue, central nervous system and often fatal disease.[2] Bangladesh is an endemic zone for Mycobacterium tuberculosis (M.TB) but NTM infection is often under-detected. Diagnosing NTM infections is very challenging and they require prolong antibiotic therapy.

Case1:

A 48-year-old Hypertensive, Diabetic, known case of hypothyroidism with the history of CABG due to triple vessel disease presented with the complained of Fever for 3 months. Fever was initially low grade then became high grade continued in nature, highest recorded temperature was 103p F and was subsided by taking antipyretics. He had no other systemic complaints. He also had history of unintended 10kg weight loss duration his course of illness. On general examination, patient was ill-looking and anaemic. His vitals were

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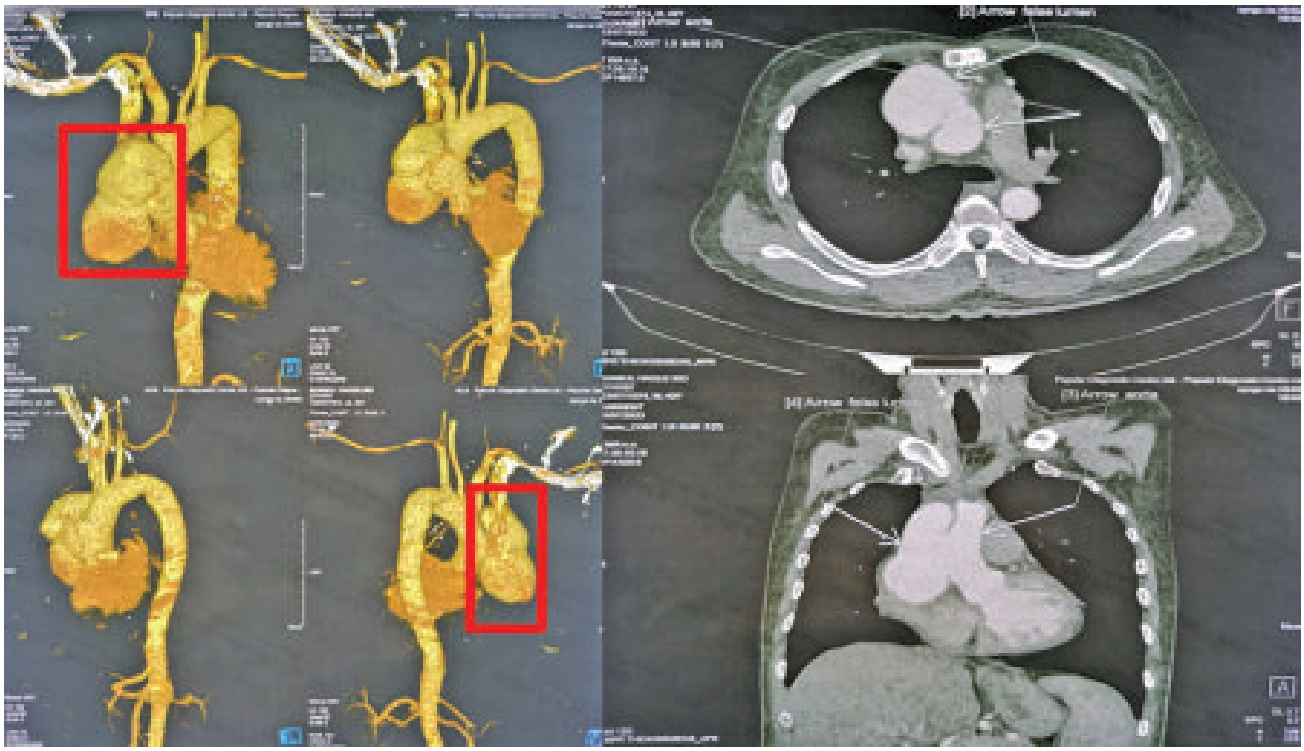

Fig.-1 **Fig.-2**

Fig. 1 and 2 : *Showing pouching and false lumen in ascending aorta*

normal. On abdominal examination there was hepatosplenomegaly. Other systems examination revealed no abnormality. On Routine investigation, CBC showed HB was 8.5g/dl with normal leucocytes level. Liver and renal function were normal. Chest X-ray showed cardiomegaly. Urine culture, 3 sets of blood sample taken from 3 different sites for culture were normal. ICT for Kala-Azar, ICT for Malaria, Febrile Antigen, all were normal. Tuberculin test were negative. Colour doppler echocardiography showed no abnormality but Transesophageal echocardiography showed No definite dissection in ascending aorta. But A large rounded luminal structure seen beside right atrium measuring about (54X50cm)

Dynamic view of CT scan of chest showed double lumen of ascending aorta with intimal flap suggestive of Aortic dissection CT aortogram : Shows,Large lobulated irregular saccular ascending aortic aneurysm Figure 1 & 2.

Empirical antibiotic therapy considering infection of aortic aneurysm including Amoxicillin, Gentamycin and vancomycin was started and shifted to cardiac surgery unit. Redo sternotomy - Ascending aortic and proximal arch replacement using 28mm VASCUTEK GRAFT done. Excised sample was sent for Gram stain and Z-N stain which showed AFB but no pus cell or bacteria. In Gene x pert no MTB was detected but PCR showed NTM (Mycobacter abscessus). Finally patient was treated with four drugs regimen (clarithromycin 500mg 12 hourly, ciprofloxacin 500mg 12 hourly, linezolid 400mg 12 hourly, and amikacin 500mg 12 hourly) for initial 6 weeks.Followed by 5months with three drugs regimen (clarithromycin 500mg 12 hourly, ciprofloxacin 500mg 12 hourly, and linezolid 400mg 12 hourly).

Case 2: A 56-yr-old man presented with persistent discharging sinus from anterior abdominal wall for 1 year. He had History of laparoscopic bilateral TEP hernia repair for inguinal hernia. He had no history of fever, cough, abdominal pain or any other systemic illness. On General examination there were no abnormality but local examination of the wound revealed single discharging sinus (Fig. 3). There was no local rise of temperature, tenderness or regional lymphadenopathy.

On routine investigation, Complete blood count, liver function, renal function and chest x-ray all were normal. Serosanguinous exudate was collected and was subjected to a Grams stain, Ziehl– Neelsen (ZN) stain. Pus cell was not found in gm stain but Z-N stain showed AFB. Biopsy was taken and Histopathology showed granulomatous inflammation, inflammatory granulation tissue, foreign body giant

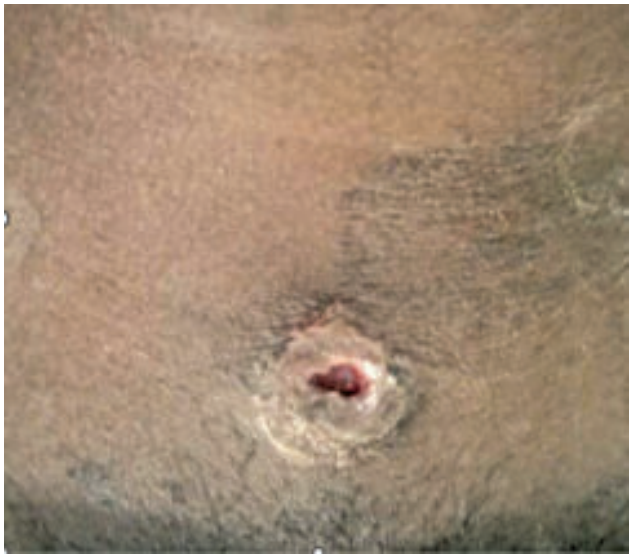

Fig.-3 : *Discharging sinus in the port.*

cell reaction & fibrosis. Anti –TB was started but patient didn't showed any response. Again, discharge was sent for Gene-Xpert and PCR for NTM. No Mycobacterium tuberculosis was detected in Gene-Xpert but PCR showed *M. abscessus*. Finally patient was treated initially for 6weeks with four drugs regimen (clarithromycin 500mg 12 hourly, ciprofloxacin 500mg 12 hourly, linezolid 400mg 12 hourly, and amikacin 500mg 12 hourly), Followed by 5months with three drugs regimen (clarithromycin 500mg 12 hourly, ciprofloxacin 500mg 12 hourly, and linezolid 400mg 12 hourly).

Case 3: A 70-yr old man underwent for an uneventful cataract surgery with intraocular lens (IOL) implantation of the left eye. One year later he developed progressive painless visual loss in the operated eye. His vision was 6/36 in the left eye. Slit-lamp examination showed ciliary injection, 2+ cells in the anterior chamber, and posterior synechiae (Fig.-4).

There was white plague deposited on the posterior capsule which was noted as posterior capsule opacity. The fundus examination was normal. Initially treated conservatively but as it was progressive, B-scan ultrasound was done which revealed heterogenous vitreous echogenicity. As a result, pars plana vitrectomy (PPV) done. Vitreous scraping sent for culture and PCR revealed M. Abscessus . He was treated with intravitreal injection of vancomycin for 14 days followed by 6 month-course of oral clarithromycin and ciprofloxacin.

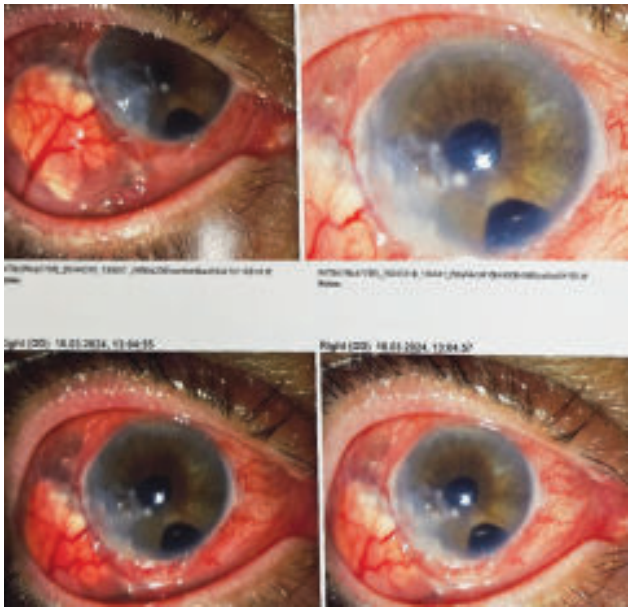

Fig.-4: *Slit lamp examination of left eye*

Discussion:

Now a days Nontubercular mycobacteria are increasingly reported because of improved microbiological diagnostic methods and enlarged immunocompromised hosts in recent years.[3]

Our first case was infective aortic aneurysm due to NTM. The aorta, as a major blood vessel is resistant to damage or destruction compared to other body blood vessels. However, a few factors can weaken the aortic wall, cause aneurysms, and also predispose the aorta to infectious etiologies. These factors include uncontrolled diabetes mellitus or hypertension, cancer, iatrogenic inoculation as a result of surgical intervention or the use of medical equipment or devices in and around the aorta, atherosclerotic diseases, vascular malformations, or medial cystic necrosis of the vascular wall. The route by which aortitis occurs includes hematogenous seeding of an existing intimal injury, septic emboli, direct spread from an infectious site, and bacterial inoculation.

In this case, aortic aneurysm developed most likely following CAG.

CT angiography is currently the best imaging technique for diagnosing mycotic aneurysms.4 In particular, the CTA enables the early detection of changes in the vascular wall and thus a faster diagnosis.[4]

In our second case, post operative wounds were healed initially, then within the next 1–2 months, incision sites became erythematous, and indurated, small blisters formed, burst out, and started serous discharge in

small quantities. Several antibiotics were recommended but did not respond to any of them. Even anti TB was started and didn't respond, moreover discharge continued and persisted. During operation, wounds are contaminated with NTM from environmental sources and take some time to make their clinical appearance. After infection with NTM, the operation scar breaks down and develops a nonhealing superficial ulcer with the sinus tract from which non-purulent serous discharge comes out.[5] Bhalla et al.[6] reported that 10.9% of postoperative wound infections occurred by NTM in South India.

In our third case, the infection often occurred within 1 month after ocular surgery. Cataract surgery was accounted for the most common procedure related to the infection. On the other hand, NTM endogenous endophthalmitis mainly took place in immuno-compromised patients. Our patient was diabetic. In 2015, Kheir et al reported that NTM endophthalmitis had no gender differences and the median age of presentation was 44 years. Among all exogenous endophthalmitis patients, the infection usually occurred after ocular intervention which 48.6% was cataract surgery with an average time of 11.5 weeks after ocular surgery. [7]

Skin or soft tissue infection is the most common manifestation seen in NTM-infected individuals whose wounds may be exposed directly or indirectly to the soil, colonized tap water, unsterilized operative instruments, or medical devices contaminated with environmental NTM after traumatic injury, during surgery, or cosmetic procedures.[8] Strict sterilization of all OT equipment, proper hand washing, and prevention of wound contamination with dust, soil, and tap water are needed to prevent wound infections with NTM.

In All three cases are infected by Mycobacterium Abscessus. The most preferred choice is a varying combination of antibacterial drugs like imipenem, amikacin, fluoroquinolones, doxycycline, linezolid, and clarithromycin.

Until now, there has been a lack of data regarding prevalence, diagnostic methods and treatment of NTM infections in Bangladesh. Therefore, such cases usually treated initially as general wound infections and sometimes by therapeutic anti tubercular regime. Recently, NTM infections have attracted more attention to the clinicians due to the increase in such cases; but still, there is a lack of awareness. When persistent chronic discharge from postoperative wound infections occur after operations that cannot be cured by usual antibiotics, NTM infections should be suspected and Z-N stain, culture, Gene-Xpert, and PCR must be considered as diagnostic tools to treat the patients with appropriate anti-NTM drug regimen.[9]

Conclusion:

All three case reports emphaseze that despite the rarity, clinicians should still consider the possibility of mycobacterial infection, in cases of no improvement following treatment with broad-spectrum antibiotics. Our Aim is to raise awareness among healthcare professionals through these case reports. A high degree of suspicion is necessary for accurate diagnosis as NTM infections often mimic the symptoms of other bacterial infections, making them difficult to distinguish.

Conflict of Interest:

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

Funding:

This research received no external funding.

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

YOUNG WOMAN WITH HEADACHE AND DOUBLE VISION: A RARE CASE REPORT ON ORBITAL PSEUDOTUMOR

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Abstract:

An uncommon inflammatory disorder that affects the orbit of the eye is called orbital pseudotumor. It can present in a variety of clinical ways. Its precise etiology is yet unclear, although an immune-mediated response is thought to be involved. A 35-year-old woman arrived to the neurology clinic with symptoms of double vision and persistent headache. There was a mild protrusion of the left eye from the orbital cavity, the eyeball medially rotated in the primary position, and restriction of left-sided eyeball movement towards the left side with complaints of increasing double vision during the attempt. She had no recent medical history or traumatic experiences. Over the course of three weeks, the initial discomfort had increased. There were no known allergies, however the patient was normotensive. Upon examination, the left eye had flare, slight anterior chamber cell, erythema, and eyelid edema. Magnetic resonance imaging showed involvement of the optic nerve, thickening of the extraocular muscles, and augmentation of orbital soft tissues. Inflammatory markers were high in the laboratory results. An orbital pseudotumor was diagnosed. The patient was treated with Inj Methylprednisolone followed by corticosteroids, her symptoms improved and the inflammatory condition subsided. A thorough approach including imaging scans, laboratory testing, and clinical evaluation is necessary for its diagnosis. The importance of recognizing an uncommon presentation and management of orbital pseudotumor with was highlighted in this case report.

Keywords: *Double Vision, Headache, Orbital Pseudotumor, Idiopathic Orbital Inflammatory Syndrome*

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Introduction:

An uncommon inflammatory disorder that affects the orbit of the eye is called orbital pseudotumor, or idiopathic orbital inflammatory syndrome. Several anatomical sites and components, including as the extraocular muscles, glands, and connective tissues, may be affected by the inflammation linked to orbital pseudotumor. The clinical signs of orbital pseudotumor are varied and include proptosis, ocular discomfort, edema, and visual abnormalities.[1] It is thought to be

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caused by an immune-mediated reaction, while the precise cause is yet unclear. Orbital pseudotumor is difficult to diagnose since it necessitates ruling out other orbital disorders by combinations of clinical examination, laboratory tests, and neuroimaging.[1] The usual course of treatment is systemic corticosteroids, but biological treatments and other immuno-suppressive medications have also showed promise[2]. The aim of this case report is to provide a comprehensive clinical case of ocular pseudotumor, emphasizing the difficulties in diagnosis and treatment while discussing thorough the strategy for management.

Case report:

A 35-year-old woman first consulted a primary care physician for double vision and persistent headaches for 3 days. As routine analgesics were not beneficial, she was referred to a neurology clinic and after assessment instructed for admission. Her double vision was more during her left lateral gaze. She described pain in the left side of the head including the left eye and cheek. Her pain was dull aching, moderately severe, and persisting in nature. Conventional analgesicswere partially beneficial initially. There was no trauma to her eye. No redness or watering from the eyes. On examination, her heart rate was 88 bpm, normotensive BP 120/75 mmHg and she was afebrile. There was a mild protrusion of the left eye from the orbital cavity, the eyeball medially rotated in the primary position, and restriction of left-sided eyeball movement towards the left side with complaints of increasing double vision during the attempt. Her past medical history was not significant.

We have organized several routine blood tests: Hb 10.8 gm/dl, ESR 60 mm in 1st hour, WBC count 6500/cumm and normal lymphocyte count, blood glucose, and serum creatinine. Serum TSH 2.1 mIU/L (normal value 0.5 to 5.0 mIU/L) MRI of the brain was unremarkable, however, MRI of orbits revealed swelling and contrast enhancement of the extraocular muscles and lacrimal gland of the left side (Fig.-1). Mild thickening and contrast enhancement noted in the left optic nerve sheath (Fig.-2). We have excluded Graves's ophthalmopathy, cerebral venous sinus thrombosis, Tolosa Hunt syndrome, and retro-orbital space-occupying lesion in this case. The patient was diagnosed with orbital pseudotumor based on the imaging data, laboratory results, and clinical presentation. The presence of orbital inflammation, normal intraocular pressure, swelling and contrast enhancement of the extraocular muscles and lacrimal gland, involvement of the optic nerve sheath, and increased inflammatory markers all supported the diagnosis.

After a consultant review, she was treated with intravenous methylprednisolone for five consecutive days which significantly improved her headache as well as double vision. Subsequently, oral prednisolone was instituted daily as a morning dose of 1 mg/kg body weight for one month.

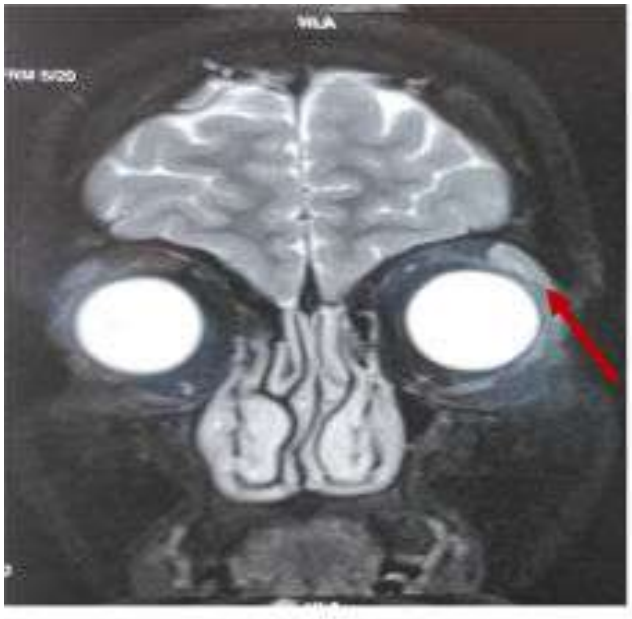

Fig.-1: *MRI orbit (coronal view) showing enlargement and enhancement of left lacrimal gland*

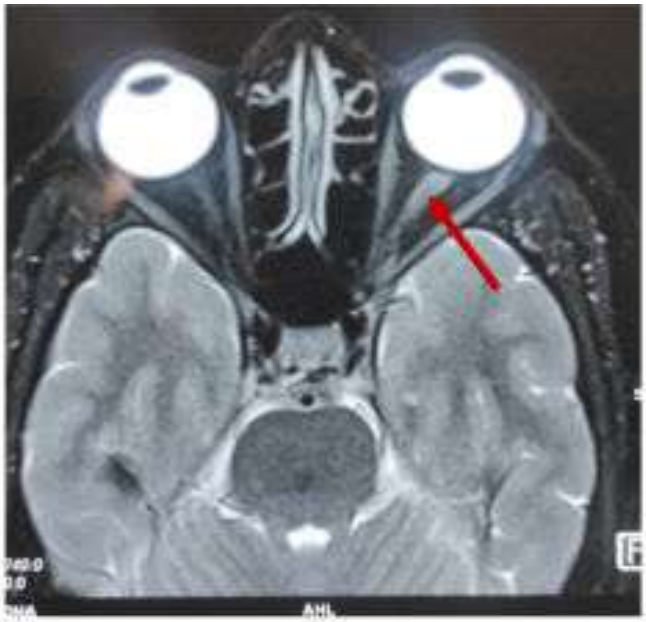

Fig.-2: *MRI orbit (axial view) showing left optic nerve thickening and enhancement*

She was discharged from the hospital after a week, with only oral medication and there was no threat to her vision and safety. There were no symptoms on her follow-up visit after two weeks in the outpatient department. No physical sign was noted. Considering the high recurrence a slow tapering of steroid was adopted. She was instructed regarding the possible side effects of steroids and how to avoid them. A subsequent visit to the outpatient department was scheduled after one month.

Discussion:

Because of its varied clinical appearance and unclear origin, orbital pseudotumor, sometimes referred to as an idiopathic orbital inflammatory syndrome, is an uncommon inflammatory disease that presents diagnostic difficulties.[3] Differentiating orbital pseudotumor from other ocular diseases can be challenging due to the vast range of clinical presentations.[4] Patients most frequently complain eye discomfort, eyelid swelling, diplopia, proptosis, visual abnormalities, and decreased visual acuity. A mix of clinical findings, imaging tests, and laboratory analyses are used to diagnose orbital pseudotumor. Assessing the degree and location of ocular inflammation requires the use of imaging methods such MRI with contrast.[3]

In patients with orbital pseudotumor, it is also quite sensitive in identifying orbital inflammation, which helps distinguish it from other orbital diseases. Laboratory tests that show the existence of systemic inflammation, such as those measuring C-reactive protein and erythrocyte sedimentation rate, operate as supporting measures. However, because they are not specific for orbital pseudotumor, their diagnostic use is restricted.[4]

The main goals of managing orbital pseudotumor are to maintain vision and regulate the inflammatory response.[1,5] Systemic corticosteroids, including prednisone, are thought to be the cornerstone of therapy. Oral corticosteroids at high doses have been shown to quickly reduce inflammation and symptoms in orbital pseudotumor patients.[1]

While it can strike at any age, adults are the ones most affected, with a peak occurrence in the fourth to sixth decades of life.[3] No gender preference is known to exist.[3] It is thought that an immune-mediated response has a role in orbital pseudotumor, albeit the precise cause is yet understood. No definite risk factors or predisposing variables have been identified for orbital pseudotumor.[3] Furthermore, more thorough research is needed to evaluate the long-term effects of various treatment approaches and pinpoint factors that predict treatment response and recurrence.[4]

Nevertheless, prolonged use of corticosteroids is linked to serious adverse effects, which makes the investigation of other therapeutic approaches necessary.[1,2] With encouraging outcomes, immunosuppressive medications including methotrexate and azathioprine have been used as steroid-sparing medicines in recent years.[2,5] Refractory patients have also demonstrated the effectiveness of biologic medicines that target certain inflammatory pathways, such as tumor necrosis factor-alpha inhibitors.[2]

Debate surrounds the function of a biopsy in ocular pseudotumor.[6] When other diagnostic techniques are unable to produce a conclusive diagnosis, or when there is a suspicion of malignancy or unusual presentations, the biopsy may be taken into consideration. However, each person must consider the advantages and disadvantages of performing a biopsy before making the decision.

Conclusion:

Finally, this case report of orbital pseudotumor provides a thorough assessment of a challenging clinical case, emphasizing the diagnostic challenges and therapeutic techniques associated with these uncommon inflammatory diseases. Numerous treatment plans are available due to the disease's varied nature and the development of immuno-suppressive medications. According to retrospective research, individuals often see a reduction in their symptoms. Steroids are often regarded as the first line of therapy for this disease.

Conflict of Interest:

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

Funding:

This research received no external funding.

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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CLINICAL IMAGE

MEDICAL QUIIZ: IMAGE -1

A K M MONWARUL ISLAM[1], ABDUL WADUD CHOWDHURY[2] , HUMAYRA JESMIN[3]

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Citation: *Islam AKMM, Chowdhury AW, Jesmin H. Clinical Image-1. Bangladesh J Medicine 2025; 36: 75.*

A 57-year-old normotensive, non-diabetic man (Figure 1A) presented with effort intolerance and leg swelling for 3 months. His serum creatinine was 1.1 mg/dl, and urine R/E showed 2+ proteinuria. He underwent electrocardiography (ECG) (Figure 1B), and transthoracic echocardiography (TTE) (Figure 1C-E). His coronary angiography (CAG) revealed normal epicardial coronary arteries. The urine was negative for Bence-Jones protein, plasma protein electrophoresis was normal, but serum light chain ratio was grossly altered. Subsequent tongue biopsy confirmed the diagnosis.

Questions:

Q1. How can the facies be described?

Q2. What is the ECG diagnosis?

Q3. What are the important findings in echo-cardiographic images C to E?

Q4. What is the clinical diagnosis?

Q5. What is the expected finding in tissue biopsy?

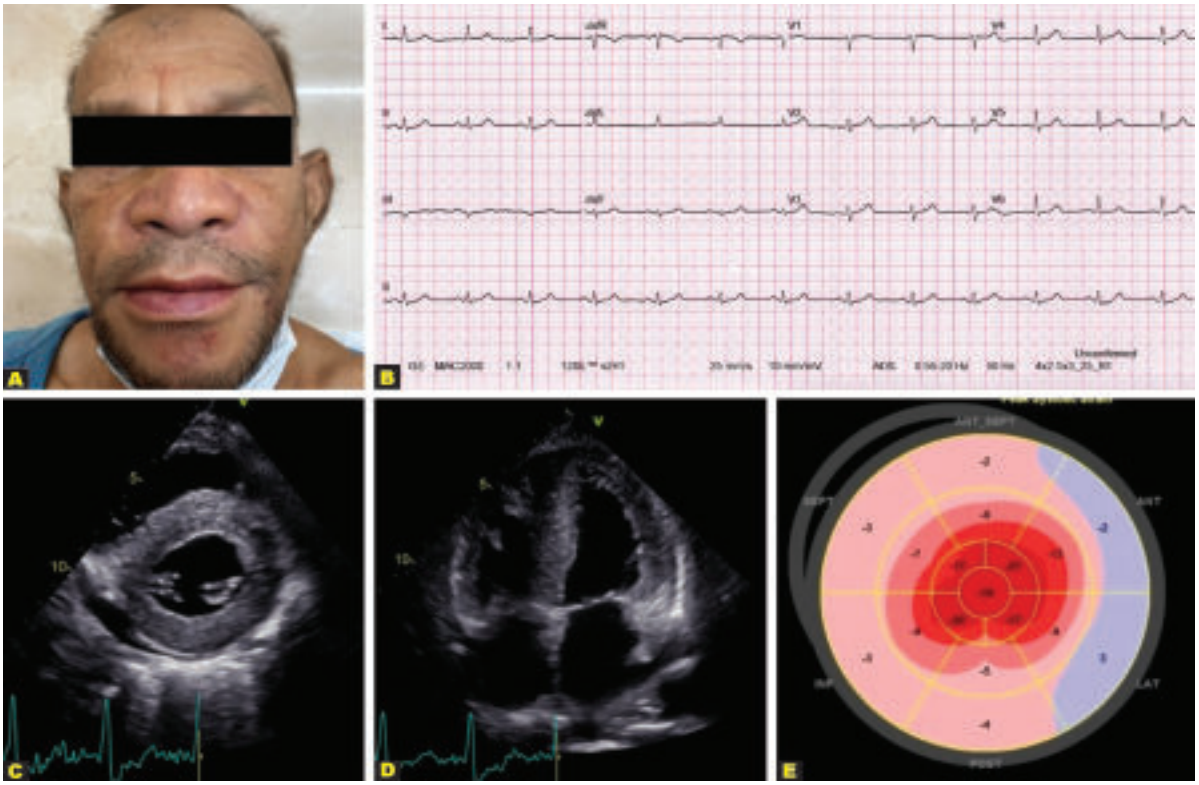

Figure 1

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CLINICAL IMAGE

MEDICAL QUIIZ: IMAGE -2

AMINUR RAHMAN[1]

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Keywords: *MRI of Spinal Multiple sclerosis, Spinal MS, radiological of Spinal MS*

A 30 years old female university student with no significant personal past or family history presented with backache for past 3 months which was aggravated during exertion relieved with analgesics. Since 1month she had shooting type of sensation across the back of thigh while bending forwards. These complaints were continuing till two weeks back, when she had felt weakness of left lower limb including proximal and distal muscles associated with urinary incontinence and paraesthesia. But she was able to appreciate all the normal sensations. She also felt band like sensation over the level of umbilicus. MRI of cervical spine with contrast was done (Fig. A1, A2, B1, B2). Please answers the following questions

A. What are the findings of the MRI?
B. What is the diagnosis?
C. What is the treatment?
D. Mention two newer drugs approved by FDA

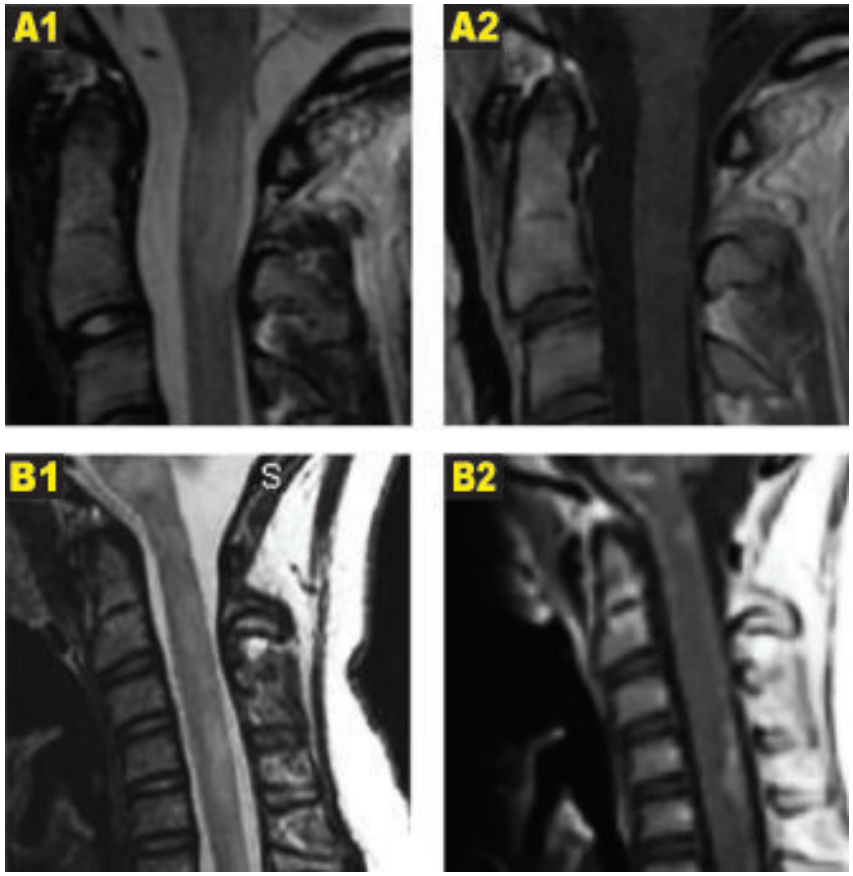

Figure (A&B): *MRI of cervical spine with contrast was done*

Address of Correspondence: Prof. Aminur Rahman**,** Professor and Head, Dept. of Neurology, Sir Salimullah Medical College, Dhaka-1100, Bangladesh**,** E-mail: draminur@yahoo.com, https://orcid.org/0000-0001-9261-7734.

Answer to Medical Quiiz -1

Answers:

1. Leonine facies.
2. Low voltage ECG.
3. Two-dimensional echocardiography left parasternal short-axis (C) and apical 4-chmber (D) views show significant left ventricular hypertrophy, granular appearance of myocardium and mild pericardial effusion. Image 1E represents bull's eye mapping of speckle-tracking echocardiography showing cherry-on-top appearance or apical sparing pattern.
4. Amyloidosis with cardiac involvement.
5. Apple-green birefringence under polarizing microscopy with Congo red staining.

Overview of amyloidosis with cardiac involvement

Amyloidosis is a heterogenous group of disorders characterized by deposition of abnormal amyloid proteins in the body.[1] Amyloid deposits can build up in the heart, brain, kidneys, spleen and other parts of the body. A person may have amyloidosis in one or more organ. Mainly two types of amyloidosis affect the heart: AL amyloidosis and ATTR amyloidosis.[2] AL amyloidosis is closely related to plasma cell dyscrasia and is characterized by deposition of either kappa or lambda light chains in tissues.[2] On the other hand, ATTR amyloidosis occurs when the liver-derived protein transthyretin (TTR) misfolds and builds up in the organs and tissues.[2] These 2 types of cardiac amyloidosis produce similar findings in echocardiography, i.e., biventricular hypertrophy, biatrial enlargement, granular myocardium, systolic and diastolic dysfunction, and "cherry-on-top" appearance in bull's-eye mapping of strain echocardiography.[3] In fact, cherry-on-top pattern has 93% sensitivity and 82% specificity for cardiac amyloidosis.[4] Significantly altered kappa-lambda light chain ratio in serum and monoclonal band in urine or serum in immunofixation electrophoresis are needed for the diagnosis of AL amyloidosis.[3] For ATTR amyloidosis, preferential grade 2 or grade 3 radiotracer uptake by the myocardium in 99mTc-pyrophosphate scanning is suggestive.[5] The diagnosis of amyloidosis is confirmed by histopathological examination of representative tissue showing apple-green birefringence under polarizing microscopy with Congo red staining.[1]

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Answer to Medical Quiiz -2

Answers:

A. MRI of Cervical spine magnetic resonance imaging. (A1-B2) of sagittal slices demonstrate demyelinating lesions in the cervical spinal cord <2 segments). (A1, B1) T2-weighted images. (A2, B2) T1-weighted and postcontrast images.

B. Primary progressive Multiple sclerosis

C. I.V methylprednisolone followed by oral prednisolone

D. Ocrelizumab and Ublituximab-xiiy

Overview:

Multiple sclerosis (MS) causes inflammatory demyelination and neurodegeneration in the brain and spinal cord. [1,2] MS is a multiphasic, chronic, relapsing demyelinating disease characterized by acute or subacute neurologic impairments. This condition primarily affects young to middle-aged females. Approximately 80% of MS patients acquire spinal cord lesions [3], which are more frequently symptomatic than brain lesions and can cause severe impairment such as ambulation, coordination, bladder and bowel function.

Spinal MS is frequently accompanied with concurrent brain lesions; nevertheless, up to 20% of patients with spinal lesions lack intracranial plaques. In contrast to the brain, both white and gray matter can be impacted in the spine. There is no substantial link between the size of the plaques and the level of clinical impairment. [3]Spinal cord atrophy is mainly important to progressive forms of MS (primary and secondary progressive), when it is closely associated with physical disability. [4]

The normal MRI involvement pattern is less than two cord segments, peripheral and ovoid appearance, and paracentral placement.[5] MS is distinguished by the development of numerous demyelinating lesions in the brain and spinal cord that progress in time and space.[6]Typical features for MS in Spinal cord in Box:1.[1,7]

Ocrelizumab is a humanised anti-CD20 monoclonal antibody used to treat multiple sclerosis (MS). The Food and Drug Administration (FDA) approved it in March 2017 for use in adults with RRMS and PPMS. Ocrelizumab is the sole disease-modifying treatment (DMT) approved for PPMS. [8] The FDA authorized Ublituximab-xiiy (Briumvi) in 2022. It is used to treat the relapsing-remitting and active secondary-progressive forms of MS. Ublituximab's method of action involves the reduction of B cells by antibody-dependent cellular cytotoxicity, as B cells play an important part in the pathogenesis of MS. Ublituximab is the first anti-CD20 medication provided twice a year as one-hour infusions after the initial doses.[9]

Box:1 *Typical radiological features for MS in the spinal cord*

1) There are multiple lesions in the spinal cord.
2) Typical spinal cord lesions in MS are relatively small and peripherally located.
3) They are most often found in the cervical cord and are usually less than 2 vertebral segments in length
4) In the cord there are some well-defined lesions, but also some ill-defined foggy lesions.
5) The transverse image shows the dorsal location and the typical triangular shape.
6) Continue with the contrast-enhanced image
7) Proton density weighted image (PDWI) is crucial for studying the spinal cord. On PDW-images the spinal cord has a uniformly low signal intensity (like CSF), which gives the MS lesions a good contrast against the surrounding CSF and normal cord tissue.

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