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EDITORIAL

DENGUE, WHAT WE LEARNT FROM THE RECENT TRENDS

When a sero survey on dengue conducted at Chattogram city in late 1990s found around 13% cases of acute febrile illness positive for dengue it was a surprise.[1] Following first significant outbreak in 2000, dengue is now recognized as a major public health problem. There was a rapid global spread of dengue disease. To note some salient aspects of dengue: absence of simple diagnostic tool for the early phase, absence of specific therapy, and absence of effective & efficient vector control. Dengue is now also considered as a climate sensitive emerging neglected tropical disease, related with rainfall, temperature, humidity; breeding places and time of incubation period has now found to be correlated with temperature. A similar phenomenon happened with Vibrio Cholerae in the past and with sudden upsurge of cases of malaria in the Chattogram Hill Districts in 2014.[2]

A brief revisit of program on vector borne diseases-malaria program amalgamated initially with primary health care, later with CDC, DGHS was renamed as vector borne diseases cinbrel (VBDC) program, and recently named as Malaria & aedes transmitted diseases unit DGHS. During outbreak the Emergency Cell of DGHS, Government of Bangladesh take care of reporting of selected illness including dengue on daily basis based on compilation of cases, although few hospitals reporting, recently increased number of hospitals are found to be reporting.

Infectious diseases Act 2019 has been promulgamated with 23 diseases to be reported by health care professionals which is yet to be operationalized.

There was a recent survey on different entomological indices in Dhaka city and all over which gave a warning of possible increase of cases in 2019.

In 2000- in Bangladesh a total of ~5000 cases of dengue, with <100 deaths were repported. In 2019 cases increased to ~100,000 with little more than ~120 official confirmed death (Figure: 1).

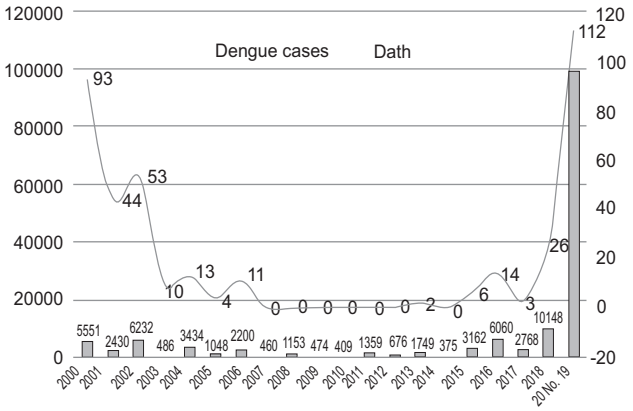

Fig.-1: *Reported Dengue Cases and Deaths, Bangladesh: 2000 – 2019*

Even in the last week of November, December there are reports of cases of dengue being admitted in different hospitals (Figure: 2).[3]

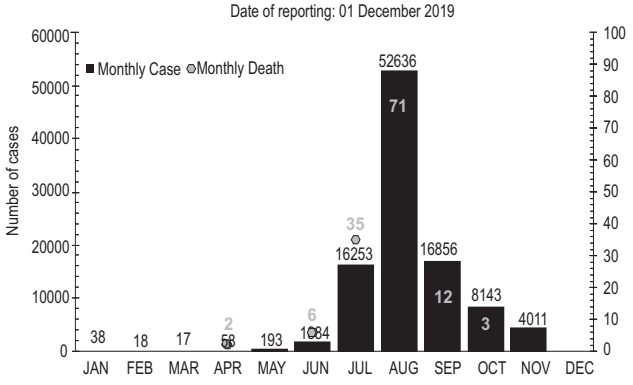

Fig.-2: *Health Emergency Operation Center and Control Room, DGHS: Reported Monthly Dengue & suspected Dengue Cases Confirmed Deaths, Bangladesh.*

The number of cases of dengue in 2019 is likely to be under reported, the actual number may be many folds higher.[4]

Dengue become an endemic in Bangladesh with spread to even rural township.

During the outbreak in 2000 expectations was, to do haematocrit for assessing the cases, providing fluid

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management and heavily reliant mostly on platelet transfusion with a hue and cry for cell separator. In 2019 NS1 has been found to be used during acute phase, and IgG, IGM to see the status of infection, and the professionals and the community aspiring to use more ICU care for management with a large number of media reports of death. Triage was tried as well in hospitals flooded with cases to identify severe cases. While providing care- management focused at ICU based in some occasion, fluid management at ICU and even in some hospitals dedicated unit for dengue was established. There was also lack of proper training initially of ICU physicians.

During early part of outbreak general wards were used for management later on dengue dedicated ward was established. In Bangladesh there are a large variety of specialists but infectious diseases is not considered as specialty. The quick setting up of dedicated dengue ward gave some confidence among the public and the professionals. Specific dedicated ID ward is now more urgent to consider in medical college hospitals and in medical universities which will be able to cater the unmet need to address a large variety of infectious diseases prevailing in the country.

Concurrent DENV infection, Chikunguniya virus, Zika virus infections are also recorded in a small proportion of cases.

In earlier outbreak more childhood cases were found then adult cases detected this year, a proportion elderly patients were also affected who had other co-morbidity

The WHO dengue Guidelines was used to update the National Guidelines, Bangladesh Society of Medicine (BSM) developed a short version as well. The BSM having a nationwide network with specialists was entrusted to provide training to health care professionals within short time which was sucessful.[5]

A number of atypical characteristics not attributable to plasma leakage(increase vascular fragility and permeability), gastrointestinal problem 10-49%, pleural effusion, neurological manifestations- encephalitis, encephalopathy, GBS, myocarditits were also reported.

It was not unexpected to have co- infection with influenza (season from April to September), and co-infection with enteric fever. Other differential diagnosis needs to be considered during the outbreak. During outbreak only 20% were positive with dengue, what are the other organisms are in circulation with dengue? Unfortunately we do not have a capacity to diagnose cases of acute febrile illness nor such a broad range of point of contact user friendly diagnostic tests are available.

There was a continued steroid controversy for management of severe cases with a mixed opinion among physicians, quickly BSM planned for conducting an RCT.

Despite a large evidence generated through dengue research- issue of vaccine- to whom, and when are still not solved.

A new arena of sexual transmission of dengue- recent report from Europe from a returning traveler from Brazil is to be further confirmed.

We have to learn how to live with dengue due to country wide spread of infections. In a future introduction of new/different sero type of dengue virus in the population infected this year will be at risk of having secondary infection with a potential risk of severe dengue.

A vector control strategy according to the Global Vector Control Strategy involving the local Government Rural Development (LGRD), community, increasing the capacity with adequate vector biologists is a pre requisite for control of dengue.[6]

Till better diagnostics are available which is an urgent gap to mitigate and improved management without specific drug is not going to solve the problemand thus individual/self care and community engagement is crucially important.

Bangladesh Health Sector Programe is committed to provide quality care. For addressing diseases like dengue all of Government approaches, whole of society approaches, health in all policies should be adopted as we committed in the UN High Level Political Declaration.[7]

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ORIGINAL ARTICLES

ROLE OF NERVE CONDUCTION STUDY IN POLYNEUROPATHY

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Abstract:

Background: *Polyneuropathy has many different causes. It is often very difficult to find out the cause. Nerve conduction study (NCS) can classify neuropathy as axonal and demyelinatig variety and direct the search for cause.*

Methodology: *Purposively selected 80 patients from the department of Neurology Dhaka Medical College during the period of January 2009 to June 2010 were taken for NCS whose were compatible with polyneuropathy by history and clinical examination. Clinical, electrophysiological feature and pattern of polyneuropathy were analyzed.*

Results: *Mean age of the patients was 34.5 ±6.8 and M: F was 1.8:1. Students, laborer and cultivators were the most affected people. 55% patients were acute cases and 35% patients were chronic Cases. 30% patient had no known risk factor for neuropathy 25% patient had antecedent infection, 15% had diabetes mellitus, 7.5% were exposed to drugs/toxins or solvents and 5% had family history of neuropathy. In clinical examination 37.5% patients were in motor type, 10% pure sensory type and 52.5% mixed sensorimotor type. In NCS47.5% were motor, 7.5% pure sensory 45% mixed sensorimotor type. Axonal were 47.5%, demyelinating 27.5% and 25% as mixed axonal and demyelinating type.*

Conclusion: *NCS in polyneuropathy play critical role by classifying it as axonal or demyelinating and shorten the cause.*

Key words: *polyneuropathy, nerve conduction study*

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Introduction:

Polyneuropathy is the disorder in which the functions of numerous peripheral nerves are affected at the same time and leads to distal and symmetrical deficit with loss of tendon reflexes[1]. It is a relatively common syndrome which is often distressing and sometime disabling or even fatal.[2] Polyneuropathy has an estimated incidence of 25-200/100,000 persons per year and a prevalence of about 5%.[3]

Peripheral nerves have motor, sensory and autonomic component. Nerve fibers (axons) can be classified as either small fibers or large fibers. Large nerve fibers neuropathy affect many functions including - motor function, vibration perception, position sense, perception of temperature. Symptoms associated with large fibers neuropathy includes -numbness, tingling, weakness, pain, loss of deep reflexes. Symptoms of small fiber neuropathy are many and includes—pain describes as burning, stabbing, prickling, jabbing or lancinating (piercing), sensation of broken glass, burning sands, or ice pick in the bone, tight band like pressure, insensitivity to heat or cold and autonomic dysfunctions related to the organs.

Sensory nerves damage produce symptoms such as pain, numbness, tingling, burning or loss of sensation or feeling. Lack of sensation can produce cuts or burns unnoticed and ulcer or poor wound healing. Motor nerves damage results in decreased movement and

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muscle wasting. Symptoms usually begin as weakness or heaviness of the hands and or feet and may deteriorate over time.[4]

Polyneuropathy (PN) as a syndrome has many different causes and worldwide diabetes mellitus is the commonest cause other being are hereditary neuropathy, deficiency of vitamins, B_1, B_{12}, uremia, autoimmune neuropathies, infections including leprosy and HIV, drugs and toxins, porphyria ,paraneoplastic state and 25% cases are idiopathic. [5, 6] About 80% of polyneuropathies are axonal and the remaining 20% are demyelinating. Most of the axonal polyneuropathies are either purely sensory or mixed sensory motor type.[2]

NCS play a critical rule firstly to confirm the diagnosis of PN and then to classify it as axonal or demyelinating variety and thereby directing the search for cause.[5,7] Furthermore electrophysiology is quite sensitive to detect sub clinical involvement of either motor or sensory component of apparently pure sensory or pure motor PN giving further clue to the aetiology.[8,9]

PN are also classified into acute and chronic form. Acute forms PN are those that have relatively dramatic onset and usually recovers within six weeks. The classical and commonest example of that group is Guillaine Barre Syndrome (GBS). The other less common causes of acute PN are vasculitic, drugs and toxins, porphyria diphtheria, acute idiopathic sensory neuropathies. Chronic PN are those which usually develop over several months. Most of the classical chronic PN which presents with signs symptoms of distal symmetrical way falls into this category. The causes of chronic PN are diabetes mellitus, uremia, alcoholism and other toxins, drugs, underlying neoplasm, hereditary (Charcot Marie tooth disease) and idiopathic.[10, 11, 12] After exclusion of common causes of PN routine and specific investigations is the first stage of screening, neurophysiological studies in the form of nerve conduction study (NCS) and electromyogram (EMG) becomes the vital and important way of approach to the underlying cause in the second stage. The subsequent investigation in the third stage depends on the findings of NCS which distinguishes demyelinating from axonal polyneuropathies and divides axonal type into purely sensory, pure motor and mixed sensory motor groups. Chronic axonal PN has many causes. After NCS confirmation further approach in the third stage should includes investigations to identify cases of diabetes mellitus that were not detected by the screening 1st stage tests and to show the less common medical condition. Even after extensive investigations about 25% of cases remain idiopathic.[13, 14]

Methods:

This cross sectional observational study was carried out in the Department of Neurology, Dhaka Medical College and Hospital, Dhaka From January 2009 to June 2010 Sample Size: A total of 80(eighty) subjects were included purposively. Patients aged 18yrs to 60yrs of age with symptoms and signs of polyneuropathy were included and undergone electrophysiological investigation. Patients with mononeuropathy, traumatic or entrapment neuropathy, Conditions such as confusional state, pregnancy, skin diseases, oedema, prosthetic device that interfere with electrophysiological investigations, Neuropathy symptoms mimicking specific disease like motor neuron disease, myopathy, muscular dystrophy, spinal muscular atrophy or neuromuscular junction disorder were excluded. And patient who were not willing to participate in the study also excluded.

All the study cases were underwent meticulous history and asked for neuropathy symptoms and risk factors of polyneuropathy and physical examination were done by standard methods. Patients who presented with weakness, wasting and cramps were categorized clinically into motor type and those with tingling, numbness or paresthesias were categorized into sensory type and combination of sensory and motor features were classified into mixed type. Michigan neuropathy screening instrument questionnaire were used for quantitative assessment.

Nerve conduction study was carried out using standard techniques by Neuro pack II of 'Nihon Kohden' MEB 9200 machine (Japan). Skin temperature was maintained between 32^0C to 34^0C. The studies included motor and sensory nerve conduction in at least cross limbs or one arm and two legs. Electrophysiological study was set as a gold standard test for neuropathy assessment. General guidelines for performing nerve conduction study were followed. Other relevant investigations were done to find out the cause. Clinical features, electrophysiological features and pattern of poly neuropathy were analyzed.

Data Collection and Data Analysis

Data was collected by semi-structured questionnaire by the investigator. Face to face interview, medical history and clinical examination and subsequent laboratory investigations were done. Proper permission was taken from the concern departments. All the patients (cases) were informed about the about the nature of the study and their informed written consent were taken in a consent form before collecting data. Data was analyzed with the help of computer SPSS program version 16.0 software facility. A p-value of less then 0.05 was considered as statistically significant.

RESULTS:

A total of eighty patients of polyneuropathy (acute, subacute and chronic) were included in the study. Meticulous history and clinical examination was

undertaken before neurophysiological investigation. The findings of study obtained from data analysis are presented below.

Table-I

Patients Characteristics (n=80)

	No of patients	Percentage (%)
Men	52	65
Women	28	35
Age in years		
18 – 30	32	40
31 – 40	28	35
41 – 50	8	9
51 – 60	12	16
Mean age ±SD=34.4±6.8		
Range of age = 18- 60		
Occupation		
Service	12	15
Business	6	7.5
Student	10	12.5
Labourer	14	17.5
Cultivator	10	12.5
House wife	8	10
Unemployed	10	12.5
Retired	4	5
Others	6	7.5
Mode of onset/Duration		
Acute/upto 4 weeks	44	55
Subacute / 4 to 8 weeks	08	10
Chronic / > 8 weeks	28	35
Risk factor distribution		
Diabetes	12	15
Connective tissue disease	2	2.5
Hypothyroidism	4	5
Hereditary/ Family history	4	5
Preceding illness- diarrhea or RTI	20	25
Drugs/Toxins/Solvents exposure	6	7.5
Deficiency (vitamin)	4	5
Malignancy	2	2.5
Heavy metal(lead)	2	2.5
Not known (Idiopathic)	24	30

SD= standard deviation, RTI= respiratory tract infection

Table-1 shows the age distribution of the patient in to four groups. Ages of the patient ranged from 18 – 60 years. Most of the patient fell into 18 – 30 and 31-40 years age group and are 32 (40%) and 28 (35%) respectively. Lowest 8 (9%) was in 41 – 50 years age group. The mean age was 34.4 years with a standard deviation of 6.8. Patients were divided into male and female gender. Out of them 52 (65%) were male and 28 (35%) were female patients. M: F=1.8: 1. In occupation distribution service category comprised 15%(12), in business category 7.5%(6), student 12.5%(10), laborer 17.5%(14) which was the highest category, cultivator 12.5%(10), house wife 10%(8), unemployed comprises 12.5%(10), and retired 5%(4) which was lowest category and other not specified were 7.5%(6). Distribution of the patients according to the duration of illness i.e. mode of onset most of patient presented acutely which were 44(55%), chronic onset were 28(35%) and rests 8(10%) were in sub-acute category. Risk factors distribution of disorder causes polyneuropathy, highest number of patient were in not known or idiopathic group which comprises 30%(24), next in preceding illness of diarrhea or respiratory tract infection were 25%(20), history of diabetes were present in 15%(12), drugs/toxins/solvents in 7.5%(6), hypothyroidism in 5%(4), hereditary or family history of neuropathy also in 5%(4).

Table-II

Clinical features of the study population (n=80)

Clinical feature	No of Patient affected	Percentage (%)
Symptoms		
Paresthesia	70	87.5
Tingling	72	90
Numbness	24	30
Lack of feeling	20	25
Weakness	60	75
Wasting	20	25
Cramps	24	30
Signs		
Cranial nerve palsy	26	32.5
Loss of muscle power	60	75
Loss of Pinprick	20	25
Loss of Vibration sense	10	12.5
Deep tendon reflex hypo/ areflexia	70	87.5
Autonomic dysfunction (any level)	10	12.5
Gait abnormality (any level)	70	87.5
Nerve thickening	2	2.5
Weakness Distribution		
Proximal and distal	40	50
Distal to proximal	20	25
No weakness	20	25
Clinical type of Polyneuropathy		
Motor	30	37.5
Sensory	8	10
Mixed	42	52.5

The multiple response table 2 shows that most of the patient had tingling, paresthesia and weakness which ranges from 75% to 90%, numbness in 30% patient, wasting in 25% patient, loss of muscle power were observed in 75%, deep tendon hypo or areflexia were in 87.5%, cranial nerve palsy in 32.5%, pinprick loss in 25%, loss of vibration in 12.5%, autonomic dysfunction at any level in only 12.5% and nerve thickening in only two patients. Distribution of weakness in study subject, 50% patient there were both simultaneous proximal and distal weakness, distal to proximal weakness were in 25% patient, and 25% patient were with no weakness at all. Clinical types of polyneuropathy among study population. Out of 80 patients, 42(52.5%) had mixed sensory motor neuropathy, followed by 30 (37.5%) had motor neuropathy and only 10% had sensory neuropathy.

Table-III

Electrophysiological classification of neuropathy in study population (n=80)

Type	No of patients	Percentage (%)
Axonal	38	47.5
Demyelinating	22	27.5
Mixed axonal & demyelinating	20	25
Motor	38	47.5
Sensory	6	7.5
Mixed sensorimotor	36	45

The above Table III shows the electrophysiological category of polyneuropathy in study population. Axonal varieties were highest and comprised 47.5 %(38), mixed variety were lowest 25 %(20) and demyelinating category were 27.5 %(22). Types determined by electrophysiological examination into motor, sensory and mixed sensorimotor polyneuropathy were 47.5 %(38), 7.5% (6) and 45% (36) respectively.

Discussion:

Polyneuropathy is relatively common and often a distressing chronic condition. It has many diverse underlying causes and in different diseases the incidence of PN varies considerably.[15]This cross sectional study was designed to see the clinical and electrophysiological features of polyneuropathy patients. This study also addressed the clinical and electrophysiological pattern of polyneuropathy patient.

In this study patients of all age group ranging from 18-60 years were included. Majority of the patients 32 (40%) were in 18 to 30 years of age with mean ±SD = 34.4 ±6.8. In this study 65 % were male and 35 % were female with M: F = 1.8: 1. In one local study[15] the M: F was 1.88: 1 and in another local study [16] the M: F ratio was 1.9:1 which resembles with the present study and it is observed that polyneuropathy is about two times more common in male. McLeod et al.[17] also found an overall predilection for men (3:1). In this study polyneuropathy were widely distributed in different occupations, labourers, cultivator and students were affected more. In this regard there are a few studies elsewhere. In the study of Chistee, [18] more or less similar findings were observed but in his series cultivators were less affected but housewives were more affected as well as labourer and students.

It was observed in this study that 55% patients presented acutely and 35% had chronic onset and 10% patients had sub-acute onset. Study on polyneuropathy patients comprising acute, sub-acute and chronic cases are few. Local study Chistee[18] of 50 polyneuropathy cases GBS cases were 50% and the findings were similar with the present study.

In this study majority (30%) patients had no known history of risk factors i.e. idiopathic, antecedent infections (preceding illness either diarrhoea or RTI) was the next common risk factors (25%), next was diabetes mellitus (15%), followed by combined drugs & toxins (7.5%). In a study of chronic polyneuropathy by Vrancken et al.[3] idiopathic were 43%, diabetes mellitus 32%, alcohol abuse 14%, paraproeinaemia 9%, deficiency of vitamin 6% and autoimmune or systemic disease 4% were observed. In a Dutch study on chronic polyneuropathy, Rosenberg NR et al.[6] observed 60(57.1%) patients of diabetes mellitus, followed by HIV infection in 21(20%) patients, alcoholism in 11(10.5%) patients; drug induced in 7(6.7%) patients and renal failure in 6(5.8%) patients in a study of 105 chronic polyneuropathy cases. In Lubec et al.[19] frequency of causal factors in 124 cases were : - diabetes mellitus in 26(21%) cases, alcohol in 20(16.1%) cases, vitamin deficiency in 13(10.5%) cases, GBS in 9(7.3%) cases, paraproteinamias in 6(4.8%) cases, hypothyroidism in 5(4.03%) cases, borreliosis in 6(4.8%) cases, paraneoplasia in 4(3.2%) cases, CIDP in 5(4.03%) cases, hereditary in 3(2.4%) cases, hyperthyroidism in 3(2.4%) cases, critical illness in 2(1.6%) cases, vasculitis in 3(2.4%) cases, and each one(0.8%) case of sarcoidosis, vincristine, azathioprine, Refsum's disease, Sneddon's syndrome, Ehlers-Danlos syndrome, crohn's disease inflammatory polyarthritis and solvent. In an Asian study of 124 cases of chronic polyneuropathy Habib and Ferdousi[15] observed diabetes were 45.2%, idiopathic 45.2%, hereditary 5.7% and CIDP in 3% cases. So the distribution of polyneuropathy in different diseases varies worldwide.

In this study less diabetic and infectious cases were observed as because major bulk of diabetes mellitus are cared by internationally reputed separate diabetic hospital and infectious disease hospitals.[16]

The features of polyneuropathy may be exclusively motor, sensory, autonomic or combined. Most PN present with mixed sensory motor symptoms. Sensory symptoms were usually the presenting features. These were tingling, pins and needles, burning sensation, pain and numbness in the extremities. Motor symptoms were usually those of weakness and wasting. [20] This is reflected in the present study where paresthesias were present in 87.5 %, tingling in 90%, numbness in 30% cases. Weakness in this study was in 75% cases, deep tendon reflex hypo/areflexia in 87.5% and abnormality of gate at any level were also 87.5%. Similarity was observed in the study of Habib and Ferdousi [15] also. A relative lack of muscle wasting in relation to the degree of weakness, weakness of proximal muscle as well as distal muscle, disproportionate loss of joint position and vibration sensation compared to relative preservation of pain and temperature are suggestive of demyelinating neuropathy.[21] In this present study proximal and distal weakness was in 50% cases and distal to proximal weakness was observed in 45% cases.

One of the most important aims of the study was to detect the clinical and neurophysiological type of polyneuropathy. In Rosenberg et al.[6] 77.5% were mixed sensorimotor type, 13.75% were pure sensory type and 8.75% were pure motor type. In Konig et al.[22] 42% were mixed sensory motor, 30% sensory, no case of motor type. In the study of Konig et al.[22] cases of mononeuropathy and mononeuritis multiplex were included. In Macleod et al.[17] 64% were mixed sensory motor type and 27% pure sensory type and 9% were pure motor type. In our present study mixed sensory motor types were 52.5%, motor types were 37.5% and pure sensory types were only 10%. Though in this present series mixed sensory motor type was the most common, the high motor type reflects the inclusion of significant acute polyneuropathy cases.

In this study of 80 polyneuropathy cases either cross limbs or both the lower limbs and an upper limb nerves were examined electrophysiologically. 80 median nerves, 80 ulnar nerves, 120 tibial nerves, 130 common peroneal nerves and 140 sural nerves were studied. In this study electrophysiological types of polyneuropathy were axonal type 47.5%, demyelinating type 27.5% and mixed type 25% which were near similar with Vrancken[3] et al. Where axonal type was 57%, demyelinating type 13% and not specified were 31%. In another European study[6] (Rosenberg NR et al.) of 56 chronic polyneuropathy cases, axonal types were 87.5% and demyelinating type were 12.5% and the findings resembles the present study. In a Bangladehi study by Habib and Ferdousi[15] 26.6% were axonal, 16.1% demyelinating and 31.5% were mixed axonal and demyelinating. The above mentioned local study does not match with our study due to the fact that 25.8% patient were not labeled in any particular pathological type.

It is important to know neuropathy as axonal or demyelinating as it helps proper management. Highly significant association was seen in motor and mixed sonsorimotor type of clinical and electrophysiological classification. In sensory polyneuropathy distribution in clinical and electrophysiological types varies. Comparison of the severity of polyneuropathy in clinical and electrophysiological grade there were poor relation among them. To determine the relation between neurophysiological data and clinical examination Lefaucheur[23] et al. observed that clinical and neurophysiological classifications and severity scores were correlated whatever the type of neuropathy. These differences with the present study might be due to that Lefaucheur[23] et al studied the sensory neuropathy according to fiber type involvement. Latov[24] et al observed that the number and type of demyelinating abnormalities in patients with polyneuropathy vary with the clinical phenotype. Rajabally et al.[25] in their studied patients with CIDP demonstrated the predominance of demyelination in upper limbs nerves, of axonal loss in lower limbs nerves and presence of about 50% of demyelinating – range abnormalities in clinically unaffected territories. Vittadini[26] et al. found significant correlation between alcoholic polyneuropathy, the duration of alcoholism and the type of alcoholic beverage consumed.

In this present study there are some relation and there are some variation among the clinical and electrophysiological spectrum of polyneuropathy .

Conclusion:

Nerve conduction study is a very important investigation in the evaluation of polyneuropathy. It confirm the diagnosis and classify neuropathy as axonal and demyelinatig category and thus direct the cause and help in management

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URINARY TRACT INFECTION DUE TO EXTENDED-SPECTRUM BETA-LACTAMASE PRODUCING ORGANISMS IS A RISK FACTOR FOR BACTERAEMIA AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract

Introduction: *Urinary tract infection (UTI) is common among patients with diabetes mellitus and the aetiological agents are often extended-spectrum beta-lactamase (ESBL) producing bacteria. Diabetic patients with UTI are sometimes complicated by bacteraemia. This study was designed to evaluate whether UTI due to ESBL-positive organisms is a risk factor for bacteraemia among patients with type 2 diabetes mellitus.*

Methods: *This was a cross-sectional analytical study, done in BIRDEM General Hospital, Dhaka, Bangladesh from January to April 2016. Adult (e"18 years) type 2 diabetic subjects of either sex with culture proven UTI were included in this study. All study participants were subjected to undergo blood cultures as well. ESBL-positivity of the infective organisms for UTI was evaluated as possible risk factor for bacteraemia.*

Results: *Total patients were 145 including 119 (82%) females. Eshcerichia coli (112, 77.2%) was the most common aetiological agents followed by Klebsiella pneumoniae (28, 19.3%). In 54 (37.2%) patients UTI was due to ESBL-positive organisms. Ten (6.9%) patients were complicated by bacteraemia [7 (7/54, 13%) among patients with UTI due to ESBL-positive organisms and 3 (3/91, 3.3%) among patients with UTI due to non-ESBL organisms]. UTI due to ESBL-positive organisms appeared as a significant risk factor for bacteraemia (OR 4.37, 95% CI 1.08-17.38, p 0.03).*

Conclusion: *Nearly two-fifths of UTI cases were due to ESBL-positive organisms in this study. ESBL-positivity of the causative organisms was a significant risk factor for bacteraemia among type 2 diabetic subjects.*

Key words: *Bacteraemia, extended-spectrum beta-lactamase, pyelonephritis, risk factor, type 2 diabetes mellitus, urinary tract infection.*

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Introduction

Urinary tract infection (UTI) is the most common bacterial infection in adults and elderly population and patients with diabetes mellitus are at increased risk for UTI.[1-3] UTI, specially pyelonephritis may be complicated by bacteraemia and sepsis.[4,5] Antimicrobials remain the cornerstone for treatment of UTI and increasing antimicrobial resistance, specially extended-spectrum beta-lactamase (ESBL) producing organisms is an ever increasing problem.[6-9] ESBL-positive organisms are inherently resistant to penicillin and cephalosporin; thus UTI caused by ESBL-positive organism require injectable agents like carbapenems and aminoglycosides or nitrofurantoin, pivmecillinam and fluoroquinolones; many organisms causing UTI are also resistant to these oral agents.[2,8]

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Moreover, UTI complicated by bacteraemia indicates complicated infection and merits intravenous antimicrobials in hospital settings; thus increasing treatment cost by many folds. So, this study was designed to evaluate whether UTI due to ESBL-positive organisms is a risk factor for bacteraemia among patients with type 2 diabetes mellitus.

Methods

This cross-sectional analytical study was done in the Department of Nephrology, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh from January to April 2016. Hospitalized adult (e"18 years) type 2 diabetic subjects of either sex, who got admitted with features of pyelonephritis, were primarily enrolled for the study purpose. A clean catch technique was applied for collection of urine in a sterile container and sent to the microbiology laboratory of the institute within half an hour for culture and a blood sample of the patient was also sent for culture before starting any antibiotic. Urine and blood cultures and antibiotic sensitivity tests were performed following standard microbiological procedures. Other investigations were done as per hospital protocol and as indicated. Patients with culture proven UTI were finally included in this study. ESBL-positivity of the infective organisms was tested by double disc diffusion method described elsewhere.[10] Pregnant patients, patients with kidney and ureteric stones, enlarged prostate, indwelling urinary catheter and recurrent UTI were excluded from the study. ESBL-positivity of the infective organisms was evaluated as possible risk factor for bacteramia. Data were analyzed by statistical package for social scientists (SPSS) version 16.0 and the results

Results

Total patients were 145 including 119 (82%) females. Mean age of the study participants was 59.2 years. Base-line characteristics are shown in Table I.

Table-I

Base-line characteristics of the study participants (N=145)

Characteristics	Parameters
Mean (range) age	59.2 (21-72) years
Male: Female	1: 4.6
Mean (range) duration of diabetes	6.3 (1-13) years
Random blood glucose at admission	13.1 (7.2-21.3) mmol/L
Mean (range) HbA1c	9.7 (8.1-11.5) %
Hypertension	68 (46.9%)
Chronic kidney disease	41 (28.3%)

Eshcerichia coli (112, 77.2%) was the most common aetiological agents followed by *Klebsiella pneumoniae* (28, 19.3%). Other organisms are presented in Table II. In 54 (37.2%) patients UTI was due to ESBL-positive organisms and in 91 (62.8%) patients UTI was due to non-ESBL organisms. Ten (6.9%) patients were complicated by bacteremia; 7 (7/54, 13%) among patients with UTI due to ESBL-positive organisms and 3 (3/91, 3.3%) among patients with UTI due to non-ESBL organisms. UTI due to ESBL-positive organisms appeared as a significant risk factor for bacteramia (p 0.03) (Table III).

Table II

Patterns of infective organisms for UTI (N=145)

Organism	ESBL-positive	Non-ESBL	Total
E. coli	38 (33.9)	74 (66.1)	112
K. pneumoneae	11 (39.3)	17 (60.7)	28
Enterobacter	4 (100)	0 (0)	4
Citrobacter	1 (100)	0 (0)	1

Table III

ESBL-positivity as a risk factor for sepsis among patients with UTI (N=145)

ESBL positivity	Sepsis (10)	No sepsis (135)	OR, 95% CI, p value
Yes (54)	7	47	4.37, 1.08-17.38, 0.03
No (91)	3	88	

Discussion

Bacteramia is not uncommon in UTI, both in community and hospital settings and in all age groups–adults, elderly and neonates; but the burden varied widely in different studies.[11-13] Generally, outcome of UTI complicated by bacteramia is worse than those without.[14] In the present study, we found nearly 7% of our type 2 diabetic subjects diagnosed with UTI had concomitant bacteramia. In different studies percentage of patients of UTI complicated by bacteramia was much higher[11,12]; elderly patients are likely to have urinary obstruction that might explain such high rates in western studies.[11]

In the present study, almost two-fifths of the study participants had UTI due to ESBL-positive organisms which is lower than a previous report from Bangladesh.[8] Patients with diabetes mellitus and specially those with poor glycaemic control are at increased risk for infection with ESBL-positive organisms.[2,15-17] The percentage of ESBL-positive

organisms was higher in our study compared to some other international reports.[16,18] Inadvertent and non-judicious use of antimicrobials may be one of the most important contributory factors for such findings in the present study.

Community acquired UTI cases are generally treated at outpatients with oral fluroquinolones, cephalosporins and nitrofurantoin. ESBL-positive organisms are resistant to penicillins and cephalosporins.[2] One-third of our patients had chronic kidney disease, but nobody was on renal replacement therapy in any form. Patients with chronic kidney disease are not suitable for prescriptions with nitrofurantoin or aminoglycosides. So, carbapenems remain the option, thus increasing treatment cost by many folds.[6]

Bacteramia itself implies severe disease. Published reports varied regarding outcome of UTI cases complicated by sepsis; some authors found worse outcome while others did not.[4,19-21] Morbidity and mortality evaluation was beyond the scope of the present study but we feel outcome evaluation in UTI complicated by bacteramia remains area for further exploration in our setting.

Published literatures indicated urinary obstruction like enlarged prostate, indwelling catheters, stone disease and lithotripsy as risk factors for bacteramia and sepsis in UTI.[5,12,22 -24] We excluded all these confounders in our study during selection of study participants. We assume duration of diabetes and status of glycaemic control could be further confounders in our study, which could be adjusted during analysis. Moreover, small sample size, short term study in a single center– all these remain as limitations of present study.

In conclusion, almost two-fifths of UTI cases were due to ESBL-positive organisms in this study and ESBL-positivity of the causative organisms for UTI was a significant risk factor for bacteramia among type 2 diabetic subjects.

Conflict of interest: Nothing to declare.

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EPIDEMIOLOGY OF HYPONATRAEMIA AMONG ELDERLY PATIENTS WITH LOWER RESPIRATORY TRACT INFECTION

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Abstract

Background: *Decrease in serum sodium concentration is frequent observation among hospitalised elderly patients. The common causes for hyponatremia are degenerative physiology, dehydration, medications and infections. Hence the present study was undertaken to know the extent of hyponatremia among elderly with Lower Respiratory Tract Infections.*

Objectives: *The present study was undertaken to assess the prevalence of hyponatremia in lower respiratory tract infection among geriatric age group and to determine the association between severity of hyponatraemia and LRTI.*

Methods: *This was hospital based cross sectional study carried out in the Department of General Medicine of a tertiary care teaching hospital situated in north Karnataka, India during November 2016 to May 2018. 100 elderly patients (age e" 60 years) with history of cough for more than four to five days, clinical findings and X-ray findings suggestive of LRTI, were selected for the study.*

Results: *In the present study 59% comprised of male whereas females constituted 41%. The prevalence of hyponatraemia among elderly patients with LRTI was 45%. The most common cause of hyponatraemia was GI loss (vomiting) 53.33%, Euvolemic hyponatramia 51.11%. The mean age was 69.99±8.44 years. Most of the patients were aged between 61 to 70 years. .Hyponatraemia was not associated with sex, age and type of LRTI. Duration of hospital stay was significantly longer in patients with hyponatraemia compared to those who did not develop hyponatraemia.*

Conclusion: *Hyponatraemia among elderly individuals with LRTI is higher as compared to other age group hence leading to prolonged duration of hospitalisation.*

Keywords: *Hyponatraemia, Elderly, Lower Respiratory Tract Infection (LRTI), Lobar Pnemonia.*

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Introduction

Acute lower respiratory tract infections (LRTI) such as pneumonia and acute bronchitis are among the most common reasons to visit a general practitioner, notably among elderly persons.[1] Elderly person are more likely to develop complications from LRTI compared with younger patients as they have a greater burden of underlying diseases and a different response to therapy.[2]

Hyponatremia is the common electrolyte imbalance encountered in clinical practice.[3] It occurs due to disruption of sodium and water homeostasis, normally maintained by complex multi-system physiological mechanisms.[4] It represents an excess of water relative to sodium, though both sodium and total body water may be increased, normal or diminished. Consequently, there are numerous potential underlying causes of hyponatremia, spanning a broad spectrum of diseases.[5]

Hyponatremia is common among older people. Prevalence of hyponatremia is known to increase in frail patient groups, particularly elderly patients where hyponatremia is observed in almost half of acute geriatric admissions.[6,7] Older people have an increased predisposition to hyponatremia due to degenerate physiology, multiple co-morbidities and polypharmacy.[4] Hospitalized older people have a further susceptibility to hyponatremia due to dehydration, inappropriate fluid therapy and iatrogenic interventions. In an Indian study, with only elderly

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hospitalized patients, the most common causes of hyponatremia were Syndrome of Inappropriate Anti diuretic Hormone secretion (SIADH) and diuretics. The two most common causes of SIADH were lower respiratory tract infection and stroke.[8] However despite of hyponatraemia in elderly patients with LRTI being an important predictor of morbidity and mortality, to our knowledge none of the study is reported on prevalence of hyponatraemia in elderly patients with LRTI so far. Hence the present study was undertaken to assess the prevalence of hyponatremia in lower respiratory tract infection among geriatric age group and to determine the association between severity of hyponatraemia and LRTI.

Methodology

This hospital based cross sectional study was undertaken in the Department of General Medicine of a tertiary care teaching hospital situated in north Karnataka, India from November 2016 to May 2018.Considering the availability of cases, feasibility, and available time period a total of 100 elderly patients (age e" 60 years) who presented with history of cough for more than four to five days, clinical findings and X-ray findings suggestive of LRTI, were selected for the study. Patients with upper respiratory tract infection, known cardiac disease, diabetes mellitus, hypertension, renal diseases and terminally ill patients were excluded from the study. The ethical clearance was obtained from the Institutional Ethical committee, Jawaharlal Nehru Medical College, Belgaum prior to the commencement.

Patients who were eligible were briefed about the nature of the study and a written informed consent was obtained. Patients were interviewed and demographic data like gender and age were noted. A thorough general physical examination was conducted to assess vital parameters, anthropometry and clinical signs followed by systemic examination. All these findings were recorded on a predesigned and pretested proforma. Further, Blood sample was collected for laboratory investigations. Blood samples were collected under all aseptic precautions; blood samples were collected by venepuncture and collected in vacutainer.the sample was collected within 6hours of admission and send for further analysis to department of biochemistry and department of pathology. Patients with lower respiratory tract infections were evaluated for hyponatremia and graded according to severity of pneumonia. All cases were provided treatment according to the diagnosis and routine hospital protocols. All cases were followed up till the hospital stay to assess outcomes, mortality, morbidity and complications. Severity of hyponatremia was defined as Mild (serum sodium concentration 131-135mmol/L), Moderate (serum sodium concentration 126-130 mmol/L) and Severe (serum sodium concentration less than 125 mmol/L).

Outcome variables

Patients were evaluated for the presence and Severity of hyponatremia. The association between hyponatremiawith demographic determinants that is age and sex, type of LRTI was determined. Also length of hospital stay was determined.

Statistical analysis

The data obtained was tabulated on Microsoft Excel spreadsheet. The categorical data was expressed as ratios and percentages. The prevalence of hyponatremia among elderly patients with LRTI was expressed in terms of percentage. Chi-square test and/or Fisher's exact test was used to find the association between the hyponatraemia and age as well as sex. The comparison of mean hospital stay among those with and without hyponatremia was expressed as mean ± standard deviation (SD) and independent sample 't' test was used to compare the data. At 95% confidence interval (CI), a probability value ('p' value) of less than or equal to 0.050 was considered to be statistically significant.

Results

In the present study 45 out of 100 patients developed hyponatraemia hence, the prevalence of hyponatraemia among elderly patients with LRTI was 45% (Graph 1). Among the patients with hyponatraemia, the mean serum sodium levels were 129.96±4.32 mmol/L and the median serum sodium levels were 131 mmol/L and ranged between 118 to 134 mmol/L.

With regard to severity, mild hyponatraemia was noted in 31% of the patients, moderate in 10% and severe hyponatraemia was present among 4% of the patients (Graph 2). The most common cause of hyponatraemia was GI loss (vomiting) which was noted in 24 patients (53.33%) out of 45 patients with hyponatraemia (Graph 3). The Euvolemic hyponatramia was common type noted in 23 of 45 patients (51.11%) (Graph 4).

Out of 100, 59 patients were males (59%) and 41 were females (41%) (Table 1). The age ranged between 60 to 89 years and the mean age was 69.99±8.44 years. Most of the patients were aged between 61 to 70 years (Table 2). With respect to type of LRTI, 47% of the patients had Lobar pneumonia, 45% of the patients had bronchopneumonia while bronchitis and Empyema were diagnosed in 6% and 2% of the Patients respectively (Table 3).Hyponatraemia was not

Table-I

Various socio-demographic and clinical factors associated with hyponatraemia

Sex	Hyponatraemia						P value
	Present		Absent		Total		
	No	%	No	%	No	%	
Male	33	55.93	26	44.07	59	59.00	0.841
Female	22	53.66	19	46.34	41	41.00	
Total	55	55.00	45	45.00	100	100.00	
Age Group							
61 to 70	25	57.63	34	57.63	59	59.00	0.438
71 to 80	12	57.14	16	57.14	28	28.00	
81 to 90	8	38.46	5	38.46	13	13.00	
Total	55	55.00	55	55.00	100	100.00	
Type of LRTI							
Bronchitis	4	33.33	2	33.33	6	6.00	0.729
Bronchopneumonia	19	57.78	26	57.78	45	45.00	
Empyema	1	50.00	1	50.00	2	2.00	
Lobar pneumonia	21	55.32	26	55.32	47	47.00	
Total	55	55.00	55	55.00	100	100.00	

associated with sex (p=0.841), age (p=0.438) and type of LRTI (p=0.729) (Table 1, 2 and 3).

No statistically significant difference was noted with regard to the mean age in patients with and without hyponatraemia (71.53±8.70 years vs 68.72±8.08 years; p=0.101) but duration of hospital stay was significantly longer in patients with hyponatraemia compared to those who did not develop hyponatraemia (10.26±4.63 days vs 5.81±2.78 days; p<0.001).

Discussion

The primary findings from this single centre prospective study emphasizes high incidence of hyponatraemia among geriatric patients admitted with LRTI. In this study 45 out of 100 geriatric patients admitted with LRTI developed hyponatraemia which suggests that, almost one out of every three geriatric patients admitted with LRTI is at risk of developing one or the other form hyponatraemia. Most of the patients in this study developed mild hyponatraemia and euvolemic hyponatraemia was common type while GI loss was the common cause of developing hyponatraemia. Furthermore, the presence of hyponatramia is likely to prolong length of hospital stay. The data on hyponatramia among elderly population admitted with LRTI is scant.[8,9] The available literature suggests that, prevalence of chronic hyponatremia in the elderly population between 7% to 20% and to a large extent it depends on the level of serum sodium and the setting in which the measurement is made. When studying the risk factors for orthostatic hypotension in an otherwise healthy population, Caird et al.[10] noted that approximately 7% of patients >65 years of age had serum sodium concentrations d" 137 mEq/L. In contrast, with a serum sodium concentration, 135 mEq/L used as a cutoff, the prevalence of chronic hyponatremia was approximately 20% among residents of a long term care facility.[11] A similar prevalence was noted in a Veterans Affairs nursing home, whereas the prevalence was 8% in ambulatory patients.[12] The most recent study designed to determine the prevalence of hyponatremia was limited to patients with severe decrements in serum sodium concentration to, 125 mEq/L. Of 1400 elderly (e"65 years) patients admitted to an Israeli hospital, 6.2% had such a disorder.[13] The increasing prevalence of hyponatremia with age is best illustrated in an analysis of >300,000 samples obtained from >120,000 patients of various ages.[14] With a serum sodium concentration, 136 mEq/L used as a cutoff and a #30-year-old cohort as a reference group, patients.

The prevalence noted in the present study was comparable to the observations from a hospital based descriptive study by Rao MY et al.[8] during 2010, who

reported that of the total of 1440 elderly patients admitted to the medical ICU during the 18 month period, 518 patients (36%) had serum Sodium <135 mmol/L and 100 patients (6.9%) had serum Sodium d" 125 mmol/L. The mean age of patients with hyponatremia was 72 years with a range of 60 to 99 yrs.

Many studies in the past indicate a higher mortality in the elderly patients with severe hyponatremia, with mortality ranging from 33% to 86%.[16] However, in the present study no mortality was noted. Sterns[15] reported a mortality rate of 5% when the serum sodium levels was < 105 mmol/L.

According to Berl T. et al.[9] (2013), more than 60 years had a significantly higher prevalence of hyponatremia both at presentation and as a hospital-acquired disorder. In summary, it is evident from multiple epidemiologic studies that the elderly are especially prone to the development of hyponatremia which was true in the present study also despite of LRTI being the predominant primary etiology at presentation.

In the present study prevalence of hyponatraemia was slightly high among males (55.93%) compared to female (53.66%) but the difference was statistically not significant (p=0.841). on the contrary, in a study by Rao MR et al.[8] (2010), Hyponatremia was more common in females and they seemed to better tolerate it than their male counterparts.

Chronic hyponatremia is frequently multifactorial in the elderly.[9] In an observational study, similar to the present study, more than half of the patients with hyponatremia had more than one cause for the condition. The single most common cause of hyponatremia was SIADH and Thiazide diuretic use was a common contributing factor. But in the present study GI loss was the predominant cause. Heart failure is also a common comorbid condition in this age group which was noted among 11.11% of the patients in this study. Some studies have documented no underlying cause for the development of hyponatraemia among the elderly among in >50% of cases.[13,16]

Overall the findings of the present study emphasize higher prevalence of hyponatraemia in elderly admitted with LRTI among selected patients after excluding known cardiac disease, diabetes mellitus, hypertension, renal diseases and terminally ill patients. The prevalence of hyponatraemia was independent of sex and type of LRTI. However these findings require further validation due to potential limitation of this study.

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FREQUENCY OF OSTEOPOROSIS IN IATROGENIC CUSHING'S SYNDROME: SCENARIO OF OUTPATIENT DEPARTMENT IN URBAN HOSPITALS

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Abstract

Background: *Cushing's syndrome is caused by excessive activation of glucocorticoid receptor. Iatrogenic Cushing syndrome is the prevalent one world -wide .Patients with Cushing's syndrome has a high prevalence of osteoporosis.*

Objective: *To see the prevalence of osteoporosis in Iatrogenic Cushing's syndrome patient.*

Method: *This descriptive cross-sectional study included 211 diagnosed case of Cushing's syndrome during the time period of December 2013 to December 2018 in outpatient department of Dhaka Medical College and Health and Hope Hospital. Final diagnosis was done on the basis of clinical feature, serum basal cortical level and BMD. We found male were prevalent one (56%).80.56% showed biochemical evidence of Cushing's syndrome. BMD was done in 113 patients compared with a reference population by means of T score, 17.69% patient in osteoporotic range.*

Conclusion: *The prevalence of osteoporosis and osteopenia is age and sex independent. Judicial use of steroid and co administration with calcium, bisphosphonate can prevent osteoporosis. Treatment with bisphosphonates should be considered in all patients (irrespective of age) with Cushing's syndrome with a low BMD to reduce fracture.*

Key words: *Iatrogenic Cushing's syndrome, Osteoporosis, Osteopenia, BMD.*

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Introduction:

Iatrogenic Cushing's syndrome is usually related to prolonged and/or high –dose steroid in various formulations. The association between hyper-cortisolism and loss of skeletal mass was first described by Harvey Cushing[1].Cushing's syndrome has multiple effects on bone metabolisim. Elevated cortisol level directly inhibit bone formation and indirectly influence the skeleton via effects on reproductive hormones, muscle, fat tissue, intestinal calcium absorption and renal calcium excretion[2,3]. As a result patients frequently show lower measurement of bone mineral density (assessed by dual-energy X-ray absorptiometry [DXA], abnormalities in bone micro architecture, lower estimates of bone strength and an increased risk of fracture compared to healthy individuals. Fractures often occur with minimal or no antecedent injury and can occur in patients with normal measurements of bone mineral density[4]. The currently accepted definition of osteoporosis is "a systemic disease characterized by low bone mass and microarchitectural deterioration of bone tissue leading to enhanced bone fragility, and consequent increase in fracture risk". The tests that forms the basis for the diagnosis of osteoporosis and prediction of fracture risk are bone mineral density (BMD) and bone mineral content (BMC) measurements[5,6] The study was intended to find out the prevalence of osteoporosis in Iatrogenic Cushing's syndrome.

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Methods:

This observational cross sectional study was carried out in outpatient department of Dhaka Medical College and Hospital and Health and Hope Hospital, during the period of December 2013 to December 2018.Total 211 patients were selected after diagnosis of iatrogenic Cushing's syndrome .Data was processed and analyzed by SPSS version 24.

Result:

Total 211 patients was analyzed .27.48%patients were in the age group 50-59 years.

Table-I

Age distribution of patients taking corticosteroid (n=211)

Age in years	Frequency	Percentage
<20	4	1.89
20-29	21	9.95
30-39	50	23.69
40-49	54	25.59
50-59	58	27.48
60-69	16	7.5
70-79	8	3.79

Men (56%) were slightly higher than female (44%).

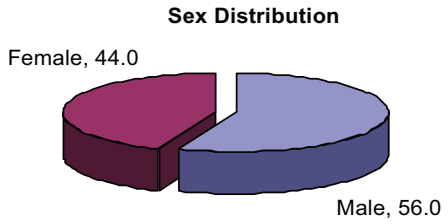

Fig.-1: *Sex distribution of study population (n=211)*

Most of them 71.56% came from rural area and 28.43% were urban dweller.

Table-II

Distribution according to dwelling (n=211)

Habitant of the patient	Frequency	Percentage
Rural	151	71.56
Urban	60	28.43

Most of the patient took corticosteroid in oral route 86%, 12% parenteral route and 2% in topical route.

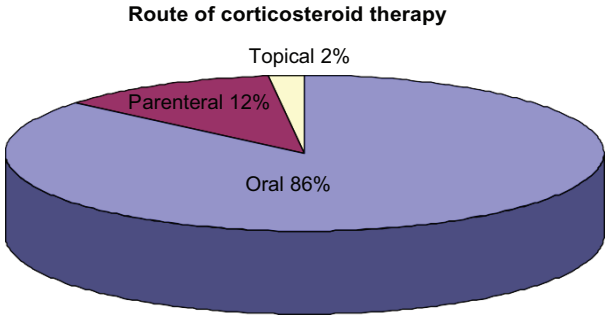

Fig.-2: *Route of administration of corticosteroid therapy (n=211)*

Prednisolone was taken by most of the patient (77.72%), than dexamethasone (18%), triamcinolone (2.84%), betamethasone (1.42%). Most of the patient took steroid equivalent to11-20 mg of prednisolone (34.12%) and duration up to 6 month was more prevalent (42.1%)

Table-III

Pharmacological preparation of corticosteroids with doses and duration of treatment (n=211)

Pharmacological name	Frequency	Percentage
Prednisolone	164	77.72
Dexamethasone	38	18
Triamcinolone	6	2.84
Betamethasone	3	1.42
Doses of steroid(equivalent of prednisolone)		
<7.5 mg	13	6.16
7.6-10 mg	55	26.06
11-20 mg	72	34.12
>20 mg	21	10
Undetermined	50	23.69
Duration of cortisteroid therapy		
Upto 6 month	89	42.1
7-12 month	46	21.8
13-24 month	42	19.9
25-36 month	21	10
37 & above	13	6.16

Basal serum cortisol was done in every patient, 80.56% patient biochemical feature of Cushing's syndrome.

Table-IV

Basal serum cortisol (n=211)

Dexamethasone suppression test	Frequency	Percentage
Plasma cortisol level>60 nmol/l	170	80.56
Plasma cortisol<60 nmol/l	41	19.44

Among 211 patients BMD was done in 113 patients. Most of them were in mild to moderate osteopenic range (42%), 39% were in normal range and 17.69 % patient were in osteoporotic range.

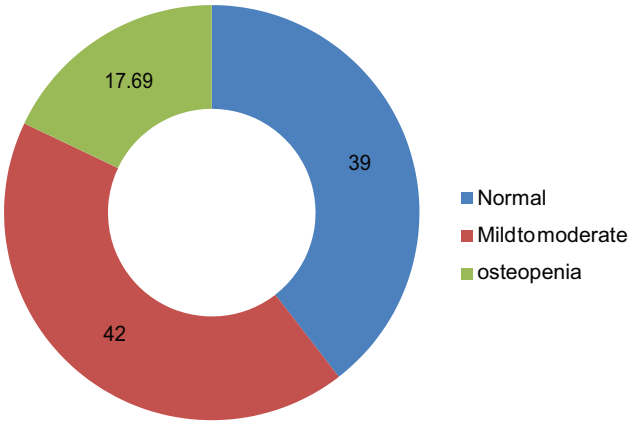

Fig.-3: *BMD in patients taking corticosteroids (n=113)*

Discussion:

In this study we found 27.48% were in the age group of 50-59 years, the youngest patient was 14 years of age and the eldest one was 79 years of age, which was similar to the findings of that of netherland[4] and india[8] , where most of them were more than 40 years of age. Overall sex distribution, male were more prevalent one, which was significantly difference from that of India ,where female were more prevalent one[8].Female are more reluctant to seek medical services due to shyness, religious belief, economic dependency on male.

A variety of pharmacological preparation was used among them most common was oral prescribed steroid (86%), even topical used steroid found in 2% cases which was rare in western countries[4] but similar to Asian ethnicity[8].Prednisolone was used in most of the cases 77.72%, less common is Betamethasone (1.42%) which was slightly differ from other studies[4,6,8].The majority of dose range was 11-20 mg (equivalent to prednisolone) 34.12%, in 23.69% cases dose ranges was not found may be due to patients reluctant to steroid intake, lack of proper counseling, lack of proper knowledge of steroid side effect. Among 211 patients we found that 42.1% patient took steroid up to 6 month and 6.16% took more than 37 month may be due to rapid relief of symptoms, easy availability.

For confirmation of diagnosis all patients were taken for Basal serum cortisol level at 9 am and revealed that 80.56% were in range group lower than the normal and 19.44% were in lower level of normal range. As iatrogenic Cushing's syndrome is mainly a clinical diagnosis, normal level does not exclude the disease.

To establish the diagnosis of osteoporosis we did BMD in 113 patients and found 39% were in normal range, 42% in mild to moderate osteopenc and 17.69% in osteoporotic range much higher than other studies.[4,8]

The paucity of laboratory investigation facilities in Bangladesh, especially in the area other than Dhaka city, the diagnosis of Cushing's syndrome was a difficult one. We mainly emphasized on the clinical feature and duration of drug used. Judicial use of steroid , legislation of prescribed steroid can prevent osteoporosis in people.

Conclusion:

The prevalence of Iatrogenic Cushing's syndrome in Bangladesh is not identified. The present study was conducted in outpatient department of various hospitals in Dhaka city with a limited Data. Among 211 patients most them were young adult, male were more prevalent. Most of them took steroid in oral form. A great number of patients had osteopenic range which can be prevented by judicial use of steroid, proper counseling, co administration with bisphosphonate, restriction of steroid availability without prescription, patients' education about side effect of steroid.

Limitation:

This is a cross sectional study with limited data. Randomized controlled trail was not done to see the frequency of osteoporosis.

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REVIEW ARTICLE

MOVING FROM ORAL POLIOVIRUS VACCINE TO INACTIVATED POLIOVIRUS VACCINE: THE RATIONALE AND CHALLENGES

KAZI ZULFIQUER MAMUN[1], NABEELA MAHBOOB[2], KAZI TAIB MAMUN[3], HASINA IQBAL[4]

Abstract

Oral polio vaccine (OPV) has served as the cornerstone of polio eradication efforts over the past 30 years, trivalent inactivated polio vaccine (IPV) has re-ascended to prominence in the past year, now acting as the sole source of protective immunity against type 2 poliovirus in routine immunization programmes. The Polio Eradication and Endgame Strategic plan 2013–2018, developed by the Global Polio Eradication Initiative (GPEI) outlines the phased removal of OPVs, starting with type 2 poliovirus–containing vaccines and introduction of inactivated polio vaccine in routine immunization to mitigate against risk of vaccine-associated paralytic polio and circulating vaccine-derived poliovirus.

Key words: *Poliomyelitis, Vaccine-associated paralytic polio, Circulating vaccine-derived poliovirus*

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Introduction

Poliomyelitis (polio) is a communicable disease caused by poliomyelitis virus, a RNA enterovirus belonging to Picornaviridae family. There are three serotypes of poliovirus, which differ antigenically and protection against one serotype does not provide protection against the others.[1] Humans are the only reservoir of polio disease. The predominant transmission mode of this disease in developing countries is the fecal/oral route, since the virus replicates in the intestines and is basically excreted in feces. If sanitation conditions and personal hygiene are inadequate, others can be infected through dirty hands or contaminated food and water. Thus, intestinal immunity is important in order to prevent transmission. The incubation period is usually 7 to 10 days, though it can be 4 to 40 days.[2] Polio disease can strike at any age, but it mainly affects children under five years' old who have not been vaccinated.[3] Infection can be inapparent (without symptoms) in approximately 72% of cases; in about 24% it causes mild disease with transitory fever, discomfort, somnolence, headache, nausea, vomiting, constipation, and sore throat, in various combinations; it manifests as aseptic meningitis in about 4% of cases; and on rare occasions (<1%) it presents as paralytic poliomyelitis.[4] Paralytic poliomyelitis manifest as acute flaccid paralysis (AFP), of sudden onset, with maximum progression within a few days (<4 days). It is usually asymmetrical, with the reduction or absence of tendon reflexes, without alterations of the sensory system.[2]Most people with paralytic poliomyelitis never recover completely, having residual paralysis of varying severity for the rest of their lives. Weakness or paralysis still present 12 months after onset is usually permanent.[5]

Globally, from estimated 350,000 polio cases in more than 125 endemic countries in 1988,it dropped to a total of 33 cases in 3 countries, in 2018.[6,7] Since 1988,

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sustained use of polio vaccines worldwide has led to a precipitous drop in the global incidence of poliomyelitis by over 99%.[5] In 2012 and 2013, 223 and 403 respectively poliomyelitis cases were reported. Globally, the last case of poliomyelitis caused by naturally circulating WPV type 2 (WPV2) occurred in India in 1999. No case due to WPV type 3 (WPV3) has been detected since 10 November 2012.[8] Though worldwide use of poliovirus vaccines has brought a drastic reduction in cases of polio, failure to implement strategic policies has led to ongoing transmission of poliovirus in Afghanistan, Nigeria and Pakistan, which are still considered endemic from 2014 for transmission of WPV type 1 (WPV1). Failure to stop poliovirus transmission in these last remaining areas has the potential of causing as many as 200,000 new cases globally every year, within next 10 years.[6] There is risk of importation and subsequent chance of spread in the countries with low immunization coverage and bordering the endemic countries.[1]

IPV and OPV: characteristics and global implementation to date

Two polio vaccines are commonly used throughout the world to protect against poliomyelitis. The ûrst was developed by Jonas Salk in 1952; the second was an oral vaccine developed by Albert Sabin in 1961.[9]

The Salk vaccine, or inactivated poliovirus vaccine (IPV), is based on 3 virulent reference strains - Mahoney (type l), MEF-I (type 2) and Saukett (type 3) grown on human diploid cells (MRC-5) and inactivated with formalin.[10] The original IPV contained 20, 2 and 4 D antigen units of PV types 1, 2 and 3.[9] The Salk vaccine provides immunoglobulin G-mediated immunity in the bloodstream, which prevents infection from progressing to viremia and protects the neurons.[10] The duration of immunity induced by IPV is not known with certainty, although a complete series is thought to provide protection for many years.[11] The IPV now available is termed enhanced IPV(eIPV) because of a new method of production developed (more potent IPV containing 40, 8 and 32 D antigen units of types 1, 2 and 3) in 1978 that results in higher potency per dose and significantly greater immunogenicity than the original IPV.[9] Trials with this eIPV showed greater than 90% seropositivity against all 3 serotypes after one dose and 99-100% seropositivity after two doses.[11,12]

Oral polio vaccine (OPV) is a live attenuated vaccine produced by passage of poliovirus through nonhuman cells at a subphysiological temperature, which causes spontaneous mutations in the viral genome.[9] OPV is superior to IPV in ease of administration, and there is no need for sterile syringes, as with IPV and making the vaccine more suitable for mass vaccination campaigns. OPV also provides longer immunity than does the Salk vaccineas, it provides both humoral immunity and cell-mediated immunity.[13,14] One dose of OPV produces immunity to all three poliovirus serotypes in roughly 50% of recipients.[15] Three doses of live-attenuated OPV produce protective antibodies to all three poliovirus types in more than 95% of recipients. OPV produces excellent immunity in the intestine, the primary site of wild poliovirus entry, which helps prevent infection with wild virus in areas where the virus is endemic.[16] The live virus used in the vaccine can rarely shed in the stool and can rarely spread to others within a community. However, OPV has strict requirements for transport and storage, and this is a big problem in some hot or remote areas.[13] As with other live-virus vaccines, immunity initiated by OPV is probably lifelong.[11]

The only rare serious adverse events associated with OPV are the occurrence of vaccine-associated paralytic poliomyelitis (VAPP) and the emergence of vaccine-derived polioviruses (VDPVs).[8]

VAPP is caused by a strain of poliovirus that has genetically changed in the intestine from the original attenuated vaccine strain contained in OPV. It is associated with a single dose of OPV administered in a child or can occur in a close unvaccinated or non-immune contact of the vaccine recipient who is excreting the mutated virus. The weakened virus may paralyze the child or his or her contact, but does not spread to cause other cases of paralysis.[17] This is a very rare event that in about two to four in every million doses of oral polio vaccine (OPV) given. VAPP can be proven by a laboratory test that detects vaccine virus in a clinical case of polio.[18]

A VDPV is a very rare strain of poliovirus, genetically changed from the original strain contained in OPV through prolonged replication in an individual or in a community, re-acquire the neurovirulence and transmissibility characteristics of WPV.[8,17] On very rare occasions, under certain conditions, a strain of poliovirus in OPV may change and revert to a form that may be able to cause paralysis (VDPV) in humans and develop the capacity for sustained circulation. The latter is known as a circulating VPDV (cVDPV). that cause cases or outbreaks of paralytic poliomyelitis.[8,19]

VDPVs are genetically divergent forms of the original Sabin vaccine virus conventionally defined by >1% genetic divergence for PV1 and PV3 and >0.6% for PV2. These viruses are further subdivided into 3 categories: (1) circulating VDPVs (cVDPVs), when evidence of person-to-person transmission in the community exists; (2) immunodeficiency-associated VDPVs (iVDPVs), which are isolated in rare cases from people

with primary B-cell and combined immunodeficiencies (with defects in antibody production) who have prolonged VDPV infections (in individual cases excretion has been reported to persist for 10 years or more)[20]; and (3) ambiguous VDPVs (aVDPVs), which are either clinical isolates from persons with no known immunodeficiency, or sewage isolates of unknown source.[21]

A cVDPV is associated with sustained person-to-person transmission and is circulating in the environment. "Persistent cVDPVs" refer to cVDPVs known to have circulated for more than six months. Low vaccination coverage is a major risk factor for cVDPV emergence. A fully immunized population will be protected against both vaccine-derived and wild polioviruses. It takes many months for a cVDPV to emerge. cVDPV outbreaks have the ability to become endemic, can be spread in any under-vaccinated communities, and can be imported to other countries.[17]

In 2005, it was reported that children in a small village in the United States had contracted vaccine-derived polio.[14] In Nigeria, 170 cases have been reported.[22] In 2006,1600 cases of vaccine-induced polio occurred in India, according to the Indian Medical Association Sub-Committee on Immunization's report on the Polio Eradication Initiative.[14] In 2008, many cases of polio were reported in all provinces of Pakistan. These cases were reported during repeated mass-immunization campaigns in which repeated doses of OPV were administered.[23] In 2012, 9 countries reported cases of paralytic poliomyelitis associated with cVDPVs, most of them with type 2. The largest numbers of such cases were reported in the Democratic Republic of the Congo (n=17) and Pakistan (n=16). In 2013, 7 countries reported cases of paralytic poliomyelitis caused by cVDPV, all associated with type 2, of which Pakistan reported the greatest number of 44 cases.[24] Cases of cVDPV also occur with type 1 and type 3.[17] These vaccine-related cases became big challenge for the scientiûc community if the polio-eradication goal is to be achieved. In many countries where wild polio has been eliminated, programmes have switched to using inactivated (killed) polio vaccine (IPV), a more expensive vaccine that does not carry the risk of VAPP and cVDPV.[25]

Switching from tOPV to bOPV and IPV introduction

Trivalent oral poliovirus (tOPV) vaccine was licensed for use in 1963 and preferred by most of the countries and was the preferred poliovirus vaccine in the expanded programme on immunization as well as the polio eradication programme.[1]Trivalent OPV (tOPV) contains all three poliovirus serotypes (against wild types 1, 2, and 3) was an important component of routine immunization programmes in 155 countries and territories around the world until April 2016. The tOPV has been used to nearly eradicate polio infection worldwide.[26] The use of tOPV has led to the eradication of wild poliovirus type 2 (WPV2), with the last case occurring in 1999. The last detected case of WPV3 was in 2012. Furthermore, four of the six WHO regions have been certified as polio-free. Led by The Global Polio Eradication Initiative, 155 countries switched to use the bivalent (against wild type 1 and 3) between 17 April and 1 May 2016.[27] The bivalent OPV (bOPV) was licensed in 2009, which is effective against type 1 and 3 but does not cover type 2.[28] Even as the remaining strains of wild poliovirus are being eradicated, the switch from tOPV to bOPV was a major step to combat cVDPV and VAPP. Over 90% of cVDPV cases, and approximately 40% of VAPP cases are due to the type 2 component of tOPV.[29] The type 2 component of tOPV also interferes with the immune response to poliovirus types 1 and 3.[30] Given the risk the type 2 component of tOPV poses to a world free of WPV2, thus tOPV was replaced with bOPV in routine programmes and supplementary immunization activities (SIAs). However, the switch from tOPV to bOPV will not eliminate all cVDPV cases. The purpose of the switch is to eliminate persistent cVDPVs associated with the type 2 serotype and to boost protection against wild poliovirus types 1 and 3 (the switch will not prevent type 1 or type 3 cVDPVs).[31]

The switch from tOPV to bOPV was coupled with the introduction of IPV at age e"14 weeks, which will provide immunity against type 2 after removal of type 2 OPV (OPV2) as recommended by the Strategic Advisory Group of Experts on Immunization (SAGE).[5] The introduction of IPV will help to reduce risks associated with the withdrawal of OPV type 2 and hasten eradication by boosting immunity to poliovirus types 1 and 3.[27] However, studies have not evaluated yet if type 2 antibody titers and immunological priming responses persist, and for how long they persist after the single dose of IPV.

The global demand for IPV has therefore substantially increased in just a few years. However, the current global inactivated poliovirus vaccine (IPV; 0.5 mL, full-dose) supply shortage dramatically limits the number of doses available for an effective outbreak response. Therefore, GPEI has proposed use of intradermal administration of a booster of fractional IPV (fIPV; 0.1 mL, one-fifth the full-dose) as a dose-sparing strategy to stretch the limited global IPV supply while further improving population immunity by increasing the number of children vaccinated.[32] Multiple studies have assessed immunogenicity of intradermal fIPV compared with the full intramuscular dose and

demonstrated encouraging results. These studies conducted in Cuba,[33,34] Oman,[35] Philippines,[36] and Bangladesh[37]-evaluated the immunogenicity by examining seroconversion rates and antibody levels following vaccination.

The studies found that cumulative seroconversion rates (a e"4-fold increase over the expected decline in maternally derived antibody titers) for all polio serotypes following the complete vaccination series were comparable between the fIPV and intramuscular IPV groups when there was less interference with maternal antibody (that is, when the first dose was given at or after 2 months of age). On the other hand, the results were varied when the vaccination series started earlier (such as at 6 weeks of age). The Philippines study showed equivalent immunogenicity between fIPV and intramuscular IPV when each vaccine was administered at 6, 10, and 14 weeks of age.[36] However, studies in Cuba (using the same schedule of immunization at 6, 10, and 14 weeks) and in Bangladesh (using a 2-dose schedule at 6 and 14 weeks) showed slightly lower cumulative seroconversion rates in the fIPV group than in the intramuscular group.[33,37] Because most OPV-using countries have added a single dose of IPV in their primary vaccination series, it was also useful to compare the immunogenicity of 2 fIPV doses with that of a single full intramuscular dose. In all studies, 2 fIPV doses (i.e., total of 0.2 mL) resulted in substantially higher seroconversion rates for all poliovirus serotypes than a single intramuscular dose.[33-37,38] After reviewing these data in October 2016, WHO's Strategic Advisory Group of Experts on Immunization (SAGE) reiterated the recommendation it first made in April 2016 that countries should start preparing for a 2-dose fIPV schedule (at 6 and 14 weeks of age), in lieu of a single intramuscular dose at 14 weeks.[39] Prior to the SAGE recommendation, 8 states in India and the country of Sri Lanka had already made this change to their immunization schedule. India will expand the use of fractional doses to an additional 8 states in August 2016 and to all 36 states in April 2017. In addition, Bangladesh has decided to introduce fIPV in their routine schedule in 2017.[40] This option would not only address the immediate IPV shortage but also serve as an affordable and immunogenic option for routine

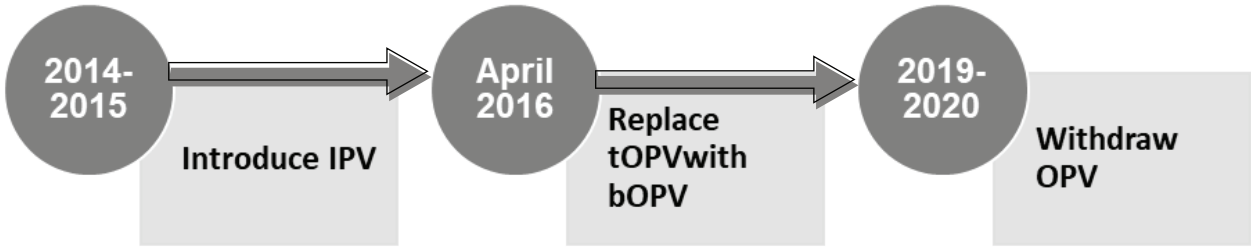

Fig.-1: *Ongoing routine immunization strengthening*[27]

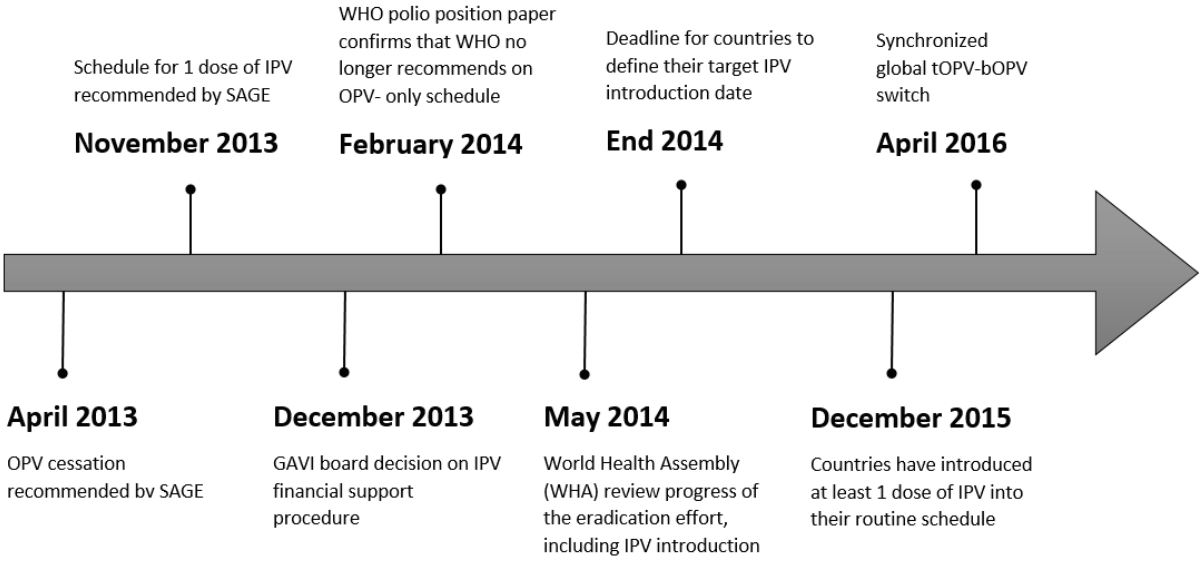

Fig.-2: *Timeline for IPV Introduction and the Switch*[5]

immunization after global polio eradication has been achieved.[32] Additional research is also desirable to better understand the role of fIPV in inducing mucosal immunity and long-term immunity to provide further evidence to support the implementation of this strategy.

However, monovalent versions of oral polio vaccine (mOPVs) had been licensed earlier in 1950s but were abandoned in favor of the tOPV to simplify immunization schedules. mOPVs confer immunity to just one of the three serotypes of OPV.[41] A few previous trials of mOPVs had suggested that mOPV type 1 was two to three times as immunogenic as tOPV[42] because it eliminated interference from the other two polio-virus serotypes. The Global Polio Eradication Initiative issued an urgent call and mOPV type 1 and mOPV type 3 were licensed again in 2005 and used to enhance the impact of supplementary immunization activities in the key remaining reservoirs of wild polio. While mOPVs have provided the GPEI with much more potent tools for rapidly building population immunity, optimizing the balance of mOPVs proved much more difficult than originally anticipated, leading to alternating outbreaks of type 1and 3 polioviruses in certain settings, and promoting the fast track development of a completely new bOPV in 2010.[43] Once WPV1 and WPV3 are certified as eradicated, use of bOPV will no longer be required, and it will need to be withdrawn. mOPV2 has been stockpiled in the event of a cVDPV2 outbreak. Stockpiles of monovalent type 1 OPV and type 3 OPV will be needed for responding to any outbreaks of polio that occur after bOPV withdrawal.[44]

Vaccination Schedule

In countries with endemic polio or where there is a high risk of imported cases, the WHO recommends OPV vaccine at birth followed by a primary series of 3 OPV and at least one IPV doses starting at 6 weeks of age, with a minimum of 4 weeks between OPV doses. In countries with >90% immunization coverage and low risk of importation, the WHO recommends one or two IPV doses starting at 2 months of age followed by at least two OPV doses, with the doses separated by 4–8 weeks depending on the risk of exposure. In countries with the highest levels of coverage and the lowest risks of importation and transmission, the WHO recommends a primary series of 3 IPV injections, with a booster dose after an interval of six months or more if the first dose was administered before 2 months of age.[8]

Conclusion

Interruption of person-to-person transmission of the virus by vaccination is important in the global polio eradication,[45] since no long-term carrier state exists for poliovirus in individuals with normal immune function, polio viruses have no nonprimate reservoir in nature,[46] and survival of the virus in the environment for an extended period of time appears to be remote. OPV contains live poliovirus, which can mutate and acquire neurovirulence. Therefore, OPV cessation is a necessary prerequisite to achieve poliomyelitis eradication. One of the most critical points for success of IPV introduction and the switch to bOPV was the global structure to support the regions. There were many international organizations working together to support the 126 countries across the globe that needed to introduce IPV and make a synchronized switch. The issues with global vaccine supply and vaccine delays were major obstacles that had to be dealt with at international, regional and national levels. It is expected that within 2 years of certification of global eradication of wild polioviruses, OPV use will cease and IPV will be used for routine polio immunization.

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CASE REPORTS

AN ELDERLY LADY WITH MULTIPLE BLISTERS ALL OVER THE BODY: HAILEY HAILEY DISEASE

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Abstract:
Hailey-Hailey disease (HHD) is an autosomal-dominant genoderma-tosis, associated with abnormal epithelial cell adhesion due to altered calcium metabolism. Clinical features involve painful red blisters, erosions, fissured and hypertrophic plaques predominantly in the intertriginous areas. Heat, friction, minor trauma, superimposed bacterial or viral infection can aggravate the condition. Here, we report a case of a 50-year old lady with no previous family history presented with severe attack of HHD since last 5 months. Histology showed acantholysis of keratinocytes resembling characteristic dilapidated brick wall appearance in the epidermis layer of skin which helped for the confirmed diagnosis.

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Introduction:
Hailey–Hailey disease (HHD) is a rare autosomal dominant skin disorder which is also known as familial benign chronic pemphigus. Clinically it is characterized by painful rash and blistering in skin folds, such as the armpits, groin, neck, under the breasts, and between the buttocks. Specially, abnormal epithelial cell adhesion occurs which involves the epidermis and occasionally the mucous membranes.[1,2,3,4]Secondary infection by bacteria and fungi often is associated with the lesion and produce pain and unpleasant odor. In majority cases clinical symptoms first appears after puberty, with highest rate of onset in the second to fourth decades of life.[1]Several precipitating factors such as friction, heat, sweat, inflammation, or infection commonly play vital role for initiating or aggravating the clinical symptoms of HHD.In addition to discomfort, pain, and limitation of physical activities,the disorder generally follows a chronic recurrent course. Histology of HHD showed loss of cohesion between suprabasal keratinocytes (acantholysis) leading to intraepidermal lacunae, splits, and blisters and dyskeratosis (abnormal keratinization of keratinocytes) of the epidermis.[5]Diagnosis of HHD is challenging asetiology, clinical features and histological findings show similarity to another dominantly inherited dermatosis, Darier's disease (DD), otherwise named as keratosis follicularis.[6]To diagnose HHD, thorough examination of clinical morphology, distribution of lesions, positive family history, and histological demonstration of a characteristic dilapidated brick wall appearance of the epidermis are recommended. Here,we report an elderly patient who presented with a 5-month history of multiple blisters spreading all over the body at 50 years of age. To the best of our knowledge, there are very few such cases reported earlier. The unusual presentation of HHD which caused significant diagnostic dilemma and challenge to the clinician is the prime focus of discussion in this case report.

Case Report:
A 50 years old lady with no previous co morbid condition admitted into Dhaka Medical College Hospital with the complaints of multiple blisters all over the

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body with some excoriations for last 5 months. According to the statement of the patient's attendant, patient initially noticed some blisters over the dorso-lateral aspects of tongue, lip and some portion of the oral-cavity 5 months back. The lesions were fragile, flaccid and easily ruptured leaving a denuded area (as shown in Fig: 1).They were painful but non-itchy, malodorous. Some excoriations were also present for which she consulted with a physician and received some oral drugs and ointments, though the name of those drugs were not documented. However, patient's symptoms were not improved rather her condition was deteriorating as the lesion involved the oral cavity and started to involve the trunk(as shown in Fig: 1). There was no positive family history of similar disease in any of the family members. Furthermore, she did not mention previous history of similar attack. Patient did not have any respiratory or urinary symptoms. In addition, her bowel and bladder habit were normal and she did not have any complaints of headache, vomiting, and abdominal pain.

Upon arrival, she was well-alert, co-operative, non anemic, non tachypnoeic, and was febrile with a temperature of 99°F. She had no koilonychia, leukonychia, clubbing, dehydration and edema. Her thyroid gland was not enlarged, lymph-nodes were not palpable, JVP was not raised. Besides, her pulse and blood pressure were within normal limit. The findings of local examination of skin reveal multiple blisters all over the body which weretender on touch, fragile, flaccid, easily ruptured, leaving a denuded area. Moreover, there were areas of excoriations and Nikolsky sign was positive. Onycholysis was present on the nail of ring finger of right hand with longitudinal white lines on the other nails of similar hand.Mucous membrane of oral cavity was also affected. Although no blister was seen in the nasal cavity, ear, urethral and anal orifice, some blisterswerefoundon the faces and over the scalp. Her other systemic examinations were unremarkable. Our initial differential diagnoses were Bullous Pemphigoid or Toxic Epidermal Necrolysis (TEN).

Her initial laboratory investigations were taken and revealed hemoglobin of 11.2gm/dl, white blood cell and platelet count were 26X 10^3/cumm and 565000/ cumm respectively. Differential count showed Neutrophil 55%,Lymphocyte 30%, and Eosinophil 10%. She had normal hepatic and renal function as her alanine aminotransferase, aspertate amino transferase, and creatinine were 18U/L, 22 U/L, and 0.5 mg/dL respectively. Her anti nuclear antibody was negative and serum albumin level was 32g/dl. Her serum electrolyte showed mild hyponatraemia with

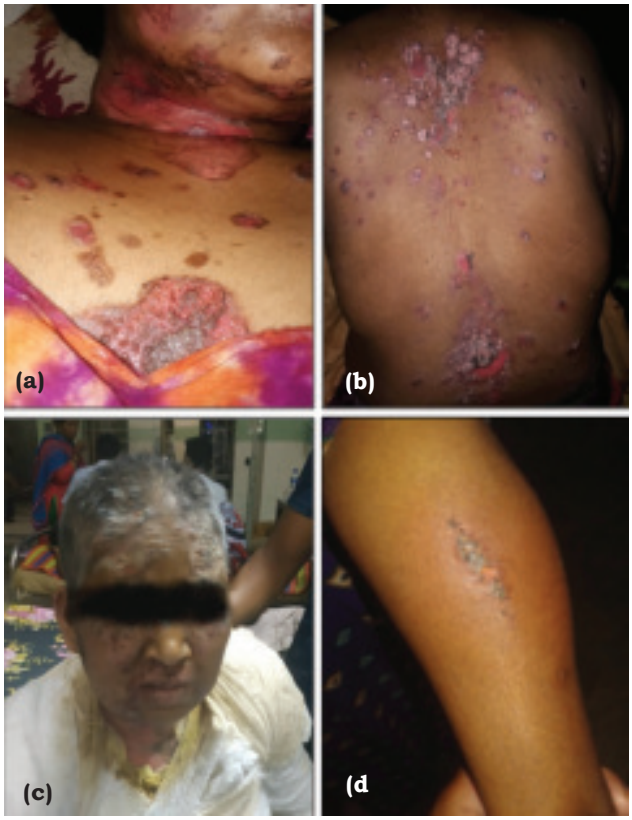

Fig.-1: *Multiple blisters spreading all over the body.*

Multiple painful red lesions on a) neck and upper part of the chest b) back, c) face and salp, and d) leg

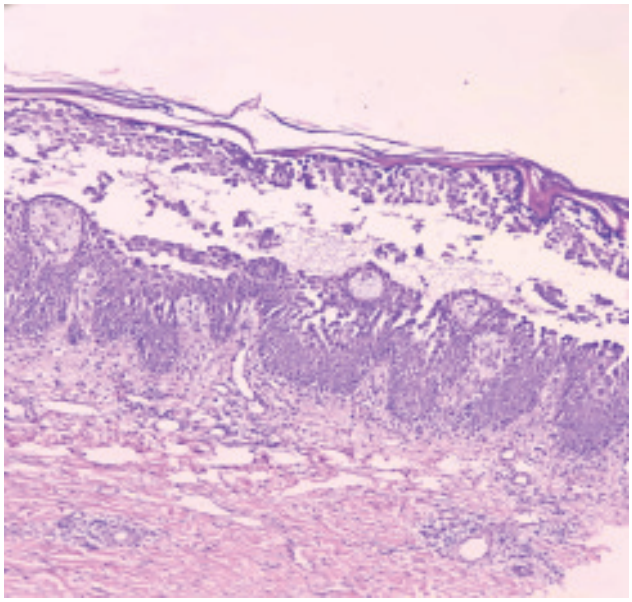

Fig.-2: *Histopathological features of skin lesin.* Suprabasilar and intraepidermal clefing and acantholysis of keratinocytes resembling dilapidated brick wall in the epidermis and mild chronic inflammatory infiltrate n dermis.

sodium 134 mmol/L, however, potassium was normal with a level of 3.5 mmol/L. Routine microscopic examination of urine showedRBC: 2-4/HPF,Pus Cell: 4-6/HPF,Albumin: (+), Sugar: Nil, and Calcium Oxalate: (+++).

To confirm the diagnosis, histopathological examination of the skin lesion was done and the microscopic features included suprabasilar & intraepidermal clefting & acantholysis of keratinocytes resembling dilapidated brick wall in the epidermis layer of skin (as shown in Fig:2) which is the characteristics feature of HHD. There was no pronounced dyskeratosis seen. However, the dermis showed mild chronic inflammatory infiltrate. As the patient had a severe outbreak of the disease involving a wide area of the body, in addition to broad spectrum antibiotic, she was treated with combination of oral and topical steroid, and regular dressing with antiseptic cleansing product. Unfortunately, her condition deteriorated and she passed away.

Discussion:

HHD occurs in 1 to 4 per 100,000 individuals. There is no preference for any sex or ethnic group was reported.[6] HHD was initially identified and described by theHailey brothers in 1939.[2]Similar to another autosomal dominant genodermatosis Darier disease (DD), HHD is caused by abnormal epidermal calcium homeostasis. Though these diseases follow hereditary inheritance, the genetic mutations are also responsible for the symptoms, as some cases were identified without any medical history. However, they are mapped to different sites in the chromosome.Using a random marker search Ikeda et allocalized the HHD gene to a 14cM interval on chromosome 3 q21-q24.[7]The linkage of HHD to chromosome 3q21-q24 was confirmed by another group who searched in six multi generational families.[8]They found location for HHD gene is consistent in all families reported to date, which supports genetic homogeneity.Genetic analysis revealed that Darier's disease is caused by mutations in the ATPase sarcoplasmic/endoplasmic reticulum Ca2+ transporting 2(ATP2A2)gene, located on chromosome12 q23-24.On the other hand, HHD is caused by heterozygousmutations in the ATPase secretory pathway Ca^{2+} transporting 1 gene (ATP2C1) gene, located on chromosome 3q21–24.[9,10]This gene encodes the secretory pathway Ca2þ/Mn2þ ATP-ase protein (hSPCA1) of the Golgi-apparatus.[11] The function of the hSPCA1 protein is to maintain calcium storage inside the cells. Calcium has significant roles for instance, regulating cell growth, division, and cellular adhesion. This protein is specifically crucial for the normal function of cells located in the outer layer of the skin known as epidermis. This particular cell type is called keratinocytes. If mutations occur in the *ATP2C1* gene, the amount of functional hSPCA1 protein decreases which hampers normal calcium storage ability.[12,13]Abnormal calcium storage affects keratinocytes more than any other cells causing impaired cellular adhesion.[14]Alterations in Ca2þ-dependent intracellular signaling happen.Therefore, keratinocytes do not stick tightly to one another resulting fragile epidermis which is less resistant to minor trauma. As a result, skin becomes damaged easily and blistered areas affect the skin, particularly in the areas where moisture and friction present like skin folds.

HHD is a distinct entity of skin disorder which is often confused with pemphigus.Pemphigus is an autoimmune disorder, in which the body produces auto-antibodies and attacks its own cells. Whereas, HHD is not an autoimmune disorder as it is devoid of any auto-antibodies. To differentiate HHD from pemphigus, direct immunofluorescence studies are performed, which would be negative in HHD.[15]

As there is no cure for Hailey-Hailey disease, prime objectives of physicians treating HHD are reducing symptoms and preventing flares. Topical medication such as vitamin D3 analogs, antibiotics, and corticosteroids are advised for mild cases.A number of systemic treatments such as doxycycline, methotrexate, cyclosporine, acitretin, thalidomide, alefacept, alitretinoin, afamelanotide, terbinafine, and naltrexone are reported effective in many patients producing long remissions.[16,17,18] In case of severe diseases or those which are recalcitrant to conventional therapy, invasive treatments have also been attempted, such as laser ablation, photodynamic therapy, electron beam radiotherapy, botulinum toxin injection, surgical excision, and grafting of the lesions have been reported beneficial for patients.[19,20,21,22]Some patients are advised to keep away fromtriggers like certain foods, stress, excessive heat, prolonged sweating and constant friction to avoid an outbreak.

Conclusion:

Hailey-Hailey disease is a rare but challenging disease for both patients and physicians as it causes significant disabilities for the patients and often become resistant or refractory. Combination of multiple treatment modalities may be required to achieve optimal benefit.Unfortunately, previous reports on literatures show that no one regimen works for all patients. Individualized treatment approaches are essential which makes it difficult for clinicians.Further researches are required for clear understanding of the molecular pathogenesis and to provide recommendations of efficient therapies for successful treatment of HHD.

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OBSTRUCTIVE HYDROCEPHALUS IN A PATIENT WITH SLE

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Abstract:

Hydrocephalous is a rare manifestation of systemic lupus erythematosus. Cerebral venous thrombosis, immune complex deposition within the arachnoid villi or direct post-inflammatory lesions of the central nervous system are possible causes of developing acute hydrochephalus. We report a case of acute non-communicating hydrocephalus secondary to stenosis of the aqueduct of Sylvius. The condition developed rapidly in a 22-year-old woman with previously diagnosed SLE.

Keywords: *Hydrocephalous; systemic lupus erythematous; stroke; pathogenesis.*

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Introduction :

Systemic lupus erythematosus (SLE) is a chronic multisystem, autoimmune disease in which neuropsychiatric involvement occurs in about 50% of patients and carries a poor prognosis[1,2]. Involvement of the central nervous system (CNS) is the second most frequent cause of death.[1,2] The frequent neurological complications of SLE are aseptic meningitis, cerebrovascular disease, movement disorders, myelopathy and psychiatric symptoms.[1,2] Hydrocephalus in SLE are very rare. We describe a case of non-communicating hydrocephalus in a 22-year-old woman with previously diagnosed SLE without antiphospholipid antibody syndrome or cerebral venous angiographic abnormality.

Case presentation :

Ms. X, 22 years lady, known case of SLE for 1 year was admitted into Square Hospital with complaints of fever & loose motion for 2 days, several episodes of convulsion for 1 day. 1 year ago she was diagnosed as a case of SLE on the basis of hyperpigmentated rash on face & limbs & oral ulcer for 1 month along with positive ANA & dsDNA. She was treated with hydroxycholoroquine. Six months ago suddenly she developed lower limb weakness & after thorough investigation she was diagnosed as a case of non compressive transverse myelitis. She was treated with steroid & immunosuppressive drugs & improved. During admission, her GCS was 8/15. Pupil was dilated with sluggish reaction to light. Pulse - 130/min, blood pressure was nonrecordable. Patient was intubated for protection of airway & inotropes started. Her Hb% was 5.6 gm/dl, WBC – $15.1x10^9$ cells/cmm, PBF show features of hemolysis. Reticulocyte count was increased. CRP was 49.8 mg/dl, procalcitonin 17.1ng/ml. Escherichia coli was found in tracheal aspirates & urine culture. CXR showed features of pneumonia. CSF study revealed protein >300 mg/dl, glucose 29.0 mg/dl, WBC: 159 cells/cmm & PMN 85%. CSF culture revealed no growth. Her troponin I was elevated (2.97ng/ml), ECG – tachycardia, non-specific changes & echocardiography showed features of cardiomyopathy - global hypokinesia of LV, mild to moderate LV systolic dysfunction (EF-40-45%), moderate pericardial effusion. She was treated as a case of septic shock, bacterial meningitis, NSTEMI, pneumonia. MRI brain revealed recent infarcts involving the head of the left caudate nucleus, cranial lobe of both cerebellar hemispheres and both cerebellar vermis with obstructive hydrocephalus. MRV was normal. Gradually her GCS deteriorated. External ventricular drainage was applied on the next day. There was no improvement in the patient's clinical course despite supportive mechanical ventilation and appropriate antibiotic coverage. Unfortunately she died of sepsis.

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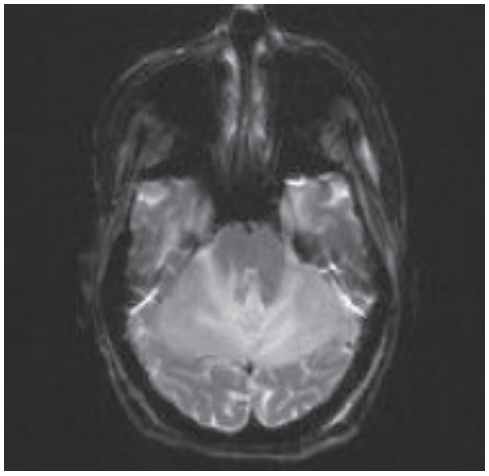

Fig.-1: *T2 image showing bilateral cerebellar infarct with compression of 4th ventricle*

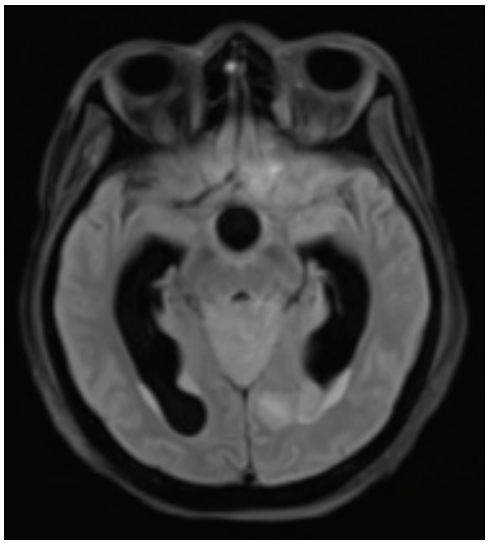

Fig.-2: *dilatation of lateral & 3rd ventricles with obliteration of basal cistern*

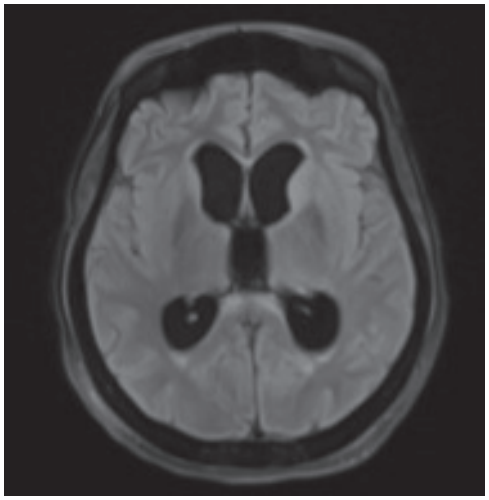

Fig.-3: *dilatation of 3rd & 4th ventricles*

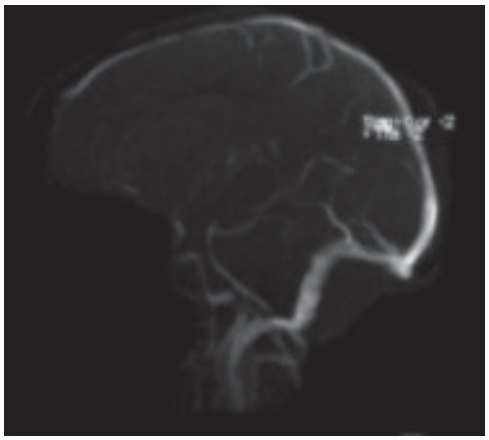

Fig.-4 : *normal MRV*

Discussion

Patients with SLE may experience a variety of neurological and psychiatric manifestations, collectively named NPSLE, that account for significant morbidity and mortality.[3] The prevalence of NPSLE varies widely, from 21% to 95% in various cohorts[4,5], in part due to the heterogeneity of manifestations and definitions used.[6] The neuropsychiatric manifestations of SLE classified as primary NPSLE & secondary NPSLE.

In primary NPSLE, direct neuronal injury due to autoantibodies against N-methyl-D-aspartate glutamate receptor (anti-NR2), accelerated atherosclerosis and thrombotic diathesis caused by the presence of anti-phospholipid are considered potential pathogenic mechanisms.[6] Secondary NPSLE may be caused by complications of the disease or its therapy, or may be unrelated to SLE and be due to infections, metabolic abnormalities and adverse drug reactions.

The pathogenesis and pathophysiologic mechanism of hydrocephalous associated with SLE are yet unproven although several alternative mechanisms have been proposed in the literature. [7] One hypothesis is that corticosteroids and other immune suppressive agents used in the treatment of SLE can lead to increased risk of opportunistic CNS infection, and these infections can lead to impairment of CSF drainage and subsequent hydrocephalus [8]. Normal pressure hydrocephalus in a 77-year-old patient with SLE has been reported, but no cause was found [9]. On the other hand, Krauss and associates showed a highly significant association between idiopathic NPH and arterial hypertension [10].

Verrees hypothesizes that the development of hypertension beyond the limits of cerebral autoregulation leads to breakdown of the blood brain

barrier in the cerebellum and development of posterior fossa edema secondary to focal transudation of protein and fluid. All of these studies show hypertension as an important contributing cause of NPH and obstructive hydrocephalus due to vascular encephalopathy [11]. In some lupus patients, hyperviscosity disrupt blood flow and might be involved in hydrocephalus[12]. Immune complex deposition can affect the brain parenchyma directly, or within the cerebrovascular system that can impair CSF flow into the arachnoid villi.

Thromboembolic formation that blocks the small arteries, choroid plexus or cerebral venous system can be conceived as another pathophysiologic mechanism to explain the development of intracranial hypertension.[10] Kitching et al. described two cases of communicating hydrocephalus in SLE patients, with cerebral phlebitis involving both deep and cortical veins demonstrated through angiography.[13] In postmortem examination of one of the patients, periphlebitis and periarteritis were noted in the brain and leptomeninges, and thrombosis and recanalization were seen in veins and arteries. Secondary antiphospholipid antibody syndrome [Hughes syndrome] is another cause of communicating-type hydrocephalus.[13,14,15] The hypercoagulable state caused by antiphospholipid antibodies increases the risk of developing generalized thrombosis in both arteries and veins. In rare cases, catastrophic antiphospholipid syndrome, associated with a high risk of death, may cause rapid organ failure usually painless, sudden onset of paralysis, loss of speech and intracranial hypertension syndrome.[16] Borenstein and Jacobs [13] reported the case of a 46-year-old woman with SLE and non-communicating hydrocephalus. They concluded that the cause of the noncommunicating hydrocephalus was aqueduct stenosis caused by post-inflammatory lesions of CNS lupus.

Our patient presented with convulsion with low GCS for 1 day. MRI revealed recent infarcts involving the head of the left caudate nucleus, cranial lobe of both cerebellar hemispheres and both cerebellar vermis resultant mass effect is causing compression over the 4th ventricle. Both lateral & 3rd ventricles are moderately dilated. CSF study showed high protein >300 mg/dl, glucose 29.0 mg/dl, WBC: 159 cells/cmm & PMN 85%. Though CSF culture revealed no growth, high protein, low sugar & neutrophilic leukocytosis – all are suggestive of bacterial meningitis. Bacterial infections can lead to impairment of CSF drainage & causing hydrocephalus. Another possibility may be due to CNS lupus. CNS lupus occurs during active stage of SLE, which may lead to bilateral cerebellar infarct with secondary occlusion of 4th ventricle leading to hydrocephalus. As patient has history of transverse myelitis 6 months back, this time involvement of brain may be most reliable explanation. May be both were present so rapid deterioration of her condition has occurred. MRV was normal & antiphospholipid antibody was negative , so cerebral venous sinus thrombosis was excluded. It should be mentioned that cerebral angiography, PET or MRS has greater sensitivity for detecting cerebritis & CNS vasculitis. As bacterial culture was negative, CSF for PCR of bacterial pathogens should be done. Unfortunately we could not obtain such investigation to strengthen our study.

Conclusion :

We can conclude that multiple pathogeneses are responsible for development of both communicating and non-communicating hydrocephalus. In the case reported here, CNS vasculitis & bacterial meningitis led to bilateral cerebellar ischemic infarct and brain edema. This resulted in secondary aqueduct stenosis and then to non-communicating hydrocephalus within 1 day. Since hydrocephalus is associated with significant morbidity and mortality, prevention is vital. Early diagnosis of hydrocephalus may play a key role in the choice of treatment strategy, may improve patient prognosis.

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SHORT COMMUNICATION

CHILDHOOD OBESITY: NUTRITIONAL TRANSITION OF BANGLADESH

S.M. TAJDIT RAHMAN[1], MD. DAHARUL ISLAM[2], RANAJIT SEN CHOWDHURY[2], ABIDA TARANNUM[3]

Abstract:

Childhood obesity has been a major public health concern in many high income countries. In middle income countries, like Bangladesh, the coexistence of obesity and underweight makes the situation more grievous. It creates a transitional status in the childhood nutrition in Bangladesh. The priority is to identify the overall picture of obesity status in our country. In this review article we try to identify the transitional situation of childhood nutrition and the importance of finding out the overall picture of childhood obesity throughout the country.

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Introduction:

Obesity is one of the major public health problems among children and adults. [1, 2] Overweight or obese may be termed as the range of weights for individuals if greater than the ideal weight, which is considered healthy for the particular height. The prevalence of obesity is very high in high income countries and many of them have declared obesity an epidemic.[3]

In the United States the rate of overweight and obesity among children and adolescents aged 6 to 18 years increased to more than 25% in the 1990s from 15% in the 1970s.[4] The prevalence of overweight/obesity in urban children in Delhi has shown an increase from 16% in 2002 to about 24% in 2006-2007.[5] Despite a major reduction in child being under-nutrition and undersize over the last three years, there has been a considerable increase in obesity among

The dual burden of developing country, Bangladesh, where underweight and overweight coexist among the children, creates so many health problems.[7]Rapid urbanization and industrialization are changing the food habits resulting in socio-economic, demographic and cultural changes leading to nutritional transition in low income countries.[8]

Overall situation:

Worldwide economic growth has been accompanied by an increase in food availability, animal fat intake, less physical activity and urbanization.[9] This nutritional transition has been changing anthropometric and health patterns throughout populations, having special impact in low and middle-income countries.

Underweight and stunting have been dropping in low and middle-income countries, mainly in children under 5 years [10]; but overweight depicts diverse distribution and rates between children populations. [10, 11] Since 1990, overweight rates have been raising in children from high and low-income countries.

However, children from some middle income societies depict a slight decrease in over-nutritional indicators, suggesting a diverse nutritional transition in children of preschool age[10];and that country's development and economic growth may play an important role.

In the last few decades, global age-standardized obesity prevalence has nearly doubled and developing countries appear to be at the forefront of this trend and rapid nutritional changes in urban settings might explain the over-nutrition climb.[12]

The prevalence of malnutrition in Bangladesh is still high. Millions of children suffer from one or more forms of malnutrition including low birth weight, wasting, stunting, underweight, Vitamin A deficiencies, iodine deficiency disorders and anemia.

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Bangladesh has made good progress in the past decade although. Malnutrition rates have seen a marked decline in Bangladesh throughout the 1990s, but remained high at the turn of the decade. Nationally, 41% of children under five years are moderately to severely underweight and 43.2% suffer from moderate to severe stunting. [13,14,15]

Childhood stunting has fallen from 71% to 37% between 1986 and 2013, in line with a

decrease of childhood stunting from 40% to 27% globally and from 49% to 28% in Asia between 1990 and 2010 (GNR). Surveillance data (FSNSP 2013) shows the national level of stunting to be below the WHO cut-off for very high prevalence. [16]

However, recent national analysis shows that 39 out of 63 Districts still have stunting rates above WHO critical threshold level for stunting (40%). [17]

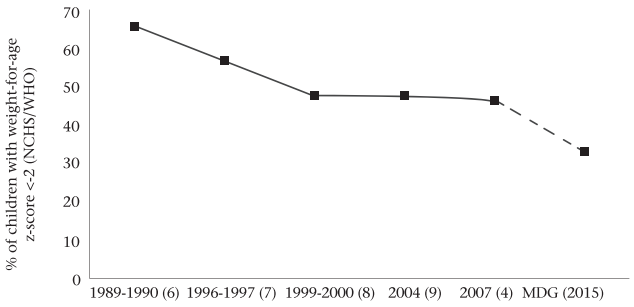

Figure: *Line Chart showing trends in prevalence of Child(0-59 months) Undernutrition in Bangladesh* [20]

Although under-nutrition is still high in Bangladesh, it is evident from various national health survey and pilot studies under-nutrition has fallen to a great extent.

On the contrary, childhood obesity is increasing day by day specially in urban areas of Bangladesh. There is no national data regarding prevalence the childhood obesity in the whole country. But various sample based studies show increasing trend of childhood obesity.

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COMMENTARY

HOW FAR SCIENTIFIC IS SNAKEBITE PREVENTION AND FIRST AID TREATMENT IN SCHOOL TEXTBOOK?

FARIHA FAIROUZ[1], RUMANA RASHID[2], ABDULLAH ABU SAYEED[3]

Background:

Snakebite is an old health problem in rural areas. In Bangladesh, the snakebite issue is included in school syllabus, in curriculum since long time, so that people can take/get immediate first aid treatment and can prevent snakebite.

The success of snakebite treatment depends more on providing first aid treatment immediately after snakebite by learning and by sending the patients quickly to hospital. Snakebite is a preventable health problem indeed. If it can be prevented the rate of snakebite will also decrease.

In the recently published snake bite management Guideline by WHO it has been targeted to reduce 50% of mortality & disability due to snakebite by 2030.[1]

Methods:

a. The snakebite topic or issue has been thoroughly reviewed in the secondary and higher secondary school books.
b. National Guidelines on snakebite in providing/ giving first aid treatment has been reviewed.[2]
c. The correlation between the topic to learn the subject and the national guidelines have been reviewed and given taken into account.
d. The similarity or correlation between the national guidelines and the topic in the prevention of snakebite in the book have been observed & reviewed.

It was a descriptive/narrative research study.

Results:

In the book of class IV in Primary and Secondary level students, 'Elementary Science, ('Prathomiik Bigghan') page no. 86 and in book of class VIII Home Science ('Gharjhastha Biggan') page no. 16 the Snakebite issue/topic is mentioned.[2,3]

There are 22 information on the first aid/primary treatment of Snakebite among which 5 (five) are non-scientific rather harmful. (Table & Picture)

Primary Treatment:

Scientific	Non-Scientific	Others:
• Immobilize the snakebite part of the body. • Rapid hospitalization • Not to take traditional treatment/ treatment from 'Ohja'.	• If there are two (2) marks of fang at bite site (':'), then to consider it as venomous snake bite; if there are 4 (four) ('::') fang marks to consider it as a non-venomous snakebite. • To provide tight tourniquet with a rope or a piece of cloth just above the snakebite area. • To give two tight tourniquet above the snakebite area • Disinfect the area with Dettol or Savlon wash and to give a sharp incision an affected area with a blade or a knife burnt in fire. Give deep incision about 0.5 cm or one centimeter and squeeze out the blood from the wound.	• Take advice from doctor as soon as possible. • To do since doctor arrives Not to move the patient if not required.

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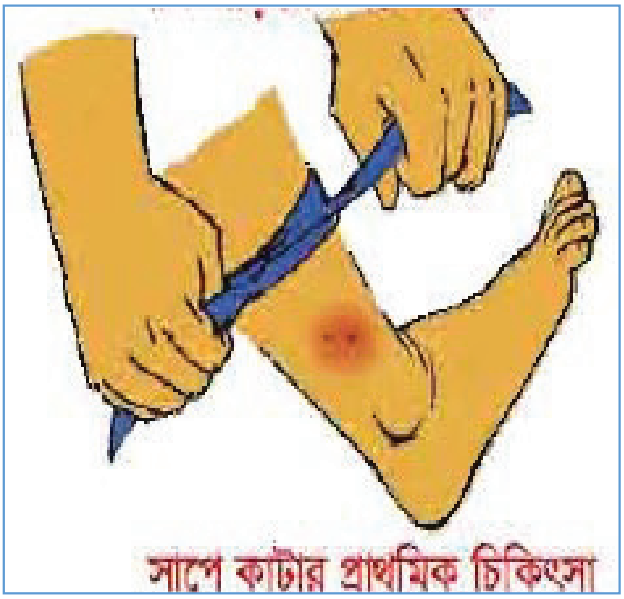
সাপে কাটায় বাঁধন দেয়া



Prevention[4]:

- It is better/wise not to keep food staff, such as grains of paddy-rice, poultry (duck-chicken, pigeon) etc. sharing for human habitation.
- Do not sleep on the floor, sleep in cot-bed using mosquito net.
- Be careful/cautions, use torch light and stick while walking at night or going for natural call at night.
- Be prudent while walking in grass, bushes.
- Do not put hand or feet in holes.

Discussion:

In the school books reviewed, we found at least 5 wrong information and 3 confusing points regarding first aid/ primary treatment following snakebite.

No specific information regarding the prevention of snakebite was provided.[2]Nothing was mentioned for transporting the patient immediately to the hospital or concern regarding the movement for hospitalization.

In school syllabus the books should be corrected/ edited immediately on scientific basis regarding the topic on prevention of snakebite and first aid/primary treatment of snakebite.

The National Curriculum and Text Book Board and syllabus must take immediate necessary action.

It is the basic right to health of every person to get appropriate health education and knowledge regarding the prevention of snakebite, and to get proper primary scientific treatment with such a severe life threatening health problem of snakebite in nearby health facilities like Primary Health Centres (PHC) and district hospital.[5]

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CLINICAL IMAGE

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME – A RARE COMPLICATION AFTER METHYLPREDNISOLONE

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Abstract :

Posterior reversible encephalopathy syndrome (PRES) is a rare neurological complication. It can occur as a complication of hypertensive disease of pregnancy, autoimmune disorder or after immunosuppressant. Typical imaging features of PRES are bilateral symmetrical involvement of parietal and occipital lobe. Here, we reported a case of PRES after methylprednisolone.

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Case Presentation :

A 19year-old gentleman with underlying nephrotic-nephritic syndrome since 2013 admitted for acute kidney injury. He presented with dyspnea, facial puffiness and leg swelling for one week. His urea was 32mmol/L, creatinine was 1567imol/L and bicarbonate was 4.2mmol/L. Ultrasound kidneys showed no evidence of obstructive uropathy. He was treated with intravenous methylprednisolone of 500mg daily for 3 days and intermittent haemodialysis. He was discharged well after 10 days in hospital. 2 days later, he presented again to hospital with status epilepticus and altered sensorium. On arrival to hospital, his Glasgow coma scale (GCS) was E1V1M4, blood pressure was 170/116mmHg. He was intubated for airway protection. Chest radiography showed right upper lobe consolidation. Urgent non-contrasted computed tomography of brain showed symmetrical white matter hypodensity at the bilateral occipital, bifrontal, left parietal and left cerebellum region consistent with posterior reversible encephalopathy syndrome (PRES) Contrasted brain imaging showed no evidence of venous thrombosis.

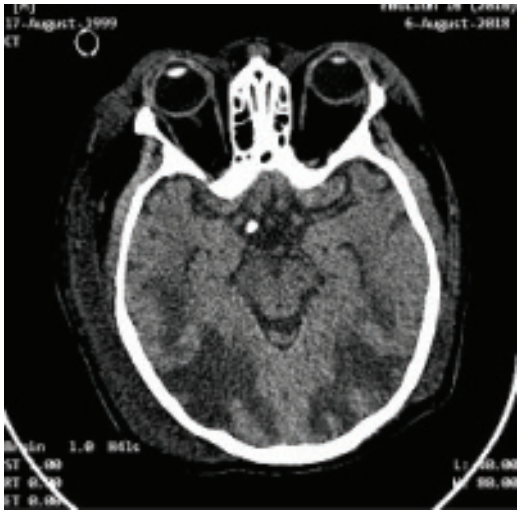

Fig.-1 : *Non contrasted Computed tomography of the brain*

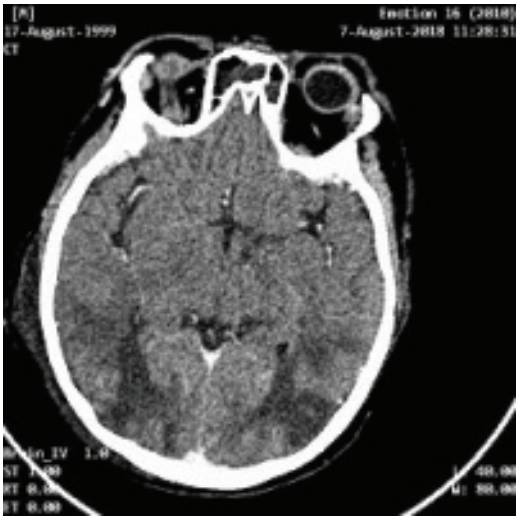

Fig.-2: *Contrast-enhanced Computed tomography of the brain*

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He was the admitted to intensive care unit (ICU) and treated with supportive management. His high dose steroid was withheld. He was treated with intravenous antibiotics for aspiration pneumonia, anti-epileptics and intermittent haemodialysis. His GCS subsequently improved to normal after one week in ICU. He was discharged home with plan of slow reintroduction of steroid.

PRES is a clinical-radiological syndrome characterized by seizures, headache, altered consciousness and visual disturbances[1]. Various conditions are associated with PRES, which include sepsis, Guillain-Barre syndrome, autoimmune diseases, cytotoxic agent, steroid and pregnancy related complication. Severe hypertension is the most common etiology of PRES. The exact pathophysiology is still uncertain, but it's believed to be due to dysfunctional cerebral autoregulation.

In computed tomography, PRES lesions are thought to be due to vasogenic edema and tend to be symmetrical, affecting both hemispheres. The commonest (>90%) site involved are parietal and occipital lobes. However, important to note PRES lesions can also occur in watershed zones, which are frontotemporal region. Magnetic resonance imaging remained the gold standard in diagnosing PRES[2].

In term of treatment, treatment of PRES is mainly supportive, which includes optimal blood pressure control, withdrawal of offending drug, treatment of underlying etiology and seizure control[3]. Most patient with PRES have good neurological recovery. In conclusion, PRES is a rare neurological complication after methlprednisolone. Recognizing the typical imaging features will help in achieving the diagnosis.

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