



# JKMC

## Journal of Khulna Medical College

Vol : 01 | No : 01

April 2022

### Editorial

- Extremely High Voltage Electric Injuries Caused by Lightning Strike: A Rising Concern for Bangladesh 01  
Islam MT

### Original Article

- Experience of Pancreatic Resection for Pancreatic Cancer: A Hospital-Based Study 03  
Hossain MM, Islam MS, Ali MS, Galib MA, Faruquzzaman, Dey PK
- Evaluation of the Results of Correction of Genu Valgum by Figure of 8-plate Temporary Hemiepiphyodesis 09  
Islam MN, Newaz MM, Kader MA, Alam SMD, Alam KS, Das PK
- Effects of Hypothyroidism on Serum Electrolytes Level 14  
Khatun MF, Sardar MMR, Akhter MS, Rashed MR, Mamun ASMA, Sabiruzzaman M
- Comparative Study of Blood Pressure Measurement Using Aneroid Sphygmomanometer & Digital Sphygmomanometer 18  
Islam MN, Chowdhury SN, Alam ABMS, Jesmin F, Parvin Z
- Incidence of Cancer in Thyroid Swelling – A Study of 100 Cases 21  
Mondal SK, Islam MM, Islam MM, Islam MAA, Paul HK

### Review Article

- Non-Alcoholic Fatty Liver Disease: Updates in Treatment Modalities 24  
Mollick MKU, Nahar K

### Case Report

- Metastatic Prostatic Carcinoma in Middle Aged Man - A Rare Case Presentation 30  
Hossain MM, Kundu RR, Parvin R, Bulbul D, Jamil F, Wahidullah SMN

### Instructions for Author

32



An Official Organ of Teachers' Association, Khulna Medical College

## About the Journal

### Focus and scope

**Journal of Khulna Medical College (JKMC)** publishes Original articles, Brief reports, Case reports, Review articles and Letters to editor. It is an official organ of Teachers' Association, Khulna Medical College. It follows the uniform requirement for manuscript submitted to Biomedical Journal as recommended by the International Committee of Medical Journal Editors. It is intended to promote prompt publication of concise, scientific article based on the study in all fields of medical sciences. It is published regularly in print.

### Copyright policy

The entire contents of the JKMC are protected under Bangladesh and International copyrights rules and regulations. An article appearing in the Journal can be reproduced after obtaining written permission from the Editor and acknowledging the source as the JKMC. Copyright for each article is reserved by the authors and other parts by the publisher.

### Peer review process

JKMC is a peer reviewed journal. Manuscripts are examined by the editorial board and are sent to reviewers. Proof correction by the authors will be appreciated.

### Disclaimer

Information within the individual article are the responsibilities of the author(s), though every effort is made by the editorial board to avoid inaccurate and misleading information appearing in the journal. Editorial board of **JKMC** accepts no liability whatsoever for the consequences of any such inaccurate and misleading information, opinion or statement.

### Ethical aspects

Manuscripts based on the study involving human subjects should have been conducted according to the ethical standards laid down in the Declaration of Helsinki revised in 2013. Manuscript must contain a statement in the method section that all studies involving human subjects have been approved by appropriate ethical committee after careful examination of the ethical aspects. Permission of the patients or their families must be sought to reproduce photographs of the patients where identity is not disguised. Otherwise the identity will be blackened out. Author should obtain written permission to reproduce any table,

illustration from any other publication. Author should disclose conflict of interest if it is there.

### Publication frequency

This journal is published twice a year in the month of April & October.

### Article processing fees

The JKMC does not charge the authors any kind of processing or publication fee.

### Reprints for the authors

Ten Copies of each published article will be provided to the main author for free of cost. Additional reprints may be obtained by prior request and on payment.

### Subscription information

Journal of Khulna Medical college is published twice a year in April and October. Annual subscription for both the issues is as follows:

Local = BDT 1200.00

Overseas = \$ 20.00

**Editorial**

## Extremely High Voltage Electric Injuries Caused by Lightning Strike: A Rising Concern for Bangladesh

Electric burn is the most devastating injury and 4th most common cause of admission in burn units worldwide. This type of injury not only involves the skin but also involves deeper tissues that causes multiple acute and chronic manifestations. Individuals tend to stay longer in hospitals, as well as morbidity and mortality rates are much higher. In Bangladesh common cause of burns are thermal, electric and chemical. Among them electric burn injuries constitute about one third of total burn injuries.<sup>1</sup> Electric injuries are typically divided into low voltage, high voltage and ultrahigh or extremely high voltage injuries. Lightning strike has 10 to 300 million volts in comparison to 120 volts for household current and it causes extremely high voltage electric burn.

Although thunderstorm and lightning strike is less common cause of electric burn, recently deaths from extremely high voltage electric burn due to thunderstorm and lightning strike are increasing alarmingly in Bangladesh. Every day when we open the the page of newspaper, news of casualties from thunderstorm and lightning strike catches our eyes. In Bangladesh, there have been reports of 351 deaths in 2016, 262 deaths in 2017, 57 deaths up to April 2018, 198 deaths in 2019, 255 deaths in 2020 and 329 deaths up to September 2021 due to lightning strike.<sup>2,3</sup> ALJAZEERA reported that, repeated lightning bolts in few seconds killed 16 persons at a wedding party and injured the groom on 4 August 2021. On average, 250 people die every year in Bangladesh from lightning strike, the number of which is more than the deaths from floods, cyclones and other natural calamities.<sup>3</sup> Worldwide, over 20,000 people are affected by lightning and several thousand succumb to their injuries. Other report showed 2,000 people are killed worldwide by lightning each year.<sup>2,4</sup> Due to increasing death toll from lightning strike, the Government of Bangladesh has declared it as a natural disaster in 2016.<sup>5</sup>

Lightning tends to strike tall or isolated objects including trees, towers, shelters, poles, high rising buildings. A person may be the tallest person in an open field. It can strike a person directly, or electricity can reach to a person from touching or near an object that has been struck or current may reach to a person through the ground and causes external and internal injuries. The injuries caused by lightning strike is due to direct transmission of electric current through the body and flush. Flush burn occurs due

to electric arc and usually involves the surface skin. Transmission of current through body tissues causes both external and internal injuries. Electricity from lightning can also travel from outdoor power, telephone, dish cables to electric equipments. Cardiopulmonary arrest is the most common cause of death in lightning victims. Damage to the central nervous system accounts for the second most debilitating group of injuries due to lightning. Other organ systems injured by lightning include the eye, ear, gastrointestinal system, skin and musculoskeletal system. The survivors of lightning strikes suffer from a variety of lasting symptoms, including memory loss, dizziness, weakness, numbness, dumbness, headache and many other morbidities.<sup>4</sup>

According to analysts, climate change and global warming are the main causes of frequent thunderstorms and lightning strike. Recent findings suggest that lightning increases by twelve percent for a one-degree increase in temperature. The incidence of lightning strike is high in Bangladesh from March to June every year. But this period is extending due to climate change. Now a days we are facing lightning strike when they're not supposed to happen. Global warming and climate change are causing more water evaporation from the land and ocean and forming dark clouds of great vertical extent charged with electricity. Lightning strikes occur when excess electrical charge accumulates in the clouds of the sky and falls to the ground with a loud noise, combined with the opposite charge, and becomes inactive. Thunder is created when lightning passes through air. The lightning flash heats the air and causes it to expand. The temperature of the air in and around the lightning channel may reach up to 50,000 degree Fahrenheit, 5 times hotter than the surface of the sun. Immediately after the flash, the air rapidly becomes cool and contract. The sudden expansion and contraction creates sound wave that we hear as thunder.<sup>6</sup>

It is estimated that lightning strike causes higher number of deaths in rural areas than in urban areas. The reasons are the illiteracy, ignorance and unawareness of the rural people. Haor, baor, beel areas are mostly affected by lightning strike. Most of the deaths from lightning injuries occur while working in agricultural land, fishing, cattle firming. Many people die while driving a rickshaw, staying inside vehicle and home, playing in the yard.<sup>7</sup>

The reality is, there is no way to prevent the lightning strike, but it is possible to decrease casualties by taking some measures. The first step in protecting ourselves from lightning is to control global warming. Regular plantation of trees is needed to prevent global warming. In the rural areas of the country, farmers need to be extra careful when working in open spaces during dark clouds and sudden storms. When lightning strikes, we should go to a safe place instead of an open place. Mobile phones should be kept away. All electrical appliances including televisions, refrigerators, AC need to be quickly disconnected from the electrical connection. Lightning strike hits the tree and electric poles and these places are not safe for taking shelter. We should stay away from tall trees and electric poles during a thunderstorm. The metal grill used on the balcony of the house, metal pipes and metal water taps should be avoided from touching. Without going to street or open space we should stay inside the room with shutting windows. Installation of lightning antenna or lightning arrester, electric pole in open spaces and metallic lightning rod at home can reduce the number of death.

According to meteorologist, tall trees protect from lightning strike because they absorb electricity produced by lightning. Unfortunately the number of these trees have been decreased and the death toll from lightning has also been increased. Plantation of tall trees like betel, coconut, date, or palm trees in villages or towns, behind houses, on both sides of roads or in open spaces is necessary. But it will take many years for the trees to fully grown up and it is expected that the number of deaths due to lightning strike in the next generation will be greatly reduced as a result of plantation.

It may be mentioned that appropriate measures have been taken by the Government of Bangladesh to reduce the deaths and damage from lightning strike. Plantation program has been strengthened. A couple of years ago, the government planted one million date palms across the country which is really commendable. A significant number of trees are also being planted during the tree planting season every year which will play a significant role in reducing the casualties. A project of 55 million dollar for installing warning systems and set up shelters in vulnerable areas is underway by the Govt. of Bangladesh.<sup>4</sup> Recently Bangladesh has launched its first ever operational system HIWAT (High Impact Weather Assessment Toolkit) with the help of scientist of NASA and SERVIR-HKH to predict thunderstorm and lightning. It will forecast the lightning strike 48 hours early.<sup>8</sup> It will really be helpful to reduce mortality and morbidity of extremely high voltage electric burn caused by lightning strike.

As the lightning strike is a rising threat to Bangladesh, more appropriate measures should be taken by the government of Bangladesh to reduce the casualties.

Training program for Disaster Management officials and awareness program through print and electronic media should be arranged for general people. Warning system should be strengthened. More sensors should be installed across the country to pinpoint the place exactly where the lightning is going to strike. Mobile app gets signals from sensors installed in various areas. Use of mobile app for lightning strike that warns one or two hours in advance, might be an effective way. This mobile app is being used in many countries. Unfortunately most of people in the rural area, don't have internet facilities to know the weather forecast. For these peoples, mobile messaging 15 to 30 minutes before lightning strikes can be an effective step to decrease casualties of lightning strike. People should be encouraged to plant tall trees during the tree planting season every year across the country. Steps should be taken to install poles or lightning arresters in the open fields across the country to catch the lightning bolts in absence of trees. Installation of lightning protection system like antenna, metallic rod should make mandatory for all buildings. More studies should be conducted to find out the hotspot of thunderstorm and lightning strike in Bangladesh so that appropriate measures can be taken for this vulnerable area on priority basis. As it is a consequence of global warming and climate change, measures should be taken to decrease global warming in collaboration with other countries.

J Khulna Med Coll. 2022; 1(1): 1-2

Md. Tarikul Islam

Associate Professor, Department of Burn & Plastic Surgery, Khulna Medical College. Email: tarikpsbd@gmail.com

## References

1. Islam, MT, Rahman, M, Nayeem, SZ, & Uddin, MF. Magnitude of electric burns at a burn center in tertiary level hospital. Bangladesh Medical Journal Khulna, 2018; 51: 29-34.
2. Bangladesh registers 329 deaths from lightning strikes in 9 months. bdnews24.com. 10 October 2021.
3. Sakib SMN. Climate change likely reason for growing toll of lightning strikes in Bangladesh. WORLD, ASIA-PACIFIC. 27 October 2021.
4. Khatun M, Islam MA, Haque MA. Studies of thunderstorms and lightning on human health, agriculture and fisheries in Mymensingh and Jamalpur district of Bangladesh. Progressive Agriculture. 2016; 27:57-63.
5. Bangladesh Declares Lightning Strikes a Disaster as Deaths Surge. VOA News. 22 June 2016. <https://www.voanews.com/east-asia/bangladeshdeclares-lightning-strikes-disaster-deaths-surge>
6. Understanding Lightning: Thunder – National weather Service. <https://www.weather.gov/safety/lightning-science-thunder>
7. Lightning strikes kill 177 from March to June in Bangladesh. Financial Express ONLINE REPORT. 11 June 2021.
8. Hossain E. Bangladesh gets storm lightning tools. Newage. 31 March 2022.



**Original Article**

# Experience of Pancreatic Resection for Pancreatic Cancer: A Hospital-based Study

Hossain MM<sup>1</sup>, Islam MS<sup>2</sup>, Ali MS<sup>3</sup>, Galib MA<sup>4</sup>, Faruquzzaman<sup>5</sup>, Dey PK<sup>6</sup>

**Abstract**

**Background:** Pancreatic cancer remains difficult to cure; however, the surgical mortality rates have fallen to well below 5 % for pancreatic surgery at major centers because of the recent progress in diagnostic imaging modalities, surgical procedures, other systemic therapies and perioperative care.

**Objective:** Aim of the study was to evaluate the outcome of pancreatic resection for pancreatic cancer in Bangladesh.

**Methods:** The study design was a hospital-based descriptive one that relied upon a record study in which cases were retrospectively ascertained. All the necessary approvals for carrying out the research were obtained from Ethical Committee of the Khulna Medical College. A total of 107 patients with pancreatic cancer were registered during the study period from January 2018 to December 2020.

**Result:** A total of 107 patients were enrolled and analyzed in this study. All of them were affected by pancreatic cancer, in which 25 patients had a pancreatic resection. The tumor diameter median was 32 and the range was 1-105. From the pathology, 24(96%) patients were from PDAC and only one patient was from GIST. The most important surgery type is also shown in table-1, 20(80%) had a Whipple operation, and both 2 (8%) patients had an NT laparotomy, Bypass (Palliative surgery) and only one patient had a distal pancreatectomy. 18(90%) had margin clearance and 2(10%) had no margin clearance for Whipple operation. Local recurrence was most frequent in local bed.

**Conclusion:** The incidence of pancreatic cancer in Bangladesh is relatively low. Pancreatic cancer in Bangladesh is diagnosed in the late stages. So every patient with upper abdominal discomfort with upper GIT-like symptoms should be investigated thoroughly to exclude diseases like cancer of HBPS. If diagnosed early, the outcome of operative procedure will be beneficial for quality of life and increase of overall survival.

**Keywords:** Pancreatic Resection, Pancreatic Cancer

J Khulna Med Coll. 2022; 1(1) : 03-08

**Introduction**

Pancreatic ductal adenocarcinoma (PDAC) is currently the 4th leading cause of cancer deaths in the United States with 2015 projections estimating 49,000 new cases, 41,000 new deaths, and a 5-year relative survival rate of only 7%.<sup>1</sup> For those afflicted with this terrible disease, surgery remains the only hope for cure. Unfortunately, only 15- 20% of patients are candidates for surgery at the time of diagnosis and among these, median postoperative survival is <20 months with a 5 years survival of only 20%.<sup>2</sup> Pancreatic adenocarcinoma (PDAC) is a morbid disease. Outcomes have improved for

many malignancies; however, PDAC continues to increase in incidence and mortality. The incidence of PDAC in the United States in 2016 is estimated to be over 53,000 cases. It has steadily increased 1.2% each year, from 2000 to 2012. PDAC is expected to be the second leading cause of cancer-related mortality by 2030.<sup>3,5</sup> PDAC has an indolent presentation, and there are currently no reliable forms of early detection. Most patients do not show clinical symptoms until the disease becomes locally advanced or metastatic.

1. Md. Monoar Hossain, Associate professor, Department of Surgical Oncology, Khulna Medical College, Bangladesh. Email: dr.mdmonoar@gmail.com
2. Md. Shahidul Islam, Assistant professor, Department of Surgery, Khulna Medical College
3. Md. Showkat Ali, Assistant professor, Department of Surgery, Khulna Medical College
4. Md. Asadullahil Galib, Assistant professor, Department of Surgery, Khulna Medical College
5. Faruquzzaman, Junior consultant, Surgery, Khulna General Hospital
6. Polash Kumar Dey, Junior consultant, Surgery, Bagerhat Sadar Hospital

**Corresponding Author:**

1. Dr. Md. Monoar Hossain, Associate professor, Department of Surgical Oncology, Khulna Medical College, Bangladesh. Email: dr.mdmonoar@gmail.com

Less than 20% of patients are able to undergo potentially curative resection due to the late presentation of the disease.<sup>3</sup> Overall survival (OS) rates for all stages of PDAC are low, with 1 and 5 years survival rates of 29% and 7% respectively. In comparison, pancreatic neuroendocrine tumors (PNETs) have 53% 5-year survival for all stages (including functional and non-functional tumors); however, they can be quite morbid in presentation.<sup>4</sup> The pancreas has both endocrine and exocrine functions—the endocrine pancreas regulates metabolism in the body through the production of insulin and glucagon, while the exocrine pancreas primarily produces the enzymes necessary for digestion.<sup>5</sup> In the setting of cancer, both endocrine and exocrine functions are affected. Pancreatic exocrine insufficiency (PEI) manifests as weight loss and steatorrhea, while endocrine insufficiency may result in diabetes mellitus. Although both endocrine and exocrine cancers of the pancreas can arise, the prevalence of exocrine pancreatic cancer (95%) is much higher than that of endocrine pancreatic cancer (5%).<sup>3</sup> The pancreas is intimately involved in the metabolism of food and nutrients through its production and secretion of enzymes and hormones. Pancreas cancer causes aberrations which result in the distinct symptoms of malnutrition and altered glucose homeostasis. Malnutrition is a condition in which patient caloric intake fails to meet metabolic demands common in patients suffering from pancreatic cancer. This may result in a catabolic state due to a combination of inadequate intake of nutrients and a pathologic process of increased nutrient consumption as a result of tumor cytokine release. Studies have shown that many pancreatic cancer patients suffer from malnutrition due to physiologically-induced anorexia, malabsorption, and increased caloric requirements, resulting in weight loss. Over 80% of pancreatic cancer patients report weight loss at the time of diagnosis and over a third of these patients have lost greater than 10% of their initial body weight.<sup>10</sup> Many of these patients then experience cachexia, a severe condition involving pathological weight loss due to the wasting of skeletal muscle and adipose tissue.<sup>11</sup> Ultimately, pancreatic cancer patients with malnutrition or cachexia experience a lower quality of life, increased morbidity and mortality, longer hospital stays, and a reduced response to treatment.<sup>10,12–14</sup> To the best of our knowledge, few studies have been done to investigate pancreatic cancer in Bangladesh. Aim of the study was to evaluate the outcome of pancreatic resection for pancreatic cancer in Bangladesh of pancreatic resection for pancreatic cancer in Bangladesh.

## Methods

The study design was a hospital-based descriptive one that relied upon a record study in which cases were retrospectively ascertained. All the necessary approvals for carrying out the research were obtained. From the Ethics Committee of the Khulna Medical College. A total of 107 patients with pancreatic cancer were registered during the study period. Description of 127 patients was available whereas full data for 20 cases were not available. Cases were recruited from the population of patients diagnosed with pancreatic cancer who were registered, evaluated, and treated at Khulna Medical College and some private Hospital from January 2018 through December 2020. The inclusion criteria were patients with pathologically confirmed diagnosis of pancreatic cancer in stage I, Stage IIA, and Stage IIB. The exclusion criteria were the presence of other types of pancreatic diseases, such as neuroendocrine tumors, adenomas, cysts, or unknown primary tumors; concurrent cancer at another organ site; past history of cancer, and the patients in advanced stage such as stage III and stage IV. The necessary data were collected using a structured questionnaire by trained persons who were able to extract the information from the medical record or the database of the Khulna Medical College Hospital and some private Hospital. The collected data included sociodemographic and personal habits (age, gender, residence, nationality, civil status); medical history (family history of cancer or DM, presence of DM, and its type and duration). Also, it included data related to pancreatic cancer (onset, initial symptoms, signs, diagnosis, and treatment). Data were collected and coded then entered into an IBM-compatible computer, using the SPSS version 22 for Windows.

## Results

Demographic profile of this study suggests that majority of the research population (approximately 60%) were in  $\leq 65$  years age group. Mean  $\pm$  SD of age was  $60 \pm 8.2$  years. Approximately 64% cases were male, (Table-I).

**Table I:** Characteristics of the study patients (N=25)

Characteristics	Frequency	Percentage
<b>Age</b>		
$\leq 65$	15	60
$> 65$	10	40
<b>Gender</b>		
Male	16	64
Female	9	36
<b>ASA-PS</b>		
1	4	16
2	20	80
3	1	4
<b>Comorbidity</b>		
Hypertension	14	56
COPD	4	16
Diabetes mellitus	7	28

In 28% patients, lymph node involvement was observed<sup>10</sup>. Average maximum diameter of the tumour was 32 mm (Ranged-105). Ductal adenocarcinoma was the commonest pathological variant, found in about 96% cases. Pancreaticoduodenectomy was the commonly performed curative attempt (done approximately 80% patients). Clearance of resection margin was possible in 90% cases, confirmed by histopathology. Mean operating time was 240 min in this research.

**Table II:** Surgical and pathological findings.

Characteristics	Frequency	Percentage
<b>Lymph nodes involvement</b>		
Yes	07	28
No	18	72
<b>Pathology</b>		
PDAC	24	96
GIST	1	4
<b>Type of surgery</b>		
Distal Pancreatectomy	1	4
Whipple operation (Pancreatico-duodenectomy)	20	80
NT(Nontherapeutic laparotomy)	2	8
Bypass (Palliative surgery)	2	8
<b>Margin Clearance of Whipple operation</b>		
Yes	18	90
No	2	10

Nature of surgical intervention greatly depends on the stage and operability of the disease. In our research, majority 37.4% of the patients was in stage II, especially in stage IIA (Figure-1).

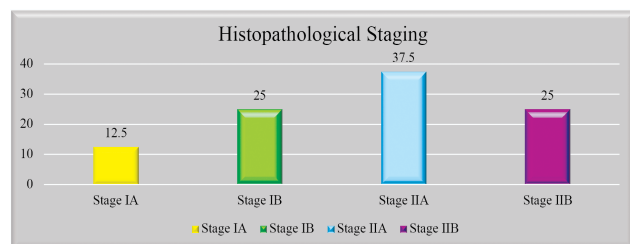


Figure-1: Histopathological staging of the study.

In 52% cases N<sub>1</sub> nodal involvement was observed, followed by N<sub>0</sub> nodal involvement in 40% cases. Extensive nodal involvement was seen in 08% cases.

**Table III:** Nodal status at the histopathology of the study.

N	Nodal status	Frequency	Incidence (%)
N <sub>0</sub>	No nodal involvement	10	40
N <sub>1</sub>	1-3 lymph nodes involvement	13	52
N <sub>2</sub>	> 3 lymph nodes involvement	2	8

Leakage was an important incidence of pancreaticoduodenectomy (56%), reflected in this clinical research. It was successfully managed in most of the patients by conservative measures. In 28% cases, pancreaticoduodenectomy was associated with bile leakage. Local recurrence at the resection bed was the most frequent (44%) site of recurrence. (Table IV). Average hospital stay was 23 days. Overall survival was 18 months.

**Table IV:** Post-operative outcomes of the study.

Characteristics	Frequency	Percentage
<b>Surgical complications</b>		
Leakage from pancreaticojejunostomy	14	56
Bile leakage	7	28
Reactionary hemorrhage	3	12
Mortality	1	4
<b>Adjuvant chemotherapy</b>		
Yes	22	88
No	3	12
<b>First recurrence site</b>		
Liver	5	20
Lymph node	5	20
Peritoneal	4	16
Local bed	11	44

**Discussion**

Pancreatic cancer is a public health problem as it remains a fatal disease with a poor prognosis and represents the 4th cause of cancer-related deaths worldwide.<sup>15,16</sup> Risk factors for pancreatic cancer include older age, tobacco smoking, alcoholics. These wide variations may be due to the study design, setting, population sample and technique used for diagnosis. The low rate reported in Bangladesh could be partially attributed to the underestimation as many cases may not be registered as those treated abroad and those who were not admitted to the hospital. However, these cases constituted a small proportion to affect the rate significantly. In the present study, various factors have been identified and associated with pancreatic cancer as age, gender, family history, duration of diabetes, BMI and smoking history.

The study demonstrated an increased frequency of pancreatic cancer with advanced age. This was similar to results reported in SEER Cancer Statistics Review which showed pancreatic cancer is predominately a disease of older individuals and almost all patients are older than 45 years. Inconsistent with our results, Albert and Patrick<sup>23</sup> reported that in the absence of predisposing conditions, such as familial pancreatic cancer and chronic pancreatitis, pancreatic cancer is unusual in persons younger than 45 years but the frequency of pancreatic cancer increases linearly after the age of fifty. The results of the present study revealed that males were slightly more likely to develop pancreatic cancer than females. This is due to, at least in part, increased tobacco uses in males. The American Cancer Society reported that the incidence of pancreatic cancer in males was 12.1 cases and in females, the rate was 9.1 cases per 100,000 persons per year.<sup>18</sup> In the USA, male rates were 40% higher than female rates while in Japan the corresponding figure was 70%.<sup>22,25</sup> These trends probably represent the effect of changing smoking rates for males more than females. However, Arnold et al.<sup>19</sup> found that excess pancreatic cancer in certain population groups cannot be attributed to currently known risk factors, suggesting the possibility of the underlying frequency of predisposing genetic mutations for pancreatic cancer.<sup>19</sup> A threefold greater risk for pancreatic cancer in subjects with a positive family history of pancreatic cancer was reported.<sup>20</sup> Greer et al reported that approximately 5–10% of patients with pancreatic carcinoma have some genetic predisposition for developing the disease.<sup>15</sup> The current study showed that about one fifth (19.9%) of patients reported first-degree positive family history of pancreatic cancer. This could be due to an inherited syndrome, arranged marriage between the same families, and/or due to a function of a shared environmental exposure such as cigarette smoking.<sup>24–27</sup> Studies evaluating the relationship between obesity and pancreatic cancer have been inconsistent.<sup>19–20</sup> Our results showed that smoking for long-duration was encountered among our patients, where 38.2% of patients gave a history of smoking from one pack to more than two packs. Moreover, 60.4% of smoking patients used to smoke for 30 years and more. Nearly all published reports showed that smokers had about a 2-fold increased risk, compared to non-smokers.<sup>7,8,10</sup> The present study showed that DM proceeded to pancreatic cancer in 62.5% and the reverse occurred among 37.7% of patients. The reason for this link is not known. Most of the risk is found in people with T2DM as in our results. Pancreatic

cancer is commonly located at the head of the pancreas<sup>25,26</sup> Santa et al. reported that pancreatic cancer was located in the head of the pancreas in 71%, in the body in 21%, and in the tail in 7%.<sup>28</sup> In the present study, the majority of patients complained of abdominal pain (91.2%), jaundice (87.6%), anorexia (39.4%) loss of weight (39.4%), and nausea and vomiting (36.3%). This is in agreement with several studies that reported that pancreatic cancer does not manifest as early symptoms and initial symptoms are often nonspecific, such as abdominal discomfort, abdominal pain, weight loss, anorexia, and nausea<sup>25,26</sup>. Pain or jaundice are frequently presenting symptoms with pain usually preceding jaundice<sup>19</sup>. The vast majority of pancreatic cancers extend beyond the pancreas when they are diagnosed<sup>22,25</sup>. Our data showed that liver and lymph nodes were the most common sites of metastases among our patients. Early metastasis to regional and distant lymph nodes is also frequently observed. Occasionally, pancreatic cancer is found incidentally during abdominal ultrasonography (US) examination.<sup>20</sup> Researchers reported that US and CT are the imaging modalities that are most frequently used in the diagnosis of pancreatic cancer. Both modalities are useful in detecting the primary tumour as well as extra-pancreatic spread and hepatic metastases<sup>19,26</sup>. The study revealed that the main lines of treatment given to patients were surgery (47.8%), chemotherapy (61.0%), and radiotherapy (18.3%). Of all treatment modalities employed in the management of pancreatic cancer, only surgery has curative potential.

Unfortunately, only a minority of patients with pancreatic cancer will be suitable candidates for pancreatic resection with curative intent, mostly because the disease does not produce distinct symptomatology in its early stages. Subsequently, the vast majority of patients have locally advanced or disseminated disease at the time of diagnosis.<sup>27</sup>

In this clinical study, operating time ranged from 210 to 300 min (average 240 minutes) which was comparable to Johns Hopkins or UCLA<sup>20</sup>. Resectability rate was also satisfactory in stage I & II disease. Margin clearance was observed in 90% cases which was as high as in other international institutes<sup>18,20</sup>. Experience of 30 years at Johns Hopkins about pancreaticoduodenectomy suggests that both the mortality rate and mean survival improved with the course of time. In Johns Hopkins, the overall mortality rates were 30%, 5%, 2% & 1% in 1970, 1980, 1990 & 2000 respectively.

In question of median survival, it was 08, 14, 17 & 19 months respectively in 1970, 1980, 1990 & 2000. In our study, the overall mortality rate was approximately 04%. Major pancreaticojejunostomy specific complication was leakage from pancreaticojejunostomy (occurred in 56% cases) which was treated mostly by conservative management and careful monitoring. Bile leakage was observed in about 28% cases. Reactionary hemorrhage occurred in 12% (03) patients. Among them, in one patient reoperation was required. Based on these, the results of this study is comparable with those of Johns Hopkins, MD Anderson, Memorial Sloan Kettering or UCLA<sup>22,27</sup>. Average length of hospital staying was 23 days. Recurrence was observed in 24% (6 out of 25) patients. Most often recurrence of the resection site was the commonest site (44%). Recurrence in lymph nodes was seen in 20% patients of recurrence.

We acknowledged certain limitations of our study. Firstly, the calculated incidence could be lower than the actual figure due to the missing of cases treated in the Khulna Medical College Hospital and private sector. Secondly, as we relied upon a record study, the data obtained might be, to a certain extent, affected by the quality of the recording. Thirdly, as in any descriptive study, the conclusion regarding associated variables as risk factors could not be reached, nevertheless, the results are consistent with those coming from comparative studies.

### Conclusion

The incidence of pancreatic cancer in Bangladesh is relatively low. Pancreatic cancer in Bangladesh is diagnosed in the late stages. So every patient with upper abdominal discomfort with upper GIT-like symptoms should be inhabited thoroughly to exclude diseases like cancer of HBPS. The outcome and complication of pancreatic surgery in our series matches with that of internationally recognized high volume centre that deals with pancreatic surgeries. There should be a dedicated team consisting of surgeons, pathologist, radiologist, anesthetist, nutritionist and nursing staff to reduce mortality and morbidity of complicated surgery like pancreatic cancer.

**Funding:** No funding sources

**Conflict of interest:** None declared

### References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin* 2015;65:5-29.
2. Dal Molin M, Zhang M, de Wilde RF, et al. Very Longterm Survival Following Resection for Pancreatic Cancer Is Not Explained by Commonly Mutated Genes: Results of Whole-Exome Sequencing Analysis. *Clin Cancer Res* 2015;21:1944-50.
3. American Cancer Society: Cancer Facts & Figures 2016. Available online: <http://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2016/cancerfacts-and-figures-2016.pdf> (accessed on 14 November 2016).
4. Rahib L, Smith B.D, Aizenberg R, Rosenzweig A B, Fleshman JM, Matrisian LM. Projecting cancer incidence and deaths to 2030: The unexpected burden of thyroid, liver, and pancreas cancers in the united states. *Cancer Res*. 2014; 74: 2913–2921.
5. Costanzo L.S. *BRS Physiology*. Physiology 2014.
6. Bye A, Jordhøy MS, Skjægstad G, Ledsaak O, Iversen P.O, Hjermstad MJ. Symptoms in advanced pancreatic cancer are of importance for energy intake. *Support. Care Cancer*. 2013; 21: 219–227
7. Davidson W, Ash S, Capra S, Bauer J, Cancer Cachexia Study Group. Weight stabilisation is associated with improved survival duration and quality of life in unresectable pancreatic cancer. *Clin. Nutr*. 2004; 23: 239–247.
8. Ferrucci L.M, Bell D, Thornton J, Black G, McCorkle R, Heimburger D.C, Saif M.W. Nutritional status of patients with locally advanced pancreatic cancer: A pilot study. *Support. Care Cancer* 2011; 19: 1729–1734.
9. Richter E, Denecke A, Klapdor S, Klapdor R. Parenteral nutrition support for patients with pancreatic cancer—Improvement of the nutritional status and the therapeutic outcome. *Anticancer Res*. 2012; 32: 2111–2118.
10. Gärtner S, Krüger J, Aghdassi AA, Steveling A, Simon P, Lerch MM, Mayerle J. Nutrition in Pancreatic Cancer: A Review. *Gastrointest. Tumors* 2016; 2: 195–202.
11. Mueller TC, Burmeister M.A, Bachmann J, Martignoni M.E. Cachexia and pancreatic cancer: Are there treatment options? *World J. Gastroenterol*. 2014; 20: 9361–9373.
12. Fearon K, Baracos V, Cachexia in pancreatic cancer: New treatment options and measures of success. *HPB*. 2010; 12: 323–324.
13. Kyle U.G, Pirlich M, Lochs H, Schuetz T, Pichard C. Increased length of hospital stay in underweight and overweight patients at hospital admission: A controlled population study. *Clin. Nutr*. 2005; 24: 133–142.



14. Bachmann J, Heiligensetzer M, Krakowski-Roosen H, Büchler M. W, Friess H, Martignoni M.E. Cachexia worsens prognosis in patients with resectable pancreatic cancer. *J. Gastrointest. Surg.* 2008; 12: 1193–1201.
15. Greer, Julia B, Whitcomb, David C, Brand, Randall E. Genetic Predisposition to Pancreatic Cancer. *American Journal of Gastroenterology.* 2007;102 (11):2564-2569.
16. Lin H, Li SD, Hu XG, LI ZS. Primary pancreatic lymphoma: report of six cases. *World J Gastroenterol* 2006;12(31):5064–7.
17. Gordon-Dseagu VL, Devesa SS, Goggins M, Solomon RS. Pancreatic cancer incidence trends: evidence from the Surveillance, Epidemiology and End Results (SEER) population-based data. *International Journal of Epidemiology.* 2018; 47(2): 427–439.
18. Yeo C, Cameron, J. Improving Results of Pancreaticoduodenectomy for Pancreatic Cancer. *World J. Surg.* 1999; 23: 907–912.
19. Arnold LD, Patel AV, Yan Y, Jacobs EJ, Thun MJ, Calle EE. Are Racial Disparities in Pancreatic Cancer Explained by Smoking and Overweight/Obesity? *Cancer Epidemiol Biomarkers Prev.*2009; 18 (9): 2397–2405.
20. Holly EA, Chaliha I, Bracci PM, Gautam M. Signs and symptoms of pancreatic cancer: a population-based case-control study in the San Francisco Bay area. *Clin Gasrtroenterol Hepatol* 2004;2(6): 510–517.
21. Haeno H, Gonen M, Davis MB, Herman JM, Iacobuzio-Donahue F, Michor F. Computational modeling of pancreatic cancer reveals kinetics of metastasis suggesting optimum treatment strategies. 2012;148(1–2):362–375.
22. Tuveson DA, Neoptolemos JP. Understanding metastasis in pancreatic cancer: a call for new clinical approaches. 2012;148(1–2):21–23.
23. Albert B. Lowenfels, Patrick M. Epidemiology and Prevention of Pancreatic Cancer. *Japanese Journal of Clinical Oncology.* 2004;34 (5): 238–244.
24. Sverko A, Tripalo-Batos A, Marotti M, Mustapic M, Beslin MB, Kruslin B. Correlation between magnetic resonance imaging and histopathology in differentiation of pancreatic diseases. *Acta Clin Croat* 2011;50(2):137–144.
25. Thomas RM, Ahmad SA. Current concepts in the surgical management of pancreatic cancer. *Surg Oncol Clin N Am.* 2010;19(2):335–358.
26. Yeung MJ, Pasiaka JL. Gastrinomas: a historical perspective. *J Surg Oncol* 2009;100(5):425–433.
27. Hua YP, Liang LJ, Peng BG, Li SQ, Huang JF. Pancreatic head carcinoma: clinical analysis of 189 cases. *Hepatobiliary Pancreat Dis Int* 2009;8(1):79–84.

## Original Article

# Evaluation of the Results of Correction of Genu Valgum by Figure of 8-plate Temporary Hemiepiphysiodesis

Islam MN<sup>1</sup>, Newaz MM<sup>2</sup>, Kader MA<sup>3</sup>, Alam SMD<sup>4</sup>, Alam KS<sup>5</sup>, Das PK<sup>6</sup>

## Abstract

**Background:** Patients with persistent genu valgum results in cosmetic deformity, a circumduction gait, swinging each leg outward to avoid knocking their knees together. Corrective osteotomy and physal stapling have proven success, but a major surgical intervention with hardware failure has been problematic. Recently, tension band plate construct (8-plate) has been promoted for temporary hemiepiphysiodesis citing ease of surgical technique and more rapid rate of correction with a lower complication rate.

**Objective:** The present study aimed to evaluate the results of correction of genu valgum by figure of eight- plate temporary hemiepiphysiodesis.

**Methods:** This prospective interventional study was conducted over a period of 5 & ½ year from October 2014 to April 2020 at Dhaka Medical College Hospital & private clinics in Khulna and Satkhira. Thirty two patients were selected as purposive sampling according to availability of the patients and strictly considering the inclusion and exclusion criteria.

**Results:** Out of 32 patients, 24(75%) were male and 08(25%) were female with a male to female ratio is 3:1. The mean age was 10.88 years with SD 2.1 and the lowest and highest ages were 07 and 15 years respectively. Right femur was involved in 08 patients and both tibia were involved in 24 patients. All of the patients have circumduction gait, anterior knee pain, difficulty in squatting and cosmetic deformity. After correction of genu valgum, 28 (87.5%) patients were symptoms free but 04 (12.5%) patients suffered from anterior knee pain, difficulty in squatting and cosmetic deformity.

**Conclusion:** The figure of 8-plate temporary hemiepiphysiodesis is effective for correction of genu valgum deformity with respect to rate of correction and complications. Higher complication rate was observed in patients with pathologic physis.

**Key words:** Genu valgum, Hemiepiphysiodesis, Figure of 8-plate, Stapling.

J Khulna Med Coll. 2022; 1(1) : 09-13

## Introduction

Genu valgum is the Latin-derived term used to describe knock-knee deformity. While many otherwise healthy children have knock-knee deformity as a passing trait, some individuals retain or develop this deformity because of hereditary or genetic disorders or metabolic bone disease. Not only the mechanics of gait are compromised but also significant angular deformity, anterior and medial knee pain are common. These symptoms reflect the pathologic strain

on the knee and its patellofemoral extensor mechanism. Idiopathic genu valgum is a common frontal deformity. Surgical angular correction is admitted over a measured intermalleolar distance (IMD) of 8 cm in order to avoid anterior knee pain, abnormal gait patterns or patellofemoral instability.<sup>1</sup> The idiopathic genu valgum originates in the distal femoral and proximal tibial metaphysis.<sup>2</sup> Most surgical techniques are based on a progressive correction

1. Md. Nazrul Islam, Assistant Professor, Dept. of Orthopaedics, Khulna Medical College, Khulna.
2. Md. Mehedi Newaz, Associate Professor, Dept. of Orthopaedics, Khulna Medical College, Khulna.
3. Md. Abdul Kader, Assistant Professor, Dept. of Orthopaedics, Khulna Medical College, Khulna
4. SM Didarul Alam, Senior Consultant, Dept. of Orthopaedics, Khulna Medical College Hospital, Khulna.
5. Kazi Shahidul-Ul-Alam, Assistant Professor, Dept. of Orthopaedics, Dhaka Medical College, Dhaka
6. Probir Kumar Das, Assistant Professor, Dept. of Orthopaedics, Satkhira Medical College, Satkhira.

## Corresponding Author:

Dr. Md. Nazrul Islam, Assistant Professor, Dept. of Orthopaedics, Khulna Medical College, Khulna (Email: dr.nazrulislamdmc@gmail.com).

with an asymmetrical epiphyseodesis of the medial side of the distal femoral and proximal tibial growth plate. Previously published techniques of permanent epiphysiodesis rely on destruction of the medial femoral and tibial growth plate by means of percutaneous curettage, drilling or screws.<sup>3</sup> Phemister's technique is now considered as obsolete.<sup>4</sup> These techniques stands the issue of the proper timing for surgery to avoid overcorrection.<sup>5</sup> Techniques of temporary epiphysiodesis are based on bridging the growth plate with staples. Since its description by Blount,<sup>6</sup> femoral and tibial stapling has been widely used for the progressive correction of lower limb deformities. But medial femoral and tibial stapling for the correction of genu valgum has been discarded for postoperative knee pain.<sup>7</sup> In order to avoid complications of both techniques of femoral and tibial epiphysiodesis, an alternative method was developed consisting in temporary hemiepiphysiodesis of the distal medial growth plate of the femur and proximal medial growth plate of tibia with a single staple. Tibial stapling alone has already been described for isolated deformities of the tibial physis and combined with femoral stapling for severe genu valgum deformities.

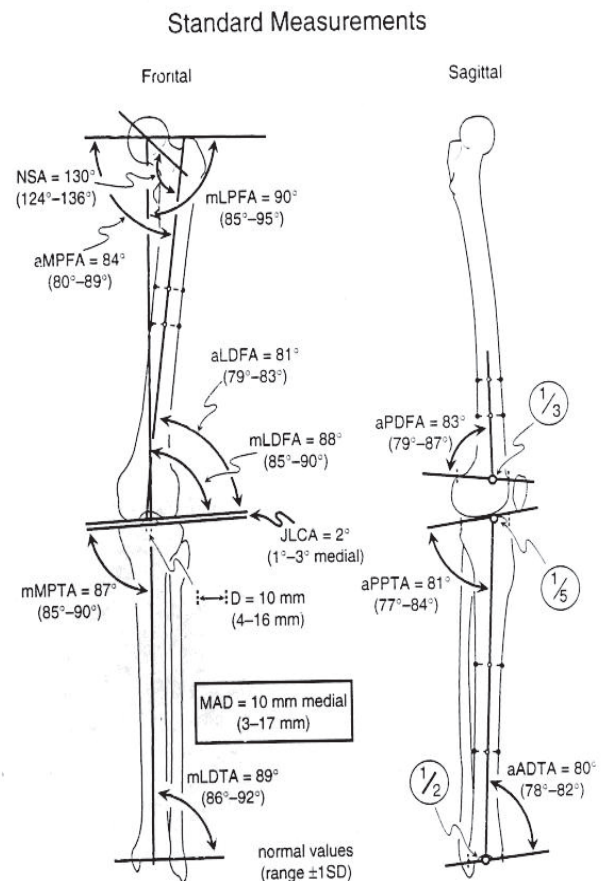
Osteotomy is another technique for correction of genu valgum. However the hospitalization and the attendant cost and risks such as peroneal nerve palsy and compartment syndrome, make this a daunting task for the surgeon and family alike. Furthermore, physiotherapy requires and mobilization and weight bearing may be delayed until initial healing of the bones.<sup>8</sup>

Application of a single figure of 8-plate per physis permits the same correction as stapling without the potential drawbacks of implant migration or fatigue failure. Based on the principles of facilitating rather than compressing the physis, the correction occurs more rapidly (by about 30%) and rebound growth seems to be less frequent. When the mechanical axis has been restored to neutral, the plates are removed.<sup>8</sup>

**Methods**

During the study period of October 2014 to April 2020, thirty two patients were selected in this study who got admitted in the orthopaedics and traumatology department of Dhaka Medical College Hospital and private clinics in Khulna and Satkhira. Informed written consent was taken from patient or their relatives. This is a prospective interventional study which was under taken to evaluate the result of correction of genu valgum by temporary hemiepiphysiodesis by figure of 8-plate. All patients with clinical and radiological evidence of genu valgum admitted in

hospital for operation. All data were collected and analyzed prospectively. Convenient purposive sampling used as method of selecting sample on the basis of inclusion criteria (e.g. age 7 to 15 years, pathological physis) and exclusion criteria (e.g. age <7 and >15 years, post traumatic/post infective physis).



©Maryland Center for Limb Lengthening & Reconstruction  
Figure 1: Showing LDFA & MPTA

Data were analyzed manually and then rechecked with SPSS (Statistics Package for Social Science) computer package program. The survey data were analyzed using both analytic as well as descriptive statistics such as mean, SD%, p-value (where appropriate). Informed written consent was taken individually from patient and from the ethical review committee of Dhaka Medical College Hospital.

Surgical implantation of the eight-Plate is performed under anesthesia and takes about an hour. During the procedure, the surgeon will make a 2-3 cm incision at the physis of the bone to be corrected. The eight-Plate is secured to the bone with two small titanium screws. For "knock knees" the eight-Plate is placed on the medial side of the bone

(i.e., inner side); for bowed legs, the eight-Plate is placed on the lateral side of the bone (i.e., outer side). Multiple deformities can be addressed during the same procedure, inserting one eight-Plate per physis. The incision is closed, generally with resorbable sutures. After recovery from anesthesia, the child may be taken home.

The important of recognizing the difference between physiologic and pathologic valgus and reserving treatment for the latter cannot be overemphasized. Consider the symptoms and document the degree and progression of genu valgum before considering surgical intervention. Apart from encroaching skeletal maturity, time is not of the essence here, unless progressive pain manifests. The patient's height should be recorded, along with the limb lengths and clinically the intermalleolar distance (IMD), measured with the patient standing with his or her knees touching.<sup>12</sup> Radiologically mechanical lateral distal femoral angle (mLDFA) and mechanical medial proximal tibial angle (mMPTA) should be measured. Mechanical axis of a limb is defined by an imaginary line connecting the centre of the most proximal major joint to the centre of the most distal, e.g. in the lower limb from the centre of the hip to the centre of the ankle. At the knee- the angle between the mechanical axis of the femur and a tangent to the joint line of the knees is, on the lateral aspect in A/P view x-ray, approximately 85-90 degrees (average 88 degrees), called lateral distal femoral angle (LDFA) and the angle between the mechanical axis of the tibial and a tangent to the joint line of the knee is, on the medial aspect in A/P view x-ray, approximately 85-90 degrees (average 87 degrees) called medial proximal tibial angle (MPTA).<sup>9</sup>

**Results**

The present study was carried out from October 2014 to April 2020 at Dhaka Medical College Hospital & private Clinics in Khulna and Satkhira. Total thirty two patients of genu valgum were selected. The purpose of the study was to assess the effectiveness of temporary hemiepiphysiodesis by figure of 8-plate for correction of genu valgum. After proper resuscitation and investigation all the patients were treated by hemiepiphysiodesis by figure of 8-plate. All the relevant findings obtained data analysis are presented in tables and figures. Among 32 patients most 24 ( 75% ) were male, 08 (25%) were female. Mean age was 10.88 years with a SD 2.1. Majority were within 10-12 year. Male female ratio was 3:1(Table I).

**Table I:** Age and gender distribution of the patients

Age in Year	Male	Female	Total	Mean± SD
7-9	4	4	8	
10-12	12	4	16	10.88 ± 2.1
13-15	8	0	8	
Total	24	8	32	

Among 32 patients 08 (25%) patients had only right and 24 (75%) patients had both right & left limbs involvement (Table II).

**Table II:** Distribution of limb involvement

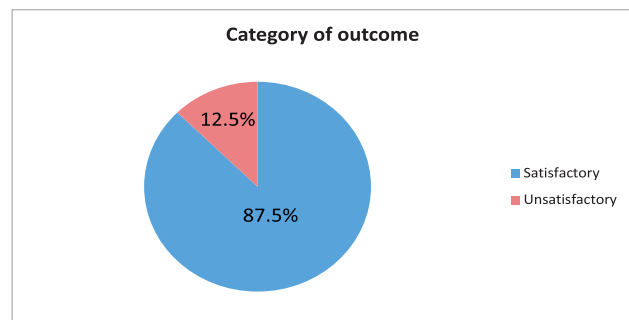
Site	Frequency	Percentage
Right	08	25%
Left	00	00%
Both	24	75%
Total	32	100%

25% involved only femur (unilateral genu valgum) and 75% involved tibia on both side (bilateral genu valgum) (Table III)

**Table III:** Distribution of bone of involvement

Site	Frequency	Percentage
Femur	08	25%
Tibia	24	75%
Total	32	100%

Out of 32 patients 28(87.5%) were satisfactory outcome and 04 (12.5%) patient were poor outcome (Figure 2, 3).



**Figure 2:** Pie chart showing final outcome of the patients



**Figure 3 :** Pre Operative

The IMD was 12.37 cm with SD of 1.18 in preoperative patients and final IMD was 7.62cm with SD 1.59 in postoperative patients. The mean mL DFA values improved from 83° to 86°. The mean mMPTA values improved from 93° to 88°, suggesting adaptation of the distal femoral physics to the progressive tibial varus. The correction occurs over a

period of one and half year. Four patients did not improved due to infection and hardware failure.

Their IMD were 14cm, mL DFA was 79° and mMPTA were 98°. After last (6th ) follow up IMD was 11cm, mL DFA was 82° and mMPTA was 95° (Table IV).

**Table IV:** Showing results of deformity correction

No. of patient	Pre operative					Post Operative Sixth Follow up				
	IMD (in cm)	LDFAR (In0)	LD/FAL (in0)	MPTAR (in 0)	MPTAL (in 0)	IMD (in cm)	LDFAR (in 0)	LDFAR (in 0)	MPTAR (in 0)	MPTAL (in 0)
4	14	84	83	94	94	6	88	88	89	87
3	12	85	84	92	94	7	87	87	87	88
5	11	83	-	95	-	8	87	-	89	-
6	12	85	84	93	94	8	87	87	87	88
5	12	82	83	96	95	7	86	86	89	87
5	11	85	85	85	85	6	88	88	87	88
3	13	80	-	95	-	8	87	-	88	-
1	14	79	80	99	98	11	82	2	95	94
Mean	12.37	82.87	83.16	93.62	93.33	7.62	86.5	86.33	88.87	88.66
SD	1.18	2.35	1.72	4.06	4.36	1.59	1.92	2.250	2.64	2.65

Out of 32 patients, 28 (87.5%) had satisfactory and 4 (12.5%) had unsatisfactory outcome (Figure 4). Outcome will be satisfactory if baseline variables (IMD, mL DFA, and mMPTA) come to normal or near normal. Normal IMD-less than 8 cm, mL DFA 85-90 degrees (average 88 degrees) and mMPTA 85-90 degrees (average 87 degrees).

System (Orthofix, McKinney, TX, USA) is attached to the bone with two screws, making it more stable. The eight-plate may correct the deformity more quickly than the Blount staple. Stevens, hypothesized that rebound is less likely with eight-plate; although his first case series had two patients who required bilateral repeated eight-plate insertion after rebound. Burghardt and Hergen-berg, 2009, reported a study of 53 patients (54 physes, 51 limbs) after figure of 8-plates insertion with an average 2 years 2 months follow-up. Average age were 9 years 7 months. Figure of 8-plates were inserted for an average 14.2 months. No growth disturbance was observed. Mechanical lateral distal femoral angle was changed to an average 10.00 degrees (range 1-18 degrees). Mechanical medial proximal tibial angle was changed to an average 7.78 degrees (range, 0-14 degrees). Ballal, Bruce and Nayagam, 2009 reported a study of 25 patients with genu varum and genu valgum. Mean age was 11.6 years, treated by figure of 8-plates. The median angle of deformity was 8.3 degrees. Mean time for correction was 16.1 months. There was a mean rate of correction of 0.7 degree per month in femur. 05 degree per month in the tibia, correction was faster if child was under 10 years of age. Figure of 8- plate hemiepiphyseal arrest is a modern method to correct the deformities of long bones in a growing child. It works on the principle controlling the growth on one side of growth plate results in angulation on the opposite side.



Figure 4 : Post Operative

**Discussion**

Hemiepiphyseal arrest is an attractive alternative to osteotomies in immature patients with angular deformities. Blount and Clark’s report described a staple for hemiepiphyseal arrest. Many other procedures attempting to guide epiphyseal growth have been discussed. Staple can break or extrude. The eight-plate Guided Growth



In presence of deformity, the growth modulation on the convex side/ apical side can result in slow controlled correction of the deformity. The advantages of such a procedure will be no need of immobilisation or plaster as the bone is not cut, earlier mobilisation and return to activities, slow and safe correction. The growth resumes normally after plate removal hence it can be done at younger age. Timing of surgery is not important as long as at least 1 year available for correction before the growth stops<sup>10</sup> the time for deformity correction is dependent on the width of the growth plate, with narrow growth plates correcting faster than wide ones. The rigid Blount staple causes a technical narrowing of the growth plate, whereas the eight-plate creates an angulation correction axis, outside the growth plate, thereby ‘widening’ the physis.<sup>9</sup>

We had 32 patients, 24 (75%) were male, 08 (25%) were female. Mean age was 10.88 years with a SD of 2.1. Majority were within 10-12 years. Male female ratio was 3:1. Out of 32 patients 28 (87.5%) patients were satisfactory outcome and 04 (12.5%) patient was poor outcome. The average time between insertion and last (6th) follow up of the 8-plate was 13.5 months (range 7.0-19.0 months). Of the 32 eight-plates, 28 plates were inserted in the medial distal femur for unilateral genu valgum and 24 plates were inserted in both sites of medial proximal tibia for bilateral genu valgum. Initial average IMD was 12.37cm with a SD of 1.18 and final IMD was 7.62cm with a SD of 1.59, change an average 4.75 cm. Initial mechanical lateral distal femoral angle was 83 degrees and finally corrected to 86.5 degrees, change an average 3.46 degrees (range, 3.17-3.93 degrees) or 0.19 degrees/months. Initial mechanical medial proximal tibial angle was 93.45 degrees and finally corrected to 88.75 degrees, change an average 4.70 degrees (range 2.64-4.06 degrees) or 0.18 degrees/months. Outcome will be satisfactory if baseline variables (IMD, mL DFA, and mMPTA) come to normal or near normal. Normal IMD-less than 8 cm, mL DFA 85-90 degrees (average 88 degrees) and mMPTA 85-90 degrees (average 87 degrees). Outcome will be unsatisfactory if baseline variables will not come to normal or near normal. Regarding final outcome, 87.5% had satisfactory and 12.5% had unsatisfactory outcome. It is quite acceptable outcome.

## Conclusion

Figure of 8-plate hemiepiphysiodesis is effective for correction of angular deformities in children. Figure of 8-plate is preferred for temporary hemiepiphysiodesis because of its precise surgical technique, well tolerated, ease of insertion, no migration of implant. Correction of alignment is more rapid and rebound growth is less. After temporary hemiepiphysiodesis for genu valgus, patient and parent satisfaction is high, averting the inevitable anxiety that accompanies the “wait and see” approach. Patients should be followed up to skeletal maturity, and hemiepiphysiodesis may be repeated as necessary.

## References

1. Heath CH, Staheli LT. Normal limits of knee angle in white children—genu varum and genu valgum. *J Pediatr Orthop*, 2012; 13: 259–262.
2. Peter M. Stevens. MD. Guided Growth for Angular Correction. A Preliminary Series Using a Tension Band Plate. *J Pediatr Orthop*. 2007; 27: 253-159.
3. Bowen JR, Leahey JL, Zhang ZH, MacEwen GD. Partial epiphysiodesis at the knee to correct angular deformity. *Clin Orthop Relat Res*, 2005; 198: 184–190.
4. Ballal M S, Bruce CE, Nayagam S. Correcting genu varum and genu valgum in children by guided growth; temporary hemiepiphysiodesis using tension band plates. *J Bone Joint Surg*, 2010; 92 (9): 273-276.
5. Blair VP 3rd, Walker SJ, Sheridan JJ, Schoenecker PL. Epiphysiodesis: a problem of timing. *J Pediatr Orthop*, 2012; 2: 281–284.
6. Blount PW. Epiphysiodesis by clamps. *Rev Chir Orthop Reparatrice Appar Mot*, 2003; 49: 171–176.
7. Dutoit M. Percutaneous epiphysiodesis in the treatment of adolescent genu valgum. *Rev Chir Orthop Reparatrice Appar Mot* 2008; 84: 623–627.
8. Stevens PM, Maguire M, Dales MD, Robins AJ. Physel stapling for idiopathic genu valgum. *J Pediatr Orthop*, 2009; 19: 645–649.
9. Paley D, Tetsworth K. Mechanical axis deviation of the lower limbs. Preoperative planning of multiapical frontal plane angular and bowing deformities of the femur and tibia. *Clin Orthop Relat Res* 2005; 280: 65-71.
10. Taral VN. Technique of genu valgum correction. Institute of Paediatric Disorders. 2009 <http://www.ipoindia.org/taralngda@gmail.com>.

## Original Article

# Effects of Hypothyroidism on Serum Electrolytes Level

Khatun MF,<sup>1</sup> Sardar MMR,<sup>2</sup> Akhter MS,<sup>3</sup> Rashed MR,<sup>4</sup> Mamun ASMA,<sup>5</sup> Sabiruzzaman M<sup>6</sup>

## Abstract

**Background:** Hypothyroidism is a common endocrine disorder. Hypothyroidism is a clinical entity resulting from the deficiency of thyroid hormones or from their impaired activity. It can lead to a variety of clinical situations, including electrolyte disturbances.

**Objective:** To evaluate the effects of hypothyroidism on serum Sodium, Potassium and Chloride level.

**Methods:** The study subjects were selected from patients undergoing thyroid evaluation in Nuclear Medicine and Allied Sciences, Rajshahi from July 2018 to June 2019. Among them 60 participants were selected, 30 were hypothyroid cases and 30 were age and sex matched controls with normal thyroid profile (euthyroids). Recently diagnosed and untreated cases were selected. Purposive sampling technique was used to select each study subject. The blood sample was collected from non-fasting subjects. T3, T4 and TSH were assayed by RIA and IRMA techniques. Serum electrolytes were measured by using ion selective electrodes method. The test of significance was calculated by using unpaired student-t test. P value less than 0.05 was considered as significant.

**Results:** In the present study, we found significant decrease in serum sodium levels but serum potassium level were significantly raised in hypothyroid patients in comparison to euthyroid patients. Moreover we have found that the mean serum chloride levels in hypothyroidism was slightly higher than euthyroidism though it was within the normal range and not statistically significant.

**Conclusion:** This recommends that the hypothyroid patients have electrolyte imbalances and should be frequently screened and checked for serum electrolytes. Moreover it can be suggested that patients with unexplained abnormal renal function should be screened for hypothyroidism.

**Key words:** Hypothyroidism, Serum electrolytes.

J Khulna Med Coll. 2022; 1(1) : 14-17

## Introduction

The number of hypothyroid patients in north Bengal is relatively high. It is endemic in some areas like Sirajganj, Bogra, Joypurhat, Gaibandha.<sup>1</sup> Thyroid hormones are known to be involved in the development and function of the kidneys and conversely, kidney function can affect the concentration and metabolism of thyroid hormones.<sup>2</sup>

Hyponatremia is the most common electrolyte abnormality.<sup>3</sup> Most guidelines consider hypothyroidism to be a cause of hyponatremia. Patients with moderate to severe hypothyroidism and mainly patients with myxoedema may

exhibit reduced sodium levels (<135 mmol/L). Thus, hypothyroidism is one of the causes of hyponatremia, and TSH determination is mandatory during the evaluation of patients with reduced serum sodium levels.<sup>4</sup> However Hanna FWF et al. found that the proportion of patients with a serum sodium lying below the reference interval (135 mmol/L) showed no significant difference between the euthyroid subjects and hypothyroid subjects.<sup>5</sup> Arvind Bharti et al. LB Sapkota and S.Thapa found that serum potassium level was significantly

1. Mst. Fatema Khatun, Assistant Professor, Department of Physiology, TMSS Medical College, Bogura
2. Md. Mijanur Rahman Sardar, Associate Professor (C.C), Department of Physiology, Khulna Medical College, Khulna.
3. Mst. Shabby Akhter, Assistant Professor, Department of Psychiatry, Gazi Medical College, Khulna
4. Md. Rakib Rashed, Assistant Professor(C.C), Department of Physiology, Rajshahi Medical College, Rajshahi
5. Abu Sayed Md. Al Mamun, Professor, Department of Statistics, University of Rajshahi, Rajshahi
6. Md. Sabiruzzaman, Professor, Department of Statistics, University of Rajshahi, Rajshahi

## Corresponding Author

Dr. Md. Mijanur Rahman Sardar, Associate Professor (C.C), Department of Physiology, Khulna Medical College, Khulna. Email: mijanrmc@hotmail.com

raised in the hypothyroid patients.<sup>6,7</sup> On contrary, Muralidhara Krishna CS et al., Sidhu et al., showed that hypokalemia was more common in hypothyroidism.<sup>8,9</sup> Furthermore Sibasish Sahoo et al. found no change in potassium level among hypothyroidism and euthyroidism.<sup>3</sup>

Arvind Bharti et al. found the mean serum chloride level in hypothyroidism was significantly higher than euthyroidism.<sup>6</sup> In contrast, Sibasish Sahoo et al., Christoph Schwarzet al. and Kavitha MM et al. found serum chloride level significantly decreased in hypothyroidism than euthyroidism.<sup>3, 10, 11</sup>

So the result of the different studies are contradictory. Moreover searching different articles, we have found that there was no study yet been done in Bangladesh regarding the effect of hypothyroidism on serum electrolytes level. So, the present study has been designed to determine it.

**Methods**

It was a cross sectional analytical type study. The study subjects were selected from patients undergoing thyroid evaluation in Nuclear Medicine and Allied Sciences, Rajshahi from July 2018 to June 2019. Among them 60 participants were selected, 30 were hypothyroid cases and 30 were age and sex matched controls with normal thyroid profile (euthyroids). Recently diagnosed and untreated cases were selected. Purposive sampling technique was used to select each study subject. Patients with newly diagnosed thyroid disorders in the age group of 20 to 60 years of both genders were included. Those having normal T3, T4 and TSH levels were categorized as euthyroid. Those having low T3, T4 and high TSH levels were categorized as hypothyroid with respect to the reference range. The protocol of the study was approved by the Ethical Review Committee (ERC) and Institutional Review Board (IRB) of Rajshahi Medical College. All the subjects were free from Diabetes Mellitus, Hypertension, Chronic liver and renal disease, Alcoholism and Smoking. Before recruitment, aim, benefit and procedure of the study was explained and informed written consent was taken from each study subject. Thorough physical examinations of all subjects were done. The blood sample was collected from non-fasting subjects. T3, T4 and TSH were assayed by RIA and IRMA techniques. Serum electrolytes were measured by using ion selective electrodes method.

Data were analyzed by computer using SPSS software program. The test of significance was calculated by using unpaired student-t test. P value less than 0.05 was consid-

ered as significant.

**Results**

Hypothyroidism and Euthyroidism were considered as Group I and Group II respectively. Both male and female were included in each group. (Table I)

Distribution of different parameters of age in (years), weight in (kg), height in (inch) and BMI in kg/m<sup>2</sup>. All the parameters showed no significant differences. (Table II)

TSH was significantly increased and T4 was significantly decreased in hypothyroid patients in comparison to Euthyroids. But no significant difference was seen in T3 in between hypothyroid patients and euthyroid individuals. (Table III)

Serum Na<sup>+</sup> showed lower value in Hypothyroidism which was statistically significant. Serum K<sup>+</sup> showed higher value in Hypothyroidism than Euthyroidism which was also statistically significant. Serum Cl<sup>-</sup> was also slightly higher in Hypothyroidism but the difference was not statistically significant. (Table IV)

**Table I :** Distribution of gender among hypothyroidism and euthyroidism

Gender	Hypothyroidism (Group I)		Euthyroidism (Group II)	
	No	%	No	%
Male	9	30	8	26.7
Female	21	70	22	73.3
Total	30	100	30	100

**Table II :** Distribution of basic health parameters:

Parameters	Hypothyroidism (n=30) (mean±SD)	Euthyroidism (n=30) (mean±SD)	P-value
Age	37.47±9.97	38.9±10.00	0.58 <sup>NS</sup>
Weight	61.33±12.20	61.10±10.8	0.28 <sup>NS</sup>
Height	62.00±2.94	61.6±2.42	0.56 <sup>NS</sup>
BMI	25.80±4.34	25.00±3.70	0.45 <sup>NS</sup>

Distribution of different parameters of age in (years), weight in (kg), height in (inch), and BMI in kg/m<sup>2</sup>. Data were expressed as mean±SD. Statistical significance was calculated by unpaired t test.

Significant = p<0.05, not significant= p>0.05.

NS=not significant, n=Total number of subjects.

**Table III :** Distribution of the Thyroid Stimulating Hormone (TSH), Thyroxine(T4) and Tri-iodothyronine(T3) among Hypothyroidism and Euthyroidism.

Parameters	Hypothyroidism	Euthyroidism	P-value
	Group I (n=30) (mean±SD)	Group II (n=30) (mean±SD)	
TSH(MIU/ml)	20.27±11.7	1.50±1.05	<0.001 <sup>S</sup>
T4(nmol/L)	48.96±38.0	118.57±30.1	<0.001 <sup>S</sup>
T3 (nmol/L)	2.25±0.693	2.10±0.486	0.32N <sup>S</sup>

Data were expressed as mean±SD. Statistical analysis was done by student's unpaired t-test. Significant = p<0.05, non-significant = p>0.05.

S=significant, NS=not significant, n=Total number of subjects

**Table IV :** Distribution of the Electrolytes: Sodium, Potassium and Chloride among Hypothyroidism and Euthyroidism

Parameters	Hypothyroidism	Euthyroidism	P-value
	Group I (n=30) (mean±SD)	Group II (n=30) (mean±SD)	
Sodium(Na+)mmol/L	134.45±5.26	136.90±1.87	0.02S
Potassium (K+)mmol/L	4.31±0.433	3.91±0.371	0.0002S
Chloride (Cl-)mmol/L	104±6.38	102±3.48	0.11NS

Data were expressed as mean±SD. Statistical analysis was done by student's unpaired t-test. Significant = p<0.05, non-significant = p>0.05.

S=significant, NS=not significant, n=Total number of subjects.

## Discussion

Hypothyroidism is a common endocrine disorder.<sup>1</sup> Hypothyroidism is accompanied by remarkable alterations in the metabolism of water and electrolytes. Electrolytes play an important role in many body processes, such as controlling fluid levels, acid-base balance (pH), nerve conduction, blood clotting and muscle contraction. Long standing hypothyroidism can cause significant changes in renal function such as a decrease in sodium reabsorption in the proximal tubule, impairment in the concentrating and diluting capacities of the distal tubules, a decrease in the urinary urate excretion and a decrease in the renal blood flow and glomerular filtration rate (GFR). In hypothyroid-

ism, physiological effects include changes in water and electrolyte metabolism, alterations of renal hemodynamics, lowered renal blood flow, renal plasma flow, glomerular filtration rate (GFR), and single nephron GFR.<sup>9</sup> So the objective of the present study was to determine the effect of hypothyroidism on serum electrolyte level.

The study subjects were selected from patients undergoing thyroid evaluation in Nuclear Medicine and Allied Sciences, Rajshahi. Among them 60 participants were selected, 30 were hypothyroid cases and 30 were age and sex matched controls with normal thyroid profile (euthyroids). Recently diagnosed and untreated cases were selected. Purposive sampling technique was used to select each study subject. The blood sample was collected from non-fasting subjects as fasting causes a rapid fall in serum T3 conc. T3,T4 and TSH were assayed by RIA and IRMA techniques. Serum electrolytes were measured by using Ion selective electrodes method.

In the present study we found significant decrease in serum sodium levels in patients with hypothyroidism. This finding is in accordance with Sibasish Sahoo et al. and Muralidhara Krishna CS et al.<sup>3,8</sup> Proposed mechanisms for hypothyroidism induced hyponatremia include increase in vasopressin (ADH) release and reduced renal glomerular filtration rate (GFR). Changes in ADH or GFR are thought to diminish renal capacity for the excretion of free water, resulting in water retention and a hence hyponatremia.<sup>12</sup>

In contrast to hyponatremia, we have found that serum potassium level were significantly raised in hypothyroid patients in comparison to euthyroid patients in this study. However the mean potassium level in hypothyroid cases were within normal range. This finding is supported by Arvind Bharti et al. and LB Sapkota et al.<sup>6,7</sup> It may be due to the fact that decreased thyroid hormones level decreased renal potassium excretion resulting elevated serum potassium level. On contrary, the findings of the present study for potassium levels are not consistent with the result of the study done by Muralidhara Krishna CS et al. They have found that hypokalemia was more common in the group with elevated TSH than those with normal TSH.<sup>8</sup> Moreover Sibasish Sahoo et al. found that there was no difference in potassium among hypothyroidism and euthyroidism.<sup>3</sup>

In the present study, we have found that the mean serum chloride levels in hypothyroidism is slightly higher than euthyroidism though it is also within the normal range and not statistically significant. This finding is compatible with Arvind Bharti et al. (2015) and L.B Sapkota.<sup>6,7</sup> However Arvind Bharti et al. (2015) stated serum chloride level significantly raised in hypothyroidism than euthyroidism.<sup>6</sup> On the other hand, Sibasish Sahoo et al. (2017) found that serum chloride levels were significantly decreased in hypothyroidism than euthyroidism.<sup>3</sup> So the findings are contradictory to each other and the observations are not conclusive. It indicates the necessity of further research with larger sample size and longitudinal study to detect changes in electrolyte concentration with time.

The strength of the study is that each study subjects was selected by doing thyroid function tests who had never taken thyroid or anti-thyroid drugs. So it was possible to determine the early changes in electrolyte abnormalities regarding the thyroid function status. However the limitation of the study was that the sample size was small and duration of the study was short. Moreover it was a cross sectional comparative study which projects the necessity of follow up study to determine the minute changes in electrolyte concentration in relation to thyroid function.

### Conclusion

The present study demonstrated that hypothyroidism is associated with significant changes in electrolyte balance, despite being within the biological reference range. Thus with these observations, it can be suggested that patients with unexplained abnormal renal function should be screened for hypothyroidism.

**Conflict of interest:** None

### References

1. Chaudhury HS, Raihan KK, Uddin MN, Ansari SM, Hasan M, Ahmed M, Kabir MF, Hoque MZ. Renal function impairment in hypothyroidism. *Bangladesh j med biochem.* 2013; 6(1): 19-25.
2. Englund FI, Berggren K, Usener B, Broberg H, Larsson A. and Brattsand GI. The Effect of Thyroid Dysfunction on Plasma Creatinine Levels. *Annals Thyroid Res.* 2016; 2(2):82-86.
3. Sahoo S, Patel S, Ganguly A, Nanda R, Mohapatra, E. Thyroid dysfunctions and renal status: implications in hyponatremia. *Asian journal of medical sciences.* . 2017; 8(4): 6-10.
4. Liamis G, Filippatos TD, Lontos A and Elisaf MS. Hypothyroidism-associated hyponatremia: mechanisms, implications and treatment. *European Journal of Endocrinology.* 2017; 176(1): 15–20.
5. Hanna FWF, Scanlon MF. Hyponatraemia, hypothyroidism, and role of arginine vasopressin. *Lancet.* 1997; 350: 755-756.
6. Bharti A, Shrestha S, Rahul R. and Singh MK. Assessment of serum minerals and electrolytes in thyroid patients. *International Journal of Advances in Scientific Research.* 2015; 01(06): 259-263.
7. Sapkota LB, Thapa S. Assessment of Serum Electrolytes in Hypothyroid Patients Attending Chitwan Medical college teaching Hospital. *Asian Journal of Medicine and Health.* 2017; 2(2): 1-5.
8. Muralidhara Krishna CS, Hemantha Kumara DS, Vishwanath HL. The electrolytes and hypothyroidism: a case control study. *Biochemistry: An Idnian Journal.* 2018; 12(2): 130-133.
9. Sidhu GK, Malek R, Khubchandani A, Manasuri S, Gaadhe P, Adarsh A. Assessment of variations in serum phosphorus, calcium, sodium and potassium levels in hypothyroid patients. *International Journal of Medical Research.* 2016;3(3): 26-29.
10. Schwarz C., Leichtle AB, Arampatzis S, Fiedler GM, Zimmermann H, Exadaktylos AK, Gregor Lindner G. Thyroid function and serum electrolytes: does an association really exist?, *The European Journal of Medical Sciences, Swiss Medical Weekly.* 2012; 142:1-7.
11. Kavitha MM, Pujar S, Hiremath, CS, Prasad S, Mahanthesh. Evaluation of serum electrolytes in hypothyroid patients. *International Medical Journal.* 2014;1(8): 393-395.
12. Hunze J, Ijsselstijn L, Wulkan RW, Alphen AMV. Does hypothyroidism cause hyponatremia? *Health.* 2014; 6:1453-1458.



In the present study, we have found that the mean serum chloride levels in hypothyroidism is slightly higher than euthyroidism though it is also within the normal range and not statistically significant. This finding is compatible with Arvind Bharti et al. (2015) and L.B Sapkota.<sup>6,7</sup> However Arvind Bharti et al. (2015) stated serum chloride level significantly raised in hypothyroidism than euthyroidism.<sup>6</sup> On the other hand, Sibasish Sahoo et al. (2017) found that serum chloride levels were significantly decreased in hypothyroidism than euthyroidism.<sup>3</sup> So the findings are contradictory to each other and the observations are not conclusive. It indicates the necessity of further research with larger sample size and longitudinal study to detect changes in electrolyte concentration with time.

The strength of the study is that each study subjects was selected by doing thyroid function tests who had never taken thyroid or anti-thyroid drugs. So it was possible to determine the early changes in electrolyte abnormalities regarding the thyroid function status. However the limitation of the study was that the sample size was small and duration of the study was short. Moreover it was a cross sectional comparative study which projects the necessity of follow up study to determine the minute changes in electrolyte concentration in relation to thyroid function.

### Conclusion

The present study demonstrated that hypothyroidism is associated with significant changes in electrolyte balance, despite being within the biological reference range. Thus with these observations, it can be suggested that patients with unexplained abnormal renal function should be screened for hypothyroidism.

**Conflict of interest:** None

### References

1. Chaudhury HS, Raihan KK, Uddin MN, Ansari SM, Hasan M, Ahmed M, Kabir MF, Hoque MZ. Renal function impairment in hypothyroidism. *Bangladesh j med biochem.* 2013; 6(1): 19-25.
2. Englund FI, Berggren K, Usener B, Broberg H, Larsson A. and Brattsand G1. The Effect of Thyroid Dysfunction on Plasma Creatinine Levels. *Annals Thyroid Res.* 2016; 2(2):82-86.
3. Sahoo S, Patel S, Ganguly A, Nanda R, Mohapatra, E. Thyroid dysfunctions and renal status: implications in hyponatremia. *Asian journal of medical sciences.* . 2017; 8(4): 6-10.
4. Liamis G, Filippatos TD, Lontos A and Elisaf MS. Hypothyroidism-associated hyponatremia: mechanisms, implications and treatment. *European Journal of Endocrinology.* 2017; 176(1): 15–20.
5. Hanna FWF, Scanlon MF. Hyponatraemia, hypothyroidism, and role of arginine vasopressin. *Lancet.* 1997; 350: 755-756.
6. Bharti A, Shrestha S, Rahul R. and Singh MK. Assessment of serum minerals and electrolytes in thyroid patients. *International Journal of Advances in Scientific Research.* 2015; 01(06): 259-263.
7. Sapkota LB, Thapa S. Assessment of Serum Electrolytes in Hypothyroid Patients Attending Chitwan Medical college teaching Hospital. *Asian Journal of Medicine and Health.* 2017; 2(2): 1-5.
8. Muralidhara Krishna CS, Hemantha Kumara DS, Vishwanath HL. The electrolytes and hypothyroidism: a case control study. *Biochemistry: An Idnian Journal.* 2018; 12(2): 130-133.
9. Sidhu GK, Malek R, Khubchandani A, Manasuri S, Gaadhe P, Adarsh A. Assessment of variations in serum phosphorus, calcium, sodium and potassium levels in hypothyroid patients. *International Journal of Medical Research.* 2016;3(3): 26-29.
10. Schwarz C., Leichtle AB, Arampatzis S, Fiedler GM, Zimmermann H, Exadaktylos AK, Gregor Lindner G. Thyroid function and serum electrolytes: does an association really exist?, *The European Journal of Medical Sciences, Swiss Medical Weekly.* 2012; 142:1-7.
11. Kavitha MM, Pujar S, Hiremath, CS, Prasad S, Mahanthesh. Evaluation of serum electrolytes in hypothyroid patients. *International Medical Journal.* 2014;1(8): 393-395.
12. Hunze J, Ijsselstijn L, Wulkan RW, Alphen AMV. Does hypothyroidism cause hyponatremia? *Health.* 2014; 6:1453-1458.

## Original Article

# Comparative Study of Blood Pressure Measurement Using Aneroid Sphygmomanometer & Digital Sphygmomanometer

Islam MN<sup>1</sup>, Chowdhury SN<sup>2</sup>, Alam ABMS<sup>3</sup>, Jesmin F<sup>4</sup>, Parvin Z<sup>5</sup>

## Abstract

**Background:** Different types of BP machines are available now. Aneroid type is most commonly used and recently use of digital type of BP machine is increasing. So it is necessary to evaluate accuracy of digital BP machine.

**Objective:** Aim of our study was to compare BP readings using digital BP machine and aneroid BP machine.

**Methods:** 100 patients took part in this study. Blood pressure was recorded by both digital and aneroid sphygmomanometers. Mean  $\pm$  standard deviation of the observation for both systolic and diastolic BP were calculated and compared.

**Results:** Mean systolic BP was  $145.23 \pm 24.45$  mm Hg by using digital machine and  $142.25 \pm 25.56$  mm Hg using aneroid machine. This difference was statistically insignificant ( $p$  value  $> 0.05$ ). Similarly mean diastolic BP was  $92.36 \pm 16.32$  mm Hg by using digital machine and  $88.96 \pm 14.52$  mm Hg using aneroid machine. This difference was statistically insignificant ( $p$  value of  $> 0.05$ ).

**Conclusion:** Digital BP machines are as accurate as aneroid machines.

**Key words:** Hypertension, Blood Pressure, Aneroid, Digital

J Khulna Med Coll. 2022; 1(1) : 18-20

## Introduction

Hypertension is one of the most important public health issue. It is considered as a major risk factor for stroke, IHD, CKD etc. Early diagnosis and treatment of hypertension could significantly reduce the risk of mortality.<sup>1</sup> For accurate control of hypertension correct measurement of BP is mandatory. There are different invasive and noninvasive methods to measure blood pressure.<sup>2,3</sup> Two studies from US which compared aneroid and mercury sphygmomanometer found minimal difference between readings.<sup>4,5</sup>

Mercury manometer is usually not used now a days. Aneroid BP machine and digital BP machine is currently

most commonly used. During COVID-19 era use of digital BP is dramatically increased. Digital BP can be of arm type and wrist type. Most of the digital machines also measure heart rate additionally. Digital BP machine can save variable number of BP results. So now a days Digital BP machine is gaining popularity day by day. But some users claim about the accuracy of BP measurement using Digital machine. So this study was performed to compare the BP measurement using Aneroid & Digital Machine. The aim of the study was to compare the results of blood pressure measurement by aneroid and digital sphygmomanometer.

1. Md Nazrul Islam, Assistant professor, Dept of Medicine, Khulna Medical College, Khulna
2. Sabikun Nahar Chowdhury, Junior Consultant, Pathology, Khulna Medical College Hospital
3. ABM Saiful Alam, Professor, Dept of Medicine, Khulna Medical College
4. Fatima Jesmin, Medical Officer, Divisional police hospital, Khulna
5. Zohora Parvin, Assistant Professor, Dept of Pharmacology, Patuakhali Medical College, Patuakhali

**Corresponding Author:** Dr. Md Nazrul Islam, Assistant professor, Department of Medicine, Khulna Medical College Khulna.  
E-mail: drmdnazrul@gmail.com

## Methods

Our study was of cross sectional type. Total 100 patients participate in this study in a private chamber (Islami bank hospital, khulna) from the month of June to December of 2021. Purposive sampling method was used in the study. Blood pressure was measured in sitting positions using both aneroid sphygmomanometer and digital BP machine. Patients aged  $\geq 18$  years and voluntarily gave consent to participate in study were included in this study. Acutely ill patients and patients not willing to participate in the study were excluded. The procedure was explained and the subjects had read a description of the experimental protocol then informed consent from the participants was taken in a private chamber. Hundred healthy adults with age  $> 18$  years had taken part in this study. Clinical history and general physical examination of all the volunteers were carried out and recorded in pre-structured Proforma. Patients having a history of acute illness were excluded from the study. The study was carried out between 4 pm – 9 pm. Height & weight of the subject was measured with measuring inch tape & weight machine respectively. The subject was asked to sit down comfortably and then blood pressure was recorded by aneroid sphygmomanometer. For this measurement of blood pressure, the following standard steps was performed:

- A well maintained, validated and calibrated machine was used
- Removal of tight clothing was done
- Blood pressure lowered slowly (2 mm/second)
- Blood pressure was read to the nearest 2 mm Hg
- Blood pressure was measured in both hands and highest one was recorded

After 5 minutes BP was measured using digital BP machine. Both the measurement was recorded in form. Data are presented as mean  $\pm$  standard deviation with their reference units. Mean  $\pm$  standard deviation of the observation for all the parameters were calculated and compared using Student's t test. Statistical analysis was done by MS-Excel and SPSS version 21. P-value  $< 0.05$  was taken as significant.

## Results

Total 100 patients participate in the study. Age range was 18 to 75 years. Of them 53 were female and 47 were male. Mean weight of female was  $58 \pm 17.61$  kg and of male was  $55 \pm 17.61$  kg. Mean height of female was  $154 \pm 13.99$  cm and of male was  $17 \pm 13.99$  cm. Mean pulse rate of female was  $88 \pm 28.69$ /min and of male was  $86 \pm 28.21$ /min.

The range of systolic BP was 100 to 190 mm Hg ( $142.25 \pm 25.56$ ) and 105 to 200 mm of Hg ( $145.23 \pm 24.45$ ) by aneroid and digital apparatus respectively. The range of diastolic BP was 65 to 140 mm Hg ( $88.96 \pm 14.52$ ) and 60 to 145 mm Hg ( $92.36 \pm 16.32$ ) by aneroid and digital BP apparatus respectively. (Table I)

**Table 1:** Mean blood pressure value

Instrument Type	SBP mm Hg (Mean $\pm$ 2SD)	DBP mm Hg (Mean $\pm$ 2SD)
Aneroid	142.25 $\pm$ 25.56	88.96 $\pm$ 14.52
Digital	145.23 $\pm$ 24.45	92.36 $\pm$ 16.32

Mean  $\pm$  standard deviation of the observation for systolic BP were compared using Student's t test. Differences of BP using digital and aneroid sphygmomanometer was found insignificant. (Table II)

**Table II:** Comparison of systolic blood pressure

Differences in Systolic BP	p value	Inference	
Digital	145.23 $\pm$ 24.45	$> 0.05$	Insignificant
Aneroid	142.25 $\pm$ 25.56		

Mean  $\pm$  standard deviation of the observation for diastolic BP were compared using Student's t test. Differences of BP using digital and aneroid sphygmomanometer was found insignificant. (Table III)

**Table III:** Comparison of diastolic blood pressure

Differences in diastolic BP	p value	Inference	
Digital	92.36 $\pm$ 16.32	$> 0.05$	Insignificant
Aneroid	88.96 $\pm$ 14.52		

## Discussion

Mercury sphygmomanometers were considered as gold standard for long for accurate BP measurement<sup>6</sup>. But the potential mercury toxicity and the problems associated with disposal of mercury, has led to decrease use of mercury instruments worldwide. For the same reason European Union directed phasing out of Mercury instruments<sup>7</sup>. Non-mercury BP instruments like aneroid and more recently, digital ones have replaced the use of traditional Mercury instruments. Additional advantage of aneroid instrument is the portability<sup>8</sup>, while that of digital instruments are ease of use as no need of auscultation skill of the examiner. Most of the digital machines also measure heart rate additionally. Digital BP machine can save variable number of BP results. In a large study in UK examined the comparability of measurement accuracy of all the three categories of sphygmomanometer and found that digital instruments are almost as accurate as mercury instruments, while higher failure rate existed with the aneroid ones and therefore the authors recommended the use of inexpensive and easy to use digital instruments by general practitioner during home visit.<sup>8</sup>

The study was conducted to determine and compare the accuracy of digital BP instruments and aneroid BP instruments and their ability to correctly diagnose hypertension. In a study among more than 8000 patients researchers used 604 sphygmomanometers (53% digital, 32% aneroid, 13% mercury and 2% hybrid devices). They found that only 78% of the aneroid models were able to give accurate measures, while 88% digital devices were accurate.<sup>8</sup>

In a study it was found that aneroid monitor could correctly estimate 54% of the systolic and 58% of the diastolic blood pressures in comparison to only 34% of the correct systolic and 48% of the correct diastolic measurement by digital instrument<sup>9</sup>. In another study among 108 pairs of data, average systolic measurement using digital (124.57 mmHg) and aneroid (124.31) was similar to mercury (125.01), there was no significant difference of average blood pressure measurement between digital and mercury sphygmomanometer ( $p = 0.71$ ), between digital and aneroid sphygmomanometer ( $p = 0.46$ ) and between aneroid and mercury sphygmomanometer ( $p = 0.71$ )<sup>10</sup>

In a meta analysis the digital blood pressure monitoring has a moderate level of accuracy and the device can correctly distinguish hypertension with a pooled estimate sensitivity of 65.7% and specificity of 95.9%.<sup>11</sup> Results of all of the above studies are similar to our study which shows that aneroid and digital BP machine both can measure the BP accurately.

In another study the researchers also observed that aneroid instruments were significantly more accurate than digital instruments of both arm and wrist type. The systolic blood pressure was particularly overestimated in case of arm type digital instruments.<sup>12</sup> Results of this study is somewhat contradictory to our study.

There are some limitation of the study as it was conducted in private chamber thus studying patient only and the result cannot be generalized to all individuals of the community. Another limitation is that we used only one instrument of each type. Also we performed the study in only one health center.

### Conclusion

Our study revealed similar effectiveness of aneroid device in comparison to digital device in measuring blood pressure among individuals. But the digital devices should be used with caution, doubt and suspicion. If any confusion arises it should be confirmed using aneroid sphygmomanometer.

### References

1. Yang Q, Cogswell ME, Flanders WD, Hong Y, Zhang Z, Loustalot F, et al. Trends in cardiovascular health metrics and associations with all-cause and CVD mortality among US adults, JAMA. 2012;307(12):1273-83.
2. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004( suppl 2, 4th report);114:555-576.
3. Chobanian AV, Bakris GL, Black HR. The seventh report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42(6):1206-1252.
4. Ostchega Y, Prineas RJ, Nwankwo T, Zipf G. Assessing blood pressure accuracy of an aneroid sphygmomanometer in a national survey environment. Am J Hypertens. 2011;24(3):322-327.
5. Shah AS, Dolan LM, D'Agostino RB Jr, Standiford D, Davis C, Testaverde L, et al; SEARCH for Diabetes in Youth Study Group. Comparison of mercury and aneroid blood pressure measurements in youth. Pediatrics. 2012;129(5): 1205-10.
6. Blood Pressure Measurement; Fact File 01/2006. British Hypertension Society; 2006. pp. 3-6
7. Directive 2007/51/EC of the European Parliament and of the Council of 25 September 2007 amending Council Directive 76/769/EEC relating to restrictions on the marketing of certain measuring devices containing mercury (Text with EEA relevance) 2007.
8. A'Court C, Stevens R, Sanders S, Ward A, McManus R, Heneghan C. Type and accuracy of sphygmomanometers in primary care: a cross-sectional observational study. Br J Gen Pract. 2011;61(590).
9. Ohnson KA, Partsch DJ, Gleason P, Makay K. Comparison of two home blood pressure monitors with a mercury sphygmomanometer in an ambulatory population. Pharmacotherapy. 1999;19(3):333-39.
10. Hamied, Lola I A, Sofiatin, Yulia, Rakhmilla, Lulu E, et al. Comparison of Mercury, Aneroid and Digital Sphygmomanometer in Community Setting, Journal of Hypertension 2015; 33:3339.
11. Muniyandi M, Sellappan S, Chellaswamy V, Ravi K, Karthikeyan S, Thiruvengadam K et al. Diagnostic accuracy of mercurial versus digital blood pressure measurement devices: a systematic review and meta-analysis. Sci Rep 2022; 12: 3363.
12. Nelson D, Kennedy B, Regnerus C, Schweinle A. Accuracy of automated blood pressure monitors. J Dent Hyg. 2008;82(4):35.

## Original article

# Incidence of Cancer in Thyroid Swelling – A Study of 100 Cases

Mondal SK<sup>1</sup>, Islam MM<sup>2</sup>, Islam MM<sup>3</sup>, Islam MAA<sup>4</sup>, Paul HK<sup>5</sup>

## Abstract

**Background:** The incidence of thyroid cancer has rapidly increased in the United States and other developed countries over the past 30 years and is also increasing in our country.

**Objective:** The aim of this study was to find out the true incidence of thyroid malignancy in thyroidectomy patients presenting with thyroid swelling.

**Methods:** This is a prospective study of 100 thyroid swelling patients underwent thyroid surgery done at Department of ENT & Head Neck Surgery of Khulna Medical College Hospital, a tertiary Care Hospital in Khulna from January 2020 to December 2021. FNAC and histopathology reports were studied to find out the incidence of benign and thyroid malignancy among the thyroid swelling.

**Results:** The age of the patients ranged from 15 to 75 years. The mean age was 47.5 years. There were 70 female and 30 male patients with female male ratio 7:3. A total 100 thyroid swelling underwent surgery, FNAC showed that 65 (65%) cases were cytologically benign, 35 (35%) cases were malignant category. Out of 100 cases histopathology showed 62 cases (62%) are benign and 38 (38%) are malignant thyroid swelling. Among the benign lesions 80.64% were colloid goiter and among the malignant lesions 72.68% were papillary thyroid carcinoma.

**Conclusion:** Although FNAC is an essential diagnostic test to rule out thyroid malignancy but histopathological examination is the only way to give true incidence of thyroid malignancy among the thyroid swelling and it is observed that there is high incidence of thyroid malignancy among the thyroid swelling patient underwent thyroid surgery.

**Key words:** FNAC, Histopathology, Thyroid cancer

J Khulna Med Coll. 2022; 1(1) :21-23

## Introduction

The incidence of thyroid cancer has increased dramatically during the past three decades and it is now the fastest growing cancer in women.<sup>1</sup> Bangladesh especially North Bengal area is an endemic zone for iodine deficiency goitre and one of the aetiology of thyroid cancer is iodine deficiency. They present as visible neck swelling which moves on deglutition. Any patient presented with thyroid swelling are routinely investigated by ultrasonogram of the thyroid gland, serum TSH and FNAC. Final diagnosis requires morphological examination for which histopathological examination becomes mandatory test.<sup>2</sup> In 1870 Rugu and his associate Joham Vent have first advocated surgical biopsy as an essential tool.<sup>3</sup> The diagnostic method of FNAC was first published in 1883 by Leyden.<sup>4</sup> But the diagnosis of thyroid swellings using aspiration cytology

was first reported by Martin and Ellis in 1930.<sup>5</sup> FNAC, however has limitation related to specimen adequacy, sampling techniques, skill of performing the procedure, interpretation of the aspirate, overlapping cytological features between benign and malignant follicular neoplasm and also in the detection of some papillary carcinoma associated with other pathology like multinodular goiter, cystic changes.<sup>6</sup> Mundasad et al. had done a comparative study between FNAC and histopathology and founded that FNAC had a sensitivity (52.6%), specificity (86.6%) and accuracy (79.1%) for thyroid malignancy.<sup>7</sup> This study aimed to see the true incidence of benign and malignant thyroid lesions among the thyroid swellings after histopathological examinations following thyroidectomy.

1. Sutanu Kumar Mondal, Associate Professor, Department of ENT & Head Neck Surgery, Khulna Medical College, Khulna.
2. Md. Mahmudul Islam, Registrar, Department of ENT & Head Neck Surgery, Khulna Medical College Hospital, Khulna.
3. Md. Mainul Islam, Assistant Registrar, Department of ENT & Head Neck Surgery, Khulna Medical College Hospital, Khulna.
4. Md. Al Aminur Islam, Assistant Registrar, Department of ENT & Head Neck Surgery, Khulna Medical College Hospital, Khulna.
5. Horidas Kumar Paul, Junior Consultant, Department of ENT & Head Neck Surgery, Khulna Medical College Hospital, Khulna.

## Address for Correspondence:

Dr. Sutanu Kumar Mondal, Associate Professor, Department of ENT & Head Neck Surgery, Khulna Medical College, Khulna.  
Email: sutanukmondal@gmail.com



## Methods

This cross sectional study was done among patients undergoing thyroidectomy between January 2020 to December 2021 at Khulna Medical College Hospital, Bangladesh. The patients were selected consequently when they presented during the study period considering inclusion and exclusion criterias. The selected patients were examined clinically and routine ultrasonography, TSH, FNAC, routine haematological investigations, Chest X-ray, ECG, CT scan if indicated were done. FNAC from thyroid swelling were done by senior expert cytologist. All surgeries were done by the senior surgical staffs and all thyroidectomies specimens were examined by senior expert histopathologist. Patients with thyroid swelling with normal thyroid hormone profile undergoing thyroidectomy were included in this study. Patients of thyroid swelling with hyper or hypothyroid function, patients with co-morbidities, unfit for surgery, patients who refused surgery and inoperable thyroid malignancy were excluded from the study. The data collected was analyzed using SPSS version 20 and depicted using descriptive statistics.

## Results

The age of the patients ranged from 15 to 75 years with a mean age 47.5 years (Table- I). The thyroid lesions were more common in females than male in a ratio of 2.33:1 (table-II). Table III shows FNAC findings of 100 cases where 65 are benign and 35 cases are malignant lesion with benign malignant ratio is 1.85:1. Among the benign lesions the most common lesion was multinodular or colloid goiter (80.64%). Table IV shows out of 35 malignant cases of FNAC finding, 85.71% is papillary carcinoma. Histopathological examinations of all 100 thyroidectomy specimens showed 50 cases (50%) are colloid goiter and 28 cases (28%) are papillary carcinoma (Table-V). Table VI shows incidence of benign and malignant lesions among 100 specimens. There are 62 (62%) benign lesions and 38 (38%) malignant lesions, so approximately benign and malignant ratio is about 1.63:1 which is very worrying. Finally among the thyroid cancer about 72.68% is papillary carcinoma (Table-VII).

Table I: Age distribution of thyroidectomy patients (n=100)

Age in yrs	No. of patients	Percentage (%)
15-25	5	5
26-35	20	20
36-45	40	40
46-55	20	20
56-65	10	10
66-75	5	5

Mean age 47.5

Table II: Sex distribution (n=100)

Sex	No. of patients	Percentage (%)
Female	70	70
Male	30	30

Female: Male = 7:3

Table III: FNAC of thyroid swelling (n =100)

Diagnosis	No. of patients	Percentage (%)
Nodular or colloid goiter	54	54
Papillary carcinoma	30	30
Follicular lesion	3	3
Lymphocytic thyroiditis	8	8
Non Hodgkin's lymphoma	1	1
Medullary carcinoma	3	3
Anaplastic	1	15

Table IV: FNAC diagnosis of thyroid malignancy (n=35)

Diagnosis	No. of patients	Percentage (%)
Papillary carcinoma of thyroid	30	85.71
Follicular carcinoma	0	0
Medullary carcinoma	3	8.57
Non Hodgkin's lymphoma	1	2.85
Anaplastic carcinoma	1	2.85

Table V: Histopathological diagnosis of thyroid swelling (n=100)

Diagnosis	No. of patients	Percentage (%)
Colloid/MNG	50	50
Lymphocytic thyroiditis	7	7
Follicular adenoma	5	5
Papillary carcinoma	28	28
Hurtle cell adenoma	1	1
Follicular carcinoma	4	4
Medullary carcinoma	2	2
Non Hodgkin's lymphoma	1	1
Anaplastic carcinoma	2	2

Table VI: Incidence of benign and malignant lesions based on histopathology (n=100)

Diagnosis	No. of patients	Percentage (%)
Benign lesions	62	62
Malignant	38	38

Benign: Malignant = 1.63:1

**Table VII:** Incidence of thyroid cancer based on histopathology (n=38)

Diagnosis	No. of patients	Percentage (%)
Papillary carcinoma	28	72.68
Follicular carcinoma	4	10.52
Medullary carcinoma	2	5.26
Anaplastic carcinoma	2	5.26
Non Hodgkin's lymphoma	1	2.63
Hurtle cell carcinoma	1	2.63

### Discussion

The incidence of thyroid cancer has rapidly increased in the United States (US) and other developed countries over the past 30 years.<sup>8</sup> Although some researchers believe this is a true increase in thyroid cancer,<sup>9</sup> but this increase is due to better diagnostic tests like ultrasonography and fine-needle aspiration cytology, resulting in the detection of disease that is unlikely to cause symptoms or death of the patient.<sup>9,10</sup>

Other countries have seen similar increases in thyroid cancer. From 1993 to 2011, South Korea witnessed a 15-fold increase in thyroid cancer with nearly the entire increase attributed to papillary cancers.<sup>11</sup> Davies and Welch also showed, using the SEER program and data, that the rates of follicular, medullary and anaplastic thyroid cancers show no significant change from 1973 to 2002.<sup>12</sup> Our study also found similar result of increasing incidence of thyroid cancer and most of which are papillary carcinoma. The most important part of our study is limitation of FNAC which includes false negative result and false positive results. Sikder had done accuracy of fine needle aspiration cytology and had found that accuracy was 90% and sensitivity was 68.75%.<sup>13</sup> Bloch had done a comparison study between FNAC and histopathology and had found accuracy of FNAC was 91.6%.<sup>14</sup> In our study 3 cases were false negative based on FNAC report out of 38 malignant cases. So accuracy of FNAC report was 92.11%.

### Conclusion

The incidence of thyroid cancer is increasing in Bangladesh like other countries in the world. Ultrasonography and FNAC are both essential diagnostic tool for thyroid swelling but final diagnosis to rule out thyroid cancer is surgical excision and biopsy. A negative FNAC report may be positive for malignancy in histopathology. So FNAC and excisional biopsy are both required to find out the true incidence of thyroid malignancy.

### References

1. Clinical Thyroidology for the Public American Thyroid association. Feb 2017;Vol 10(2):9.
2. Gupta M, Gupta S, and Gupta VB. Correlation of Fine Needle Aspiration Cytology with Histopathology in the Diagnosis of Solitary Thyroid Nodule. J thyroid Res. 2010; doi:10.4061/2010/379051
3. Rugu C. Needle Aspiration Biopsy. Am J Pediatr. 1970; 62:565-568
4. Das D, Sarma MC, Sharma A, Datta TK, Lahiri SK. A Comparative study between fine needle aspiration cytology and histopathological examination in the diagnosis of neoplastic and non-neoplastic lesions of the thyroid gland. Indian J Prev Soc Med. 2012;43(1):72-5.
5. Orell SR, Vielh P. The techniques of FNA cytology. (2012) In: Orell SR, Steratt FG, eds. Fine needle aspiration cytology. 5th edn. Elsevier; 2012: 10.
6. Kumar A, Bhadouriya, Narain P et al. Comparative study of FNAC and histopathology of thyroid swellings, diagnostic accuracy and role in it's management. International Journal of Otorhinolaryngology and head and Neck Surgery. 2017;3(4):885-892.
7. Mundasad B, Mcallidter I, Carson J. Accuracy of fine needle aspiration cytology in diagnosis of thyroid swelling. Intern J Endocrinol. 2006; 2(2): 23-25
8. Vaccarella S, Franceschi S, Bray F, Wild CP, Plummer M, Dal Masol Worldwide thyroid-cancer epidemic? The increasing impact of over diagnosis. New Engl J Med. 2016;375:614-617.
9. How J, Tabah R. Explaining the increasing incidence of differential euthyroid cancer. CMAJ. 2007; 177:1383-1384.
10. Kent WD, Hall SF, Isotalo PA, Houlden RL, George RL, Groome PA. Increased incidence of differentiated thyroid carcinoma and detection of subclinical disease. CMAJ. 2007; 177:1357-1361.
11. Ahn HS, Kim HJ, Welch HG. Korea's thyroid-cancer "epidemic" – Screening and over diagnosis. New Engl Med. 2014;371:1765-1767.
12. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. JAMA. 2006;295:2164-2167.
13. Sikder M AH, Rahman AMM, Khair MA. Accuracy of fine needle aspiration cytology in the diagnosis of thyroid swellings. J Dhaka National Med Coll Hos. 2012;18(2):47-51.
14. Bloch M. Fine needle aspiration biopsy of head and neck masses. Otolaryngol Head Neck Surg. 1997;89:62-68.

## Review Article

# Non-Alcoholic Fatty Liver Disease: Updates in Treatment Modalities

Mollick MKU<sup>1</sup> Nahar K<sup>2</sup>

## Abstract

The global prevalence of nonalcoholic fatty liver disease (NAFLD) is increasing rapidly. Alteration of food habit, increase incidence of metabolic syndrome, and lack of exercise are all contributing in this sharp rise of NAFLD. It is currently the most common liver disease and is estimated to affect up to 25% of the population. The spectrum of the disease includes a simple hepatic steatosis (NAFL, nonalcoholic fatty liver) that might progress to nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis or hepatocellular carcinoma. Therefore patients with NAFLD in our daily practice should be addressed with proper importance through available and updated diagnostic and therapeutic adjuncts. In this review, we tried to focus on existing treatment modalities along with recent updates in management of NAFLD. Worldwide there is an urgency in the need for the development of new medical strategies for NAFLD patients. We aim to present the beneficial effects of life-style modifications and newer pharmacological agents on both non-obese and obese NAFLD patients. This review also aims to focus on recently completed clinical trials testing promising drugs for NASH resolution. The marketing of new therapeutic agents would greatly increase the odds of reducing the global burden of NAFLD.

**Keywords:** NAFLD, NASH, Cirrhosis, Treatment updates

J Khulna Med Coll. 2022; 1(1) : 24-29

## Introduction

Non-alcoholic fatty liver disease (NAFLD) is an umbrella term which includes conditions mainly caused by fatty infiltration of the hepatocytes without significant amounts of alcohol use, that can be originated from multiple factors. Initially NAFLD starts with non-inflammatory hepatocellular steatosis and progresses to nonalcoholic steatohepatitis (NASH), fibrosis of the hepatocytes, and liver cirrhosis, which may further progress to hepatocellular carcinoma (HCC).<sup>1</sup>

NASH has increased risk of progression to cirrhosis, end-stage liver disease, and development of hepatocellular carcinoma (HCC).<sup>2,3</sup> In clinical practice NAFLD is usually diagnosed incidentally in asymptomatic patients. Different diagnostic tools are present. Magnetic resonance spectroscopy and Fibroscan are advanced noninvasive modalities for diagnosis and staging, assessing a larger section of the liver in comparison to liver biopsy.<sup>4,5</sup>

Yet liver biopsies are still considered gold standard for the diagnosis and staging of NASH, as it can differentiate between types of liver disorders. Other clinical diagnostic indices such as increased serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), as well as evidence of liver steatosis in ultrasonography are also routinely used. In low resource settings ultrasonography in skilled hand can provide important initial information regarding NAFLD. The diagnosis of NAFLD should be suspected in patients with metabolic syndrome (obesity, type 2 diabetes mellitus, hypertension, or dyslipidemia) and in patients with unexplained laboratory abnormalities suggesting liver disease.<sup>6</sup> Therefore many researches and clinical trails are ongoing to provide a safe effective management for NAFLD patients

1. Md. Kutub Uddin Mollick, Associate Professor, Department of Hepatology, Khulna Medical College.

2. Kamrun Nahar, Assistant Registrar, Department of Hepatology, Khulna Medical College.

### Address for Correspondence:

Dr. Md. Kutub Uddin Mollick, Associate Professor, Department of Hepatology, Khulna Medical College. E-mail : drmollick18@yahoo.com

## Epidemiology

Understanding of the epidemiology and natural history of non-alcoholic fatty liver disease (NAFLD) has increased as it is the most common form of chronic liver disease in the Western world and increasing in importance in other parts of the world. NAFLD and NASH have a world wide distribution. In Asia, similar increase in prevalence of NAFLD also noted in last few years.<sup>7,8</sup> About 30% to 40% of patients who develop cirrhosis secondary to NAFLD, will die of liver-related problems. The prevalence of NAFLD is different among men and women, and the natural history of NAFLD depends on the histologic subtype. Those who have simple hepatic steatosis or nonspecific inflammation generally have a benign long-term prognosis, whereas non-alcoholic steatohepatitis (NASH) can progress to cirrhosis.

## Pathogenesis

The pathogenesis of NAFLD is a complicated process which is not clearly known. Different studies show association of genetic factors and/or environmental elements.<sup>9</sup> The “two-hit hypothesis” of NASH, originally explained by Day and James suggests that lipid deposition in the liver (first hit) is followed by a series of other, oxidative and hepatotoxic processes (second hit), caused by a mechanism currently not known. Hepatic steatosis can occur from the excessive importation of FFA from adipose tissue, from diminished hepatic export of FFA (secondary to reduced synthesis or secretion of very low-density lipoprotein [VLDL]), or from impaired beta-oxidation of FFA. The major sources of triglycerides are from fatty acids stored in adipose tissue and fatty acids newly made within the liver through de novo lipogenesis.

## Management of NAFLD

### Lifestyle Modifications

Management of NAFLD usually focuses on treating patients with significant fibrosis or with less severe disease but at high risk of disease progression (ie with diabetes, MetS, persistently increased ALT, high necroinflammation). Renowned collaborations such as European Association for Study of Liver (EASL) has recommended early diagnosis and management of high risk groups.<sup>10</sup> There are no drugs approved by regulatory agencies for NASH. Therefore, no specific therapy can be firmly recommended, and any drug treatment would be off label. Currently, the only proven strategy for NAFLD management is lifestyle modification techniques such as weight loss through diet and exercise.

Since obesity strongly influences the development of NAFLD, weight loss is again the main objective in NAFLD management, and the first-line therapy. Therefore all NAFLD patients are encouraged to follow a low caloric diet, increase their physical activity, and stop smoking (if applicable).<sup>11</sup>

## Dietary supplementation in the treatment of NAFLD

### Antioxidants agents

**Vitamin E and vitamin C:** It is widely accepted that free radicals induced oxidative stress is vital in the pathogenesis of NAFLD, therefore antioxidants have an important role to play. A clinical trial using atorvastatin and vitamins E + C vs placebo, showed improved hepatic steatosis on computed tomography scans.<sup>14</sup> Though a meta-analysis shows, adjuvant vitamin E was not shown to have a significant effect on normalizing serum ALT levels. Using higher doses of vitamin E, a longer duration of therapy or adding vitamin C did not alter the effect of these antioxidants on the measured outcomes either.<sup>15</sup> There seems to be lacking evidence on the long-term effects of vitamin E use on histological improvements of NAFLD patients, which calls for larger, well-designed randomized controlled trials (RCTs) with histological endpoints, to really determine the efficacy of its use.

**Garlic:** Solemani et. al showed The current clinical trial indicated that intake of garlic powder at 800 mg/day for 15 weeks improved hepatic steatosis, liver enzymes, lipid profiles, and fasting blood sugar in patients with NAFLD.<sup>16</sup> Garlic-derived S-allylmercaptocysteine (SAMC) has a therapeutic role in diabetes and nonalcoholic fatty liver disease due to its properties in the regulation of lipogenesis and glucose metabolism.<sup>17</sup>

**Ginger:** Ginger has been demonstrated to improve lipid derangements. However, its underlying triglyceride-lowering mechanisms remain unclear. Gao H et. al. found that coadministration of the alcoholic extract of ginger (50 mg/kg/day, oral gavage, once daily) over 5 weeks reversed liquid fructose-induced increase in plasma triglyceride and glucose concentrations and hepatic triglyceride content in rat<sup>19</sup>. Hypothesis exist regarding effect of ginger on NAFLD which includes increasing insulin sensitivity, inducing the activation of peroxisome proliferator-activated receptor gamma, promoting considerable antioxidant

effects and antidyslipidemic properties, and reducing hepatic triglyceride content which can prevent steatosis.<sup>20</sup>

**Coffee and Green tea:** The green tea has a strong beneficial effect on NAFLD patients shown in various clinical and experimental studies. Green tea decrease hepatic steatosis by reducing hepatic insulin resistance which is a key mechanism in its pathogenesis.<sup>21</sup> The antioxidant capacity of coffee has been demonstrated in animal models of fatty liver, in which caffeine intake improves insulin resistance and reduces the production of inflammatory cytokines. Moreover, the weight of the animals and the intrahepatic levels of glucose were reduced with coffee consumption.

**Anthocyanins (ACNs) :** are water soluble vacuolar pigments of the polyphenol class that are present in many plant based products. ACNs plays a role in reducing the oxidative burden of liver through reacting with free radicles, but their benefits in patients with NAFLD has not yet been well established.<sup>22</sup>

**Polyunsaturated fatty acids (PUFA) and monounsaturated fatty acids supplementation:**  $\omega$ -3 PUFA therapy had a beneficial effect on liver fat.<sup>23</sup> PUFAs are used to promote weight loss, and to reduce hepatic triglyceride accumulation, while improving insulin sensitivity and reducing steatosis, and hepatic damage in patients with NAFLD.<sup>24</sup> Dietary supplementation of PUFAs is one of the core aspect of management of NAFLD. Vitamin D: Vitamin D supplementation improve lipid profile and inflammatory mediators when compared with placebo.<sup>25</sup>

**Probiotics, prebiotics and symbiotic:** Microorganisms that are beneficial to human when ingested as therapeutic agents have role in NAFLD management. The contribution of microflora in NAFLD progression is mainly based on increased oxidative stress in the liver, which is caused by the increased ethanol and lipopolysaccharide production in the intestine, further causing the release of inflammatory cytokines.<sup>26</sup>

## Pharmacological Therapeutics for NAFLD

### Farnesoid X receptor (FXR) agonist

Among the two generations of FXR agonists, First-generation is obeticholic acid (OCA) (INT-747) and Second-generation is cilofexor (GS-9674) and tropifexor. FXR is a nuclear receptor involved in multiple metabolic pathways. On its activation by bile acids, FXR regulates bile acid synthesis, conjugation, and transport, as well as various aspects of lipid and glucose metabolism. FXR, a key nuclear receptor of lipoprotein metabolism in the liver, therefore plays an important role in NAFLD management.

### Cilofexor and Tropifexor

Cilofexor is a potent, selective, nonsteroidal agonist of FXR that predominantly activates intestinal FXR without involvement of the enterohepatic circulation.<sup>27</sup> Patel K, Harrison SA, et al. showed that use of Cilofexor reduces hepatic steatosis (as per MRI results) and serum gamma-glutamyltransferase.<sup>28</sup> An investigational second-generation FXR agonist is tropifexor, a nonsteroidal FXR agonist. An interim analysis of a phase II study (FLIGHT-FXR) in biopsy-proven NASH patients with significant fibrosis (defined as stage 2–3 fibrosis) exhibited significant efficacy of tropifexor in hepatic steatosis reduction at 12 weeks after treatment.<sup>29</sup>

### Peroxisome proliferator- activated receptors (PPARs) agonists

Peroxisome proliferator activated receptors (PPARs) are nuclear hormone receptors that act as transcription factors in response to endogenous lipid messengers. PPARs agonists are classified into three groups: 1) PPAR  $\alpha/\delta$  is elafibrinor (GFT505), 2) Pan-PPAR agonist (PPAR- $\alpha$ , PPAR- $\beta/\delta$ , and PPAR- $\gamma$ ) is lanifibrinor (IVA337), and 3) Dual agonist of PPAR- $\alpha/\gamma$  is saroglitazar. Phase III RCTs on elafibrinor and rabifibrinor showed insignificant resolution of NASH.<sup>30</sup> A multicenter phase II study (EVIDENCE IV) comparing saroglitazar magnesium with placebo in NASH patients achieved the primary endpoint: improvement of hepatitis from baseline at 16 weeks and improvement of liver fat content measured by magnetic resonance imaging-proton density fat fraction.<sup>31</sup>



**Glucagon-like peptide-1 (GLP-1) agonists**

Glucagon-like peptide-1 (GLP-1) is a multifaceted hormone with broad pharmacological potential. Among the numerous metabolic effects of GLP-1 are the glucose-dependent stimulation of insulin secretion, decrease of gastric emptying, inhibition of food intake, increase of natriuresis and diuresis, and modulation of rodent  $\beta$ -cell proliferation. GLP-1 also has cardio- and neuroprotective effects, decreases inflammation and apoptosis, and has implications for learning and memory, reward behavior, and palatability. GLP-1 agonist has three subclasses; 1) GLP-1 receptor agonist: liraglutide, semaglutide, 2) Dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist: tirzapatide (LY3298176), and 3) Dual glucagon and GLP-1 receptor agonist: cotadutide (MEDI0382).

A multicenter phase II study (LEAN) demonstrated the efficacy of liraglutide (a GLP-1 agonist) in NASH resolution based on the disappearance of hepatocyte ballooning without fibrosis worsening among NASH patients after 48 weeks of treatment.<sup>32</sup> Cotadutide is a dual glucagon and GLP-1 agonist. A phase IIb RCT in overweight patients with T2DM showed the efficacy of cotadutide in reducing weight and serum transaminases in comparison with placebo (NCT03235050).<sup>33</sup>

**Thyroid hormone receptor  $\beta$  agonist: resmetirom**

Thyroid hormone receptor  $\beta$  agonist, highly expressed in hepatocytes, regulates many metabolic pathways, including the reduction of triglyceride and cholesterol levels, improvement of insulin sensitivity, promotion of liver regeneration and reduction of cell apoptosis. Resmetirom (MGL-3196) is a liver-directed, orally active agonist of the thyroid hormone receptor. Prof Stephen A Harrison et. al. showed resmetirom treatment resulted in significant reduction in hepatic fat after 12 weeks and 36 weeks of treatment in patients with NASH. Further studies of resmetirom will allow assessment of safety and effectiveness of resmetirom in a larger number of patients with NASH with the possibility of documenting associations between histological effects and changes in non-invasive markers and imaging.<sup>34</sup>

C-C chemokine receptor type 2 (CCR2) and type 5 (CCR5) antagonist

**Cenicriviroc**

CCR2 belongs to the G-protein-coupled seven-transmem-

brane receptor superfamily. A recent phase IIb RCT (CENTAUR) showed that cenicriviroc had no efficacy on NASH resolution but improved at least one fibrosis stage at 1 year of treatment but not after 2 years.<sup>35</sup>

**Antifibrotic drugs**

Selonsertib (GS-4997) is a selective inhibitor of apoptosis signal-regulating kinase 1 (ASK1). Two phase III studies have investigated the efficacy of selonsertib in NASH patients with bridging fibrosis (STELLAR-3) and compensated cirrhosis (STELLAR-4) over a period of 48 weeks.

Simtuzumab (GS-6624) is a humanized monoclonal antibody directed against lysyl oxidase-like molecule 2 (LOXL2). LOXL2 is an enzyme that catalyzes the cross-linkage of extracellular matrix components, such as collagen and elastin. Thus, inhibition of LOXL2 by an anti-LOXL2 monoclonal antibody may lead to a reduction in fibrosis.<sup>36</sup>

**Pan-caspase inhibitor: emricasan**

Caspases are intracellular proteases regulating apoptotic cell death. Multiple studies demonstrate that in NASH, liver injury and fibrosis are suppressed by inhibiting hepatocyte apoptosis and suggests that Emricasan may be an attractive antifibrotic therapy in NASH.<sup>37</sup>

**Insulin sensitizers and lipid lowering agents**

Cinnamon: Cinnamon is believed to have a role in glucose metabolism, especially absorption. These actions may ameliorate fasting blood glucose, LDL, and hemoglobin A1c, and might increase HDL cholesterol and insulin concentrations.<sup>38</sup>

**Conclusion**

Increasing global trends of NAFD are raising the importance of a proper management protocol for the spectrum of the disease. Newer pharmacological agents show a promising role in the management. Studies have shown the efficacy of lifestyle modifications and dietary supplements are also effective adjuncts in reducing insulin resistance, oxidative stress and inflammation involved in the pathogenesis of NAFD. Further clinical trials are required to establish the role of different drugs in preventing hepatosteatosis thus improving quality of life in patients with NAFD.

## References

- Adams LA, Lymp JF, St Sauver J, Sanderson SO, Lindor KD, Feldstein A, Angulo P. The natural history of nonalcoholic fatty liver disease: a population-based cohort study. *Gastroenterology*. 2005;129:113–121.
- Fan JG. Impact of non-alcoholic fatty liver disease on accelerated metabolic complications. *J Dig Dis*. 2008;9:63–67. doi:10.1111/j.1751-2980.2008.00323.x
- Angulo P. Long-term mortality in nonalcoholic fatty liver disease: is liver histology of any prognostic significance? *Hepatology*. 2010;51:373–375. doi:10.1002/hep.23521
- Malekzadeh R, Poustchi H. Fibroscan for assessing liver fibrosis: An acceptable alternative for liver biopsy: Fibroscan: an acceptable alternative for liver biopsy. *Hepat Mon*. 2011;11:157–158.
- Fierbinteanu-Braticevici C, Dina I, Petrisor A, Tribus L, Negreanu L, Carstoiu C. Noninvasive investigations for non alcoholic fatty liver disease and liver fibrosis. *World J Gastroenterol*. 2010;16:4784–4791.
- Stickel F, Hellerbrand C. Non-alcoholic fatty liver disease as a risk factor for hepatocellular carcinoma: mechanisms and implications. *Gut*. 2010;59:1303–1307
- Eguchi Y, Hyogo H, Ono M, Mizuta T, Ono N, Fujimoto K, Chayama K, Saibara T. Prevalence and associated metabolic factors of nonalcoholic fatty liver disease in the general population from 2009 to 2010 in Japan: a multicenter large retrospective study. *J Gastroenterol*. 2012;47:586–595.
- Farrell GC, Wong VW, Chitturi S. NAFLD in Asia--as common and important as in the West. *Nat Rev Gastroenterol Hepatol*. 2013;10:307–318.
- Cohen JC, Horton JD, Hobbs HH. Human fatty liver disease: old questions and new insights. *Science*. 2011;332:1519–1523.
- European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. *J Hepatol*. 2016;64:1388-1402.
- Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, Charlton M, Sanyal AJ. The diagnosis and management of non-alcoholic fatty liver disease: practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. *Hepatology*. 2012;55:2005–2023.
- Keating SE, Hackett DA, George J, Johnson NA. Exercise and non-alcoholic fatty liver disease: a systematic review and meta-analysis. *J Hepatol*. 2012;57:157–166.
- Firenzuoli F, Gori L. Herbal medicine today: clinical and research issues. *Evid Based Complement Alternat Med*. 2007;4:37–40.
- Pacana T, Sanyal AJ. Vitamin E and nonalcoholic fatty liver disease. *Curr Opin Clin Nutr Metab Care*. 2012;15:641–648.
- Sarkhy AA, Al-Hussaini AA, Nobili V. Does vitamin E improve the outcomes of pediatric nonalcoholic fatty liver disease? A systematic review and meta-analysis. *Saudi J Gastroenterol*. 2014;20:143–153.
- Soleimani D, Paknahad Z, Rouhani MH. Therapeutic Effects of Garlic on Hepatic Steatosis in Nonalcoholic Fatty Liver Disease Patients: A Randomized Clinical Trial, Dovepress, Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2020, 13:2389-2397. DOI:10.2147/Dnso.S245455
- Takemura S, Minamiyama Y, Kodai S, Shinkawa H, Tsukioka T, Okada S, Azuma H, Kubo S. S-Allyl cysteine improves nonalcoholic fatty liver disease in type 2 diabetes Otsuka Long-Evans Tokushima Fatty rats via regulation of hepatic lipogenesis and glucose metabolism. *J Clin Biochem Nutr*. 2013;53:94–10
- Lai YS, Chen WC, Ho CT, Lu KH, Lin SH, Tseng HC, Lin SY, Sheen LY. Garlic essential oil protects against obesity-triggered nonalcoholic fatty liver disease through modulation of lipid metabolism and oxidative stress. *J Agric Food Chem*. 2014;62:5897–5906.
- Gao H, Guan T, Li C, Zuo G, Yamahara J, Wang J, Li Y. Treatment with ginger ameliorates fructose-induced Fatty liver and hypertriglyceridemia in rats: modulation of the hepatic carbohydrate response element-binding protein-mediated pathway. *Evid Based Complement Alternat Med*. 2012:570948
- Sahebkar A. Potential efficacy of ginger as a natural supplement for nonalcoholic fatty liver disease. *World J Gastroenterol*. 2011;17:271–272.
- Gan L, Meng ZL, Xiong RB, Guo JQ, Lu XC, Zheng ZW. Green tea polyphenols epigallocatechins-3-gallate ameliorates insulin resistance in non alcoholic fatty liver disease mice. *Acta Pharmacol Sin*. 2015;36(5):597–605. doi:10.1038/aps.2015.11.
- Valenti L, Riso P, Mazzocchi A, Porrini M, Fargion S, Agostoni C. Dietary anthocyanins as nutritional therapy for nonalcoholic fatty liver disease. *Oxid Med Cell Longev*. 2013:145421.
- Lu W, Li S, Li J, et al. Effects of omega-3 fatty acid in nonalcoholic fatty liver disease: a meta-analysis. *Gastroenterol Res Pract* 2016; 1459790.
- Levy JR, Clore JN, Stevens W. Dietary n-3 polyunsaturated fatty acids decrease hepatic triglycerides in Fischer 344 rats. *Hepatology*. 2004;39:608–616.
- Mitra Hariri and Sara Zohdi Effect of Vitamin D on Non-Alcoholic Fatty Liver Disease: A Systematic Review of Randomized Controlled Clinical Trials *Int J Prev Med*. 2019; 10: 14.

26. Iacono A, Raso GM, Canani RB, Calignano A, Meli R. Probiotics as an emerging therapeutic strategy to treat NAFLD: focus on molecular and biochemical mechanisms. *J NutrBiochem.* 2011;22:699–711
27. Schwabl P, Hambruch E, Budas GR, Supper P, Burnet M, Liles JT, et al. The non-steroidal FXR agonist cilofexor improves portal hypertension and reduces hepatic fibrosis in a rat NASH model. *Biomedicines* 2021;9(1):60. doi:10.3390/biomedicines9010060.
28. Patel K, Harrison SA, Elkhatab M, Trotter JF, Herring R, Rojter SE, et al. “Cilofexor, a nonsteroidal FXR agonist, in patients with noncirrhotic NASH: a phase 2 randomized controlled trial” *Hepatology* 2020;72(1):58–71. doi:10.1002/hep.31205.
29. Lucas KJ, Lopez P, Lawitz E, Sheikh A, Aizenberg D, Hsia S, et al. Tropifexor, a highly potent FXR agonist, produces robust and dose-dependent reductions in hepatic fat and serum alanine aminotransferase in patients with fibrotic NASH after 12 weeks of therapy: FLIGHT-FXR Part C interim results. *Dig Liver Dis.* 2020;52(Suppl 1):E38. doi:10.1016/j.dld.2019.12.129.
30. Thaninee Prasoppokakorn, Panyavee Pitisuttithumand Sombat-Treprasertsuk, *Pharmacological Therapeutics: Current Trends for Metabolic Dysfunction-associated Fatty Liver Disease (MAFLD)*, *Journal of Clinical and Translational Hepatology.* 2021; 9(6):939–946. DOI: 10.14218/JCTH.2021.00189
31. Siddiqui MS, Idowu MO, Parmar D, Borg BB, Denham D, Loo NM, et al. A phase 2 double blinded, randomized controlled trial of saroglitazar in patients with nonalcoholic steatohepatitis. *Clin Gastroenterol Hepatol.* 2020;S1542-3565(20)31509-3. doi:10.1016/j.cgh.2020.10.051.
32. Armstrong MJ, Gaunt P, Aithal GP, Barton D, Hull D, Parker R, et al. Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study. *Lancet* 2016;387(10019):679–690. doi:10.1016/s0140-6736(15)00803-x.
33. Ambery P, Parker VE, Stumvoll M, Posch MG, Heise T, Plum-Moerschel L, et al. MEDI0382, a GLP-1 and glucagon receptor dual agonist, in obese or overweight patients with type 2 diabetes: a randomised, controlled, double blind, ascending dose and phase 2a study. *Lancet.* 2018;391(10140):2607–2618. doi:10.1016/s0140-6736(18)30726-8.
34. Resmetirom (MGL-3196) for the treatment of non-alcoholic steatohepatitis: a multicentre, randomised, double-blind, placebo-controlled, phase 2 trial. *The Lancet.* Published: November 11, 2019. DOI: [https://doi.org/10.1016/S0140-6736\(19\)32517-6](https://doi.org/10.1016/S0140-6736(19)32517-6).
35. Ratziu V, Sanyal A, Harrison SA, Wong VW, Francque S, Goodman Z, et al. Cenicriviroc treatment for adults with nonalcoholic steatohepatitis and fibrosis: final analysis of the phase 2b CENTAUR study. *Hepatology.* 2020;72(3):892–905. doi:10.1002/hep.31108
36. Harrison SA, Abdelmalek MF, Caldwell S, Shiffman ML, Diehl AM, Ghalib R, et al. Simtuzumab is ineffective for patients with bridging fibrosis or compensated cirrhosis caused by nonalcoholic steatohepatitis. *Gastroenterology* 2018;155(4):1140–1153. doi:10.1053/j.gastro.2018.07.006.
37. Fernando J, Barreyro, Silvia Holod, Paola V. Finocchietto, Alejandra M. Camino, Jorge B. Aquino “The pan-caspase inhibitor Emricasan (IDN-6556) decreases liver injury and fibrosis in a murine model of non-alcoholic steatohepatitis” *Liver International.* <https://doi.org/10.1111/liv.12570>
38. Ranasinghe P, Jayawardana R, Galappaththy P, Constantine GR, de Vas Gunawardana N, Katulanda P. Efficacy and safety of ‘true’ cinnamon (*Cinnamomum zeylanicum*) as a pharmaceutical agent in diabetes: a systematic review and meta-analysis. *Diabet Med.* 2012;29:1480–1492.

**Case report**

# Metastatic Prostatic Carcinoma in Middle Aged Man - A Rare Case Presentation

Hossain MM<sup>1</sup>, Kundu RR<sup>2</sup>, Parvin R<sup>3</sup>, Bulbul D<sup>4</sup>, Jamil F<sup>5</sup>, Wahidullah SMN<sup>6</sup>

**Abstract**

Carcinoma of prostate is extremely common in older aged male. It is rare in younger age. Diagnosis is most often by rectal examination, increase in serum prostate specific antigen (PSA), FNAC or Core biopsy from prostate. Prostatic carcinoma spread mainly to the lumbar vertebra but also spread to proximal femur, pelvis. In some cases it spread to viscera, lymph nodes like iliac group and para-aortic nodes. We are reporting a case of metastatic prostatic carcinoma in middle aged man which is rare and treatment is not satisfactory.

J Khulna Med Coll. 2022; 1(1) : 30-31

**Introduction**

The incidence of clinically detected adeno-carcinoma of the prostate varies significantly among nations. In particular, scandinavian countries have relatively high rates, and Asian nations have very low rates. On migration of persons from low to high incidence countries, the rate of clinical prostate cancer increase, suggesting a role for environmental factors.<sup>1</sup>

There are no known risk factors. It is rare under age 40 years; and it does not occur in the absence of testis.<sup>2</sup> Approximately one of every five American men will be diagnosed with prostate cancer in their lifetime and about 3% will die of it.<sup>3</sup>

Adenocarcinoma of the prostate in childhood and adolescence is rare, with approximately five cases in

patients younger than 10 yrs and 21 cases between the ages of 10 and 21 years reported.<sup>4</sup>

Patients tend to have obstructive symptoms and at an advanced stage, showing a metastatic pattern similar to that seen in adults. The tumours are almost uniformly poorly differentiated and are not responsive to treatment, with an average survival ranging between 3 and 10 months.<sup>3</sup> The incidence of clinically detected adeno-carcinoma of the prostate varies significantly among nations. It is of note that the incidence of incidently discovered adenocarcinoma of the prostate at autopsy is relatively uniform among different nations.

- 
1. Md. Mokter Hossain, Associate Professor. Department of Pathology, Khulna Medical College, Khulna
  2. Rama Rani Kundu, Assistant Professor. Department of Pathology, Khulna Medical College, Khulna
  3. Ruma Parvin, Curator. Department of Pathology, Khulna Medical College
  4. Dilruba Bulbul, DLM Student. Department of Pathology, Khulna Medical College
  5. Forhad Jamil, DLM Student. Department of Pathology, Khulna Medical College
  6. SM Nazim Wahidullah, DLM Student. Department of Pathology, Khulna Medical College

**Corresponding Author:**

1. Dr. Md. Mokter Hossain, Associate Professor. Department of Pathology, Khulna Medical College, khulna, Bangladesh. Email: mokterhossain4351@yahoo.com

### Case Study

A 28 years old man presented with micturation difficulties (obstruction) and pain in pelvic bone, generalized weakness and progressive anaemia for 5 months. He had history of haematuria. On examination, the patient was moderately anaemic, with presence of swelling in right hip bone. On digital rectal examination (DRE), prostate was hard in consistency. He took 5 bag blood transfusion. His routine blood reports and other routine investigations were normal except anemia. His bone Scan (showed) with Te99m MDP, dose 20 MCi, Spect-CT showed increased radiotracer uptake corresponds to sclerotic change in body of L1-L5 and S1-S2 vertebrae and both hip bones; suggestive of multiple bony metastases. MRI features Suggested enhancing altered marrow Signal intensities at L2, L3, L4, L5, S1 and S2 vertebral bodies – metastasis could be considered. FNAC from bony swellings in hip bones show metastatic adenocarcinoma, primary site most probably from prostate (Fig-1), His histopathology specimen from spinal mass (CT-guided Core biopsy) was taken and histopathology report was metastatic prostatic carcinoma with advice immunocytochemistry for further work-up. His PBF report was microcytic hypochromic anaemia due to chronic disorder or malignancy.

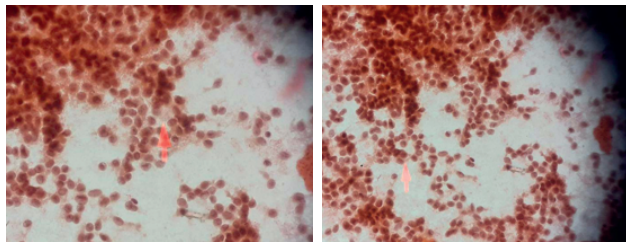


Fig-1: FNAC from pelvic bone metastasis shows hypercellular smear with single, monotonous population of cells forming glandular pattern.

### Discussion

The periurethral, transitional, and central Zones collectively are equivalent to the older designation of anterior, middle, and lateral lobes and are often the site of benign prostatic hyperplasia (BPH) and the peripheral zone of glands draining into ducts entering the urethral sinus is equivalent to the older designation of posterior lobe; it is the characteristics site for carcinoma. Adeno carcinoma of Prostate is extremely common in older age group arises from the peripheral group of glands and most often diagnosed by rectal examination.<sup>5</sup>

Prostatic carcinoma is associated at an early stage with an increase in serum prostate specific antigen (PSA). Elevations of PSA reflect a complexed form (bound to alpha-1 antichymotrypsin) which becomes elevated with prostatic cancer, and a free form, which rises with BPH. Thus, an increase total PSA with a decreased fraction of free PSA suggests malignancy, while an increased total PSA with a proportionate increase in the fraction of free PSA suggests BPH.<sup>5</sup>

The cancer detection rate using measurement of PSA is between 2% and 4% and approximately 30% of men with an elevated PSA will have prostate cancer confirmed by biopsy. Unfortunately 20% of men with clinically significant prostate cancer will have PSA values within the normal range. There is therefore controversy over the usefulness of PSA alone as a screening procedure.<sup>6</sup>

Prostatic carcinoma is characterized by increased serum prostatic acid phosphatase when the tumour penetrates the capsule into adjacent tissues. Prostatic acid phosphates, along with PSA, is useful in the follow up of disseminated disease. May frequently progress to bony osteoblastic metastasis, which, unfortunately, may be the presenting sign and serum alkaline phosphatase is an indicator of osteoblastic lesions. When disseminated, may respond to endocrine therapy, because tumour growth is partially related to the activity of androgens.<sup>5</sup>

### Conclusion

Although majority of prostatic cancer metastasis is common in elderly ages, metastasis from prostatic cancer can occur in younger ages also. These findings will be helpful in the evaluation and management of a younger patient having bony metastasis.

### References

1. Canter HB, Piantadosi, Jissacs JT. Clinical evidence for and implication of the multistep development of prostate Cancer. J Urol.1990; 143 : 742 – 746.
2. Kenneth C. Swen. Atlas and test of aspiration biopsy cytology. Williams and Wilkin. Baltimore 1990; p241.
3. Shimada H, Misug K, Sasaki Y et al. Carcinoma of the prostate in childhood and adolescence : report of a case and review of the literature. Cancer 1980;46:2534-2542.
4. Stacey E. Mills. et al. Sternberg s diagnostic surgical pathology 4th edition. Lippincott Williams and wilkins. 2004. p2084-89.
5. Arthur S, Schneider and Philip A. Szanto. Diseases of the Prostate. Pathology 5th edition, Philadelphia; Lippincott Williams and Wilkins, 2014; p292.
6. Williams S et al. Baily and Loves—Short practice of surgery. CRC Press- Taylor and Francis Group---27th edition. 2018; p1469



## Instructions for Author

### Preparation of Manuscript

- Articles should be typed in English on one side of white A4 size good quality paper with clear margin of 5 cm for header and 2.5 cm for remainder
- Interline space (1.5 point) throughout.
- Font type is Times New Roman with size 12 point.
- Manuscript should have uniform style, correct journal format, carefully proofread for grammar, spelling and punctuation.
- The manuscript must be accompanied by a Cover letter declaring that "It has neither been previously published nor been submitted elsewhere for publication".
- In general, original article should be divided into following sections: Title page, Abstract, Introduction, Methods, Results, Discussions, Acknowledgement, References.
- Tables with titles and foot notes, graph with title and Illustrations with legends will be submitted at the end.
- Each of the sections is to start on a separate page. Pages should be numbered consecutively beginning from the abstract.
- The Title page should be the first page of all manuscript and must include the following: 1. Title, 2. Article type, 3. Full name for each author and affiliation, 4. Contact information for the Principal/Corresponding Author (name, address, telephone, e mail) and 5. Word count.
- Abstract should start with appropriate title of the article and structured with headings (Background, Objectives, Methods, Result & Conclusion). Authors name should not be given at this page. It should be preferably within about 250 words. Avoid abbreviations in the title and abstract except standard abbreviation. A non structured abstract is suggested for review article and case report. It should be followed by 3 to 5 key words.
- Text should be arranged into following sections: Introduction, Methods, Results, Discussions, Acknowledgement, References.
- References would be the last segment of the text and it should be absolutely correct both in content and style.
- Length of an article should be limited to the word count (excluding reference & illustration) as designated for each type.
- Standard abbreviation should be used. The full form for which an abbreviation stands should precede its first use in the text.

### Format of Manuscript

The format of the manuscript depends on the type of the article. Each component should begin in a new page in a sequential order and contain relevant information.

A) **Original Articles** (length: 2000±500 words)

#### 1. Title

#### 2. Abstract (250±50 words)

A structured abstract should include headings such as Background, Objective, Methods, Results, and Conclusions. Title be added at the top and Key words (<5) at the bottom of the abstract.

### 3. Introduction

It will include statement of the problem with a short discussion of its importance and significance, short review of the literature related to the problem with pertinent reference and lastly objectives/ rationale/ benefits expected will be stated in 1-2 paragraph.

### 4. Methods

In this section study type, place and time, description of study subjects and grouping, sampling, selection criteria, approval of the study involving human subjects by ethical review committee and description of the ethical aspects in such study, description of study variable, description of procedure, methods, apparatus, drugs or chemicals as applicable should be given. Description of statistical procedure for obtaining all P values should be provided to allow verification. Statistical software, if used should be specified.

### 5. Results

Present result in logical sequence in text, table and illustration with the most important finding first. Describe without comment. Restrict number of table and figure needed to support assessment of paper. Do not duplicate data in table and figure.

**Table:** Simple self explanatory with brief title, not duplicate in text. Each table should be numbered in Roman numerals and include appropriate headers. It should be printed in separate page (not more than two table per page/sheet). Do not use internal horizontal and vertical rules. Uses of many tables are not encouraged. It should be referred the result section.

**Illustration (Figures):** Figures include graphs, charts and photographs. All illustrations must be numbered consecutively in Arabic numerals as they appear in the text. Submit print photograph of each illustration along with its electronic file. Figure number, title of manuscript, name of the corresponding author and arrow indicating top should be written on a sticky label affixed on the back of each photograph. Scanned picture, graph, chart with title and figure number should be printed on separate page and its original data presentation file should be inserted in the CD along with text. Readers should be able to understand figures without referring to the text. The axes on graphs should be labelled including units of measurement and that the font is large enough to read.

**Legend:** Must be typed in a separate sheet of paper. All drugs should be mentioned in their generic form. The commercial name may be used in parenthesis.

### 6. Discussion

In this section, describe only the key findings and compare and contrast the findings to other researchers, their interpretations, probable explanation of the findings and the message of the study. It also describes how the current study changes the understanding of a clinical situation. It should also include the limitations of the present study. Abbreviations used should be defined in footnotes.

## 7. Conclusion

A brief concluding paragraph presenting the implications of the study results and possible new research directions on the subject.

## 8. Acknowledgement

Individuals, institution, sponsor, organization or bodies can be acknowledged in the article for their contribution or financial or any form of assistance to the work.

## 9. Reference

For reference, use author number style (Vancouver). References should be numbered consecutively in the order in which they are first mentioned in the text. Identify references in the text, tables and legends by Arabic numerals in superscript. All citations to electronic references should be presented in numbered references following the text. The titles of the journals should be abbreviated according to the style used in Index Medicus. Write names of all authors of the article.

### Examples:

#### Standard journal article

Khalil M, Chowdhury MAI, Rahman H, Mannan S, Sultana SZ, Rahman MM et.al. Splenic Mass and its relation to age, sex and height of the individual in Bangladeshi Peoples. J Bangladesh Soc Physiol. 2008;3(1):71-78.

#### Standard book with initials for authors

Name of the authors (full stop) title of the book (full stop) edition (full stop) place of publication (colon) name of publisher (semicolon) copy right year (full stop) page number p (full stop)

Eyre HJ, Lange DP, Morris LB. Informed decisions: the complete book of cancer diagnosis, treatment and recovery. 2nd ed. Atlanta: American Cancer Society; 2002.768.

#### Contributed chapter of a book

Name of the authors of chapter (full stop) title of the chapter (full stop) In (colon) name of editors/editor (comma) editors/ editor (full stop) title of the book (full stop) place of publication (colon) name of publisher (semicolon) copy right year (full stop) page ranges.

Rojko JL, Hardy WD. Feline leukemia virus and other retroviruses. In: Sherding RG, editor. The cat: diseases and clinical management. New York: Churchill Livingstone; 1989. p.229-332.

#### Standard journal article on the Internet

Kaul S, Diamond GA. Good enough: a primer on the analysis and interpretation of noninferiority trials. Ann Intern Med [Internet]. 2006 Jul 4 [cited 2007 Jan 4]; 145(1):662-9. Available from: <http://www.annals.org/cgi/reprint/145/1/62.pdf>

#### B) Brief Reports (length : 1000±200 words)

A brief account of observational studies or large case series. The arrangement are unstructured Abstract (100±20 words), Introduction, Methods, Results and Discussion.

#### C) Case Reports (length: 1000±200 words)

It highlights unique presentations or aspects of disease processes that may expand the differential diagnosis and improve patient care. For a manuscript to be considered as a Case Report, it must meet at least one of the following 3

criteria: 1. Challenge an existing clinical or pathophysiologic paradigm, and/or; 2. Provide a starting point for novel hypothesis, testing clinical research, and/or 3. Offer a clinical "lesson" that may allow medical colleagues to provide improved care.

Case Report should consist of an unstructured Abstract (100±20 words), Introduction, Case study (including clinical presentation, diagnosis and outcome) as well as a Discussion that includes a brief review of the relevant literature.

#### D) Review Articles (length: 3000±500 words)

State of the Art Review Articles provide a comprehensive and scholarly overview of an important clinical subject with a principle focus on developments in the past 5 years. Preference for a review article is given to systematic reviews and meta-analyses of clearly stated questions over traditional narrative reviews of a topic.

Components should include: unstructured Abstract (250±50 words), Context, Objective, Data Sources, Study Selection, Data Extraction, Results, Analysis and Conclusions.

### Editorial Procedure

All submitted articles will undergo a preliminary check by members of editorial board before assigning to reviewer. Manuscript not fulfilling the requirement for publication or not prepared according to the style and format of journal and/or following authors guideline will be sent back to author for correction and resubmission. All the checked manuscripts will be sent to two individual reviewers for double blind peer review as per recommendations by subject specific experts selected by editorial board. Reviewed manuscripts will be sent to the corresponding author for appropriate response if it is indicated. Upon recommendation of both the reviewers, manuscripts will be accepted. Acceptance is based on significance, originality and clarity and fulfilment of the criteria of the publication policy of this journal. Selection of the reviewed and accepted manuscripts intended for publication in a particular issue will be decided by Editorial Board. Accepted manuscripts become the permanent property of Journal of Khulna Medical College and may not be reproduced by any means in whole or in part without the written consent of the publisher. The Editor reserves the right to style and if necessary shortens the material accepted for publication and to determine the priority and time of publication.

### Submission of manuscript

Three copies of the articles with three copies of illustrations should be submitted. An online copy should also be submitted through e-mail.

All manuscripts should be submitted by registered post to the following address:-

Editor, Journal of Khulna Medical College  
Room no – 324 (2nd floor)  
Khulna Medical College.  
(Mobile : 01711311137)

Authors from abroad may submit the manuscript through e-mail: [jkmc9222@gmail.com](mailto:jkmc9222@gmail.com)  
[tarikpsbd@gmail.com](mailto:tarikpsbd@gmail.com)