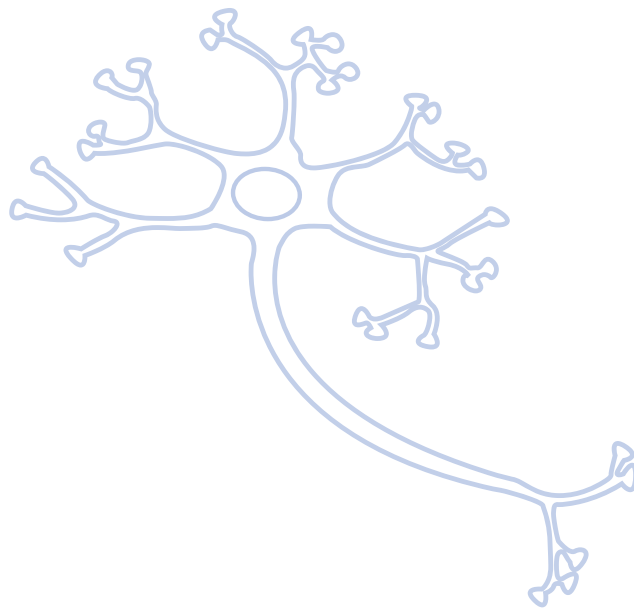


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Table of Contents

	Page
Editoria	
• Impact of Ketogenic Diet in Metabolic & Brain Health <i>Md. Akhtaruzzaman</i>	34-36
Original Articles	
• Corneal Clarity after Phacoemulsification: Nuclear Management by Stop and Chop vs Divide and Conquer Methods <i>Md. Golam Rosul, Tarana Jahan, Shawana Haque, Rumana Tussie</i>	37-40
• Effect of Smoking on Red Blood Cell Parameters: A Cross-sectional Study in a Divisional City of Bangladesh <i>Shah Abdullah Al Towhid, Talha Bin Yousuf, Roushon Ara Begum</i>	41-46
• Short-term Clinical Outcomes of COVID-19 Patients Hospitalized with Chronic Obstructive Pulmonary Disease and Asthma in Three Tertiary Level Hospitals in Bangladesh <i>Md. Ziaul Hoque, SM Nahid Hasan, Shah Didar Imam, SM Moniruzzaman</i>	47-52
• Forensic Profiling of Road Traffic Accident Victims- A Retrospective Study <i>Nazmun Nahar Nahida, Kishoara Binte Quader, Laila Yesmin, Alamgir Hossain, Borhan Uddin Ahamed</i>	53-57
• Comparison of Outcomes of Bell's Palsy Patients Treated with Steroid and Steroid with Antiviral Drug in a Tertiary Care Hospital <i>Shah Didar Imam, Md. Jalal Uddin, ABM Khairul Hasan, Sajal Kumar Shill, Md. Ziaul Hoque</i>	58-62
• Diagnostic Performance of Computed Tomography in Laryngeal Carcinoma and its Extension <i>Momotaj Begum, Sabina Yasmineen, Sadia Noor Arabi, Abu Bakar Siddique, Md. Noman Chowdhury</i>	63-67
• Incidence of Benzodiazepine Use and Misuse Among Adults in Selected Areas of Bangladesh <i>Munira Afrin, Fatema Zerine Khan, Shompa Sharmin Rasna, Tasneema Juaira, Nahida Nazmun</i>	68-72
• Knowledge and Experiences of Diseases with Associated Factors among Agricultural Workers in Manikganj District <i>Afsana Mahjabin, Khondoker Mohammad Ali, Md. Jahangir Alam, Md. Salahuddin Emdad, Faizun Nahar Nabila, Kazi AKM Sohel Anabil Digarna</i>	73-77
Review Article	
• Fever of Unknown Origin in Children <i>Mahmud Hossain</i>	78-84
Information for Authors	i-iv

Journal of Monno Medical College

Volume 09; Number 2; December, 2023

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Impact of Ketogenic Diet in Metabolic & Brain Health

Md. Akhtaruzzaman

Principal & Professor, Department of Biochemistry, Monno Medical College, Gilondo, Manikganj, Bangladesh.


The ketogenic diet, commonly known as the keto diet, has gained considerable popularity in recent years as a weight loss and health improvement strategy. While proponents praise its potential benefits, the diet has not been without its fair share of controversy and debate within the scientific and medical communities. Idea of keto diet originated from “Fasting” as a treatment of disease. In 1911, fasting was used as “cure” for epilepsy. In early 20th century, fasting included in mainstream treatment of epilepsy as reported by Dr. McMurray in NYMJ. Ketogenic diet is recommended still to treat epilepsy in children of all ages including infants. In 1921-Rollin Woodyatt noted that ketone bodies (acetone, β -hydroxybutyrate and acetoacetate) were produced by the liver as a result of prolonged fasting and starvation. He also noted that, diet low in carbohydrate & high in fat also produces the ketone bodies. In 1921, Russel Wilder from the Mayo Clinic called this type of diet as “Ketogenic Diet (KD)”. In 1970, ketogenic diet started as weight reducing strategy.¹ In Bangladesh, weight-loss “keto-craze” started in 2019 since promotional video by some physician and online activists. A good number of obese, diabetic and hypertensive started to follow ketogenic diet with aim to reduce weight in a magical way. A ketogenic diet is a specialized diet that involves consumption of highly restricted carbohydrates, moderate protein and a high proportion of fat. KD restricts carbohydrate intake to < 25-50 grams/day in an attempt to enhance tissues to use fat or ketones as fuel and shifting the body into a state of ketosis. KD typically recommend that only 5% of calories come from carbohydrates along with 75% from fat and 20% from protein.² Nutritionists designed various types of ketogenic diet out of which only 4 major types of ketodiet have gained attention till now. These are Standard Ketogenic Diet, Cyclical Ketogenic Diet, Targeted Ketogenic Diet & High protein Ketogenic Diet. Low carbohydrate intake, prolonged starvation / fasting causes

lowering of primary source of energy i.e. glucose. As a result, body breaks down fatty acid from fat and produce ketones bodies (ketogenesis). This ketosis state is called nutritional ketosis where in the serum ketone concentration is within 0.5 to 3.0 mmol/L and there is compensatory mechanism to maintain the blood p^H in the physiological range (7.35-7.45). In the absence of compensations serum ketone may exceed 10.00 mmol/L which can manifest as ketoacidosis.³

Ketone bodies can be used as an alternative energy source by many cells in the body such as kidneys, cardiac & skeletal muscles and the neural tissues via blood brain barrier. RBCs have no mitochondria and hepatocytes lack the enzyme beta-ketoacyl Co-A transferase in its mitochondrial matrix and so are unable to use ketones. The utilization of ketones leads to a reduction in production of ROS (Reactive Oxygen Species) and thus reduces oxidative stress. The epigenetic modulation is targeted via specific inhibition of the class I histone deacylases by β -hydroxybutyrate thus causing down regulation in transcripts of genes FOXO3A and MT2, responsible for oxidative stress resistance.⁴ Low carb, moderate protein & high fat intake in KD follow the same phenomena of KB synthesis. Low carb intake in KD will cause nutritional ketosis by decrease insulin & increase glucagon which stimulate lipolysis, fatty acid oxidation that ultimately leads to ketogenesis. KD helps in weight loss by increasing concentration of “satiety” hormones, such as glucagon-like peptide-1 and leptin & decreasing the hormone “ghrelin” that stimulate appetite. Both causes satiating effect and decrease hunger. Mechanism of KD in reducing seizure in epilepsy is still not clear. Several hypothesis are proposed like i. Ketone bodies stabilize neuronal activity and thus decreases seizure. ii. KD decrease excitatory neurotransmitters glutamate and increase inhibitory neurotransmitters GABA thus reduce the frequency and severity of seizures.⁵ The efficacy of keto diet was also

Correspondence: Professor dr. Md. Akhtaruzzaman Dept. of Biochemistry, Monno Medical College, Gilondo, Manikganj, Bangladesh. Email: dr.auzaman@gmail.com. Cell no: 01711442888

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proved in some other studies in neurological diseases such as Alzheimer's disease (AZ) & Parkinson's disease (PD). These patients were treated with medium -chain triglyceride drinks and scored significantly higher in the AD & PD patients compared to placebo treated patients.^{6,7} Ketone bodies are metabolized anaerobically decreasing the energy available and leading to a higher seizure threshold.⁸ The Modified Atkinson's Diet (MAD), a modified version of KD that has more flexibility and palatability, renders better suited in children compared to KD in treating children with drug resistant epilepsy.⁹ MAD is also found to be efficacious in treating drug resistant epilepsy in adolescents and adults however the rate of seizure reduction is lower than that of the children population.⁸ Kawamura et al. in several in vivo and in vitro studies in animal models and patients with epilepsy had shown that feeding KD for 2-3 weeks lead to reduce neuronal excitability in the seizure prone area region of the CA3 region. Furthermore, the binding of adenosine to the adenosine A1 receptor (A1R) leads to an inhibitory effect that decreases neuronal excitability. Therefore, increased adenosine levels in taking KD is one possible mechanism for seizure prevention specially in drug-resistant epilepsy.⁸ Individual taking KD there is excessive production of ketone bodies which leads to mitochondrial stress and increased levels of reactive oxygen species and increase ratio of NAD⁺/ NADH and AMP/ATP that ultimately results in protective adaptive (hormetic) response. In the heart, the adaptive response improves resistance to damage after ischemic attack.¹⁰

Proponents argue that the keto diet, which involves a significant reduction in consumption of carbohydrates and an increase in consumption of healthy fats, can lead to rapid weight loss, improved mental clarity, and better control of blood glucose levels. However, critics express concerns about potential long-term health risks associated with the diet, including nutritional deficiencies, increased cholesterol levels, and the strain on vital organs. One of the key aspects of the keto diet is the induction of a state called ketosis, where the body shifts from using glucose as its primary energy source to burning fat. While some studies suggest positive outcomes, the long-term effects of sustained ketosis remain unclear, raising questions about its safety and sustainability. Moreover, concerns about the potential lack of essential nutrients cannot be ignored. The restrictive nature of the keto diet may make it challenging to obtain an adequate amount of certain vitamins and

minerals, potentially leading to nutritional imbalances over time. On the flip side, supporters argue that the keto diet's positive impact on weight loss and metabolic health outweigh these concerns. They point to success stories and studies showing improvements in conditions such as epilepsy and type 2 diabetes. As we navigate this nutritional landscape, it is crucial to approach the keto diet with caution. Individuals should consult healthcare professionals before embarking on such a dietary regimen, especially those with pre-existing health conditions. The one-size-fits-all approach may not be suitable for everyone, and personalized guidance is essential to ensure that nutritional needs are met. In conclusion, the keto diet sparks a compelling debate within the scientific and medical communities. While it shows promise in certain areas, unanswered questions and potential risks underscore the need for further research and a nuanced understanding of its long-term effects. As the popularity of the keto diet continues to grow, it is imperative that individuals approach it with informed decision-making and a focus on overall health and well-being.

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Original Article

Corneal Clarity after Phacoemulsification: Nuclear Management by Stop and Chop vs Divide and Conquer Methods

Md. Golam Rosul¹, Tarana Jahan², Shawana Haque³, Rumana Tussie⁴

¹Associate Professor, Department of Ophthalmology, Monno Medical College and Hospital, Monno City, Gilando, Manikganj, Bangladesh; ²Assistant Professor, Department of Microbiology, Monno Medical College, Monno City, Gilando, Manikganj, Bangladesh; ³Assistant Professor, Department of Biochemistry, Monno Medical College, Monno City, Gilando, Manikganj, Bangladesh; ⁴Assistant Professor, Department of Ophthalmology, Shaheed Suhrawardy Medical College, Dhaka; ; Bangladesh.

Abstract

Background: Restoration of effective vision is the principal aim of all modalities of cataract surgery including Phacoemulsification. Energy level of ultrasonic power in Phacoemulsification and turbulence of fluid in the anterior chamber plays an important role in corneal endothelial cell loss influencing post-operative corneal clarity.

Objectives: To compare post-operative corneal clarity after Phacoemulsification by two techniques of nuclear divisions: stop and chop with divide and conquer. **Methodology:** This prospective observational study was conducted on Ophthalmology Department at Shaheed Monsur Ali Medical College and Hospital, Uttara, Dhaka from January, 2023 to June, 2023. The study was carried out on 30 outdoor patients undergoing Phacoemulsification at SMAMCH and Mirpur Eye Hospital, Dhaka. The selected patients underwent detailed ocular and systemic examinations with relevant investigations and divided equally into two groups comprising of 15 in group A (stop and chop) and 15 in group B (divide and conquer). Phacoemulsification was done in all patients by a single expert surgeon. Patients were followed up after 1 week, 4 weeks and 12 weeks of surgery. Corneal endothelial cell count and central corneal thickness were assessed in each visit. Mean value of these mentioned parameters in follow-up periods were compared between two groups. Unpaired t test was done to assess the level of significance. **Results:** The mean age \pm standard deviation (SD) of the study subjects was 61.5 ± 2 years, out of which 13(43.33%) were males and other 17(56.67%) females. Pre-operative value of mean endothelial cell count was $2620 \pm 70.20/\text{mm}^2$ in group A and $2625 \pm 71.10/\text{mm}^2$ in group B. Postoperative mean value \pm SD of endothelial cell count was $2420 \pm 68.90/\text{mm}^2$, $2345 \pm 66.64/\text{mm}^2$, $2310 \pm 66.04/\text{mm}^2$ respectively after 1 week, 4 weeks and 12 weeks of surgery in group A and $2410 \pm 69.54/\text{mm}^2$, $2340 \pm 65.87/\text{mm}^2$, $2310 \pm 64.45/\text{mm}^2$ in group B respectively. Mean value \pm SD of central corneal thickness was 545 ± 40.50 micrometer, 535 ± 40.02 micrometer and 532 ± 39.85 micrometer respectively after 1 week, 4 weeks and 12 weeks after surgery in group A and 547 ± 43.98 micrometer, 537 ± 41.23 micrometer and 533 ± 40.63 micrometer respectively in group B. **Conclusion:** Quantitative assessment and comparison of endothelial cell count and central corneal thickness shows that at end of the study, there was no remarkable difference in mean values of endothelial cell count and central corneal thickness between two methods.

Key Words: Phacoemulsification, Corneal clarity, Divide and Conquer, Stop and Chop

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Correspondence: Dr. Md. Golam Rosul, Associate Professor, Department of Ophthalmology, Monno Medical College and Hospital, Monno City, Gilando, Manikganj, Bangladesh. E-mail: dr.md.golamrosul@gmail.com, Cell: +880 1711-031805.

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Introduction:

There are various methods of cataract surgery- of them, phacoemulsification is considered as the 'gold standard' of all modalities of cataract surgery.^{1,2}

The Phacoemulsification technique was initially described by Kelman in 1967.³ In phacoemulsification, nucleus is ultrasonically divided and aspirated through an incision which is less than 3 mm in diameter.^{4,5} Its acceptance is increasing day-by-day. It was found as a procedure of choice for about 50% of surgeons by 1999, 79% of surgeons by 1992 and is almost universal now-a-days.⁶ All modern phaco methods depend on the principle of lens "disassembly" where hard nucleus is fragmented into gradually smaller maneuverable pieces.^{7,8}

Many procedures have been described for the management of lens nucleus. They are of 2 broad categories. The first category are the sculpting techniques, including divide and conquer, in which phacoemulsification is done by sculpting the nucleus in order to decrease its size and to create trenches along which nucleus may be divided. The pieces of divided nucleus are then made into small pieces and emulsified.⁹ In the other chopping techniques, a chopper, i.e., 2nd instrument is introduced and drawn across the nucleus to make the nucleus into smaller fragments. These smaller fragments can be separated by main mass of the nucleus and emulsified.^{10,11} Considering the inherent disadvantages of packing of the chopped pieces like jig saw puzzle, especially in chopping techniques, Dr. Paul Koch developed the stop and chop technique. In this technique, Dr. Koch divided the nucleus by sculpting into two halves so that a space is created to facilitate the chopping process and removal of the nuclear pieces.¹² We conducted the current study in 2 groups of patients subjecting them to nuclear managements by stop and chop and divide and conquer techniques to compare the rate of corneal endothelial cell loss and central corneal thickness.

Methodology:

This prospective observational study was conducted at Shaheed Mansur Ali Medical College and Hospital (SMAMCH), Uttara, Dhaka from January, 2023 to June, 2023. The study was carried out on 30 outdoor patients, undergoing Phacoemulsification at SMAMCH and Mirpur Eye Hospital, Mirpur, Dhaka on corneal endothelial cell loss and central corneal thickness.

Patients were selected based on some inclusion criteria like

nuclear grades 1-3, healthy cornea, full pupil dilatation, good red reflex, easy surgical access, average axial length (22-25mm), lack of other ocular comorbidities. Brown and black cataract, preoperative endothelial count less than 1,000 per sq.mm were excluded from this study. These 30 patients were randomly divided into 2 groups, who were operated by either of the two methods of nuclear division. In group A, 15 patients were operated by stop and chop technique and the other 15 by divide and conquer method in group B. After getting written informed consent, each of the patients in two groups underwent Phacoemulsification by one of these 2 techniques under peribulbar anaesthesia.

With divide and conquer technique, a deep groove was cut across the middle of the lens nucleus towards the opposite side of the capsulorhexis. Then by rotating the nucleus through 90°, the 2nd groove was created and followed by further rotation and sculpting to create a cross. The second instrument and phacoprobe were positioned into the grooves, and then nucleus was cracked into 4 quadrants.

In stop and chop technique,¹³ a central trench was first sculpted and the nucleus was divided into 2 halves or 2 hemi nuclei, followed by stopping sculpting and commencing chopping. The nucleus was then divided into several pieces, which were aspirated conventionally.

All patients were followed up post-operatively after 1 week, 4 weeks and 12 weeks. Each patient underwent preoperative evaluation including best corrected visual acuity (BCVA) with Snellen's chart, detailed slit lamp examination, nuclear sclerosis grading, fundoscopy, intraocular pressure (IOP) by Goldman applanation tonometry (GAT) and regurgitation test to check the patency of nasolacrimal duct. Using TOPCON SP 3000P specular microscope, specular microscopy was done pre-operatively in each patient and corneal endothelial cell count and corneal thickness for each of the patients were determined and recorded.

Results:

The mean age \pm standard deviation (SD) of the patients was 61 \pm 2 years. The mean endothelial cell counts \pm SD were 2620 \pm 70.20/mm² and 2625 \pm 71.10/mm² preoperatively in group A and group B respectively. The counts were decreased to 2420 \pm 68.90/mm² and 2410 \pm 69.54/mm² in

1st post-operative visit after 1 week in group A and group B respectively, followed by further decreases to $2345 \pm 66.64/\text{mm}^2$ and $2340 \pm 65.87/\text{mm}^2$ in 2nd post-operative visits after 4 weeks, and $2310 \pm 66.04/\text{mm}^2$ and $2310 \pm 64.45/\text{mm}^2$ in 3rd post-operative visits after 12 weeks in group A and group B respectively. (Table I)

Table I: Comparison of mean endothelial cell counts

Groups	Mean endothelial cell count + standard deviation at different patient visits			
	(% loss from previous visit)			
	1 st Visit (Preoperative)	2 nd Visit (after 1 week post operatively)	3 rd Visit (after 4 weeks post operatively)	4 th Visit (after 12 weeks post operatively)
Group A	2620 ± 70.20 / mm^2	2420 ± 68.90 / sq. mm (7.63% loss)	2345 ± 66.64 / sq. mm (3.09% loss)	2310 ± 66.04 / sq. mm (1.49% loss)
Group B	2625 ± 71.10 / mm^2	2410 ± 69.54 / sq. mm (8.19% loss)	2340 ± 65.87 / sq. mm (2.90% loss)	2310 ± 64.45 / sq. mm (1.28% loss)

The mean + SD of corneal thickness of the cases in group A and group B was 530 ± 40.90 micrometer and 532 ± 30.56 micrometer respectively. The mean corneal thickness of the cases on follows up post-operatively after 1 week, 4 weeks and 12 weeks were found 545 ± 40.50 , 535 ± 40.02 and 532 ± 39.85 micrometer in group A and 532 ± 30.56 , 547 ± 41.23 and 533 ± 40.63 micrometer in group B respectively. (Table II)

Table II: Corneal pachymetry of the cases

Groups	Mean value \pm standard deviation of corneal thickness			
	Preoperative	Post-operative follow ups after-		
		1 week	4 weeks	12 weeks
Group A (n=15)	530 ± 40.90 μm	545 ± 40.50 μm	535 ± 40.02 μm	532 ± 39.85 μm
Group B (n=15)	532 ± 30.56 μm	547 ± 43.98 μm	537 ± 41.23 μm	533 ± 40.63 μm

Preoperative visual acuity of the majority patients in both group A was 6/24 or worse [12/15 (80.00%) and all of the patients in group B was 6/24 (15/15, 100.00%) in group B]. (Table III)

Table III: Preoperative visual status of the patients

Visual Acuity	Number (%) of patients	
	Group A (n=15)	Group B (n=15)
>6/18	0 (0.00%)	0 (0.00%)
6/24	2 (13.33%)	2 (13.33%)
6/36	3 (20.00%)	3 (20%)
6/60	4 (26.67%)	3 (20%)
5/60	3 (20.00%)	1 (6.67%)
4/60	1 (6.67%)	2 (13.33%)
3/60	1 (6.67%)	2 (13.33%)
2/60	0 (0.00%)	2 (13.33%)
1/60	1 (6.67%)	0 (0.00%)
<1/60	0 (0.00%)	0 (0.00%)

The majority of cases in both groups with best corrected visual acuity after 12th postoperative week was 6/12 or better [12(80.00%) in group A and 13/15 (86.67%) in group B]. (Table IV)

Table IV: Best Corrected Visual Acuity after 12th postoperative week

Visual acuity	Number of patients (%) for patient groups	
	Group A (n=15)	Group B (n=15)
6/6	4 (26.6)	3 (20.0)
6/9	4 (26.6)	4 (26.6)
6/12	4 (26.6)	6 (40.0)
6/18	1 (6.6)	0 (0.0)
6/24	1 (6.6)	1 (6.6)
6/36	1 (6.6)	1 (6.6)
6/60 or less	0 (0.0)	0 (0.0)

Discussion:

The preoperative mean endothelial cell density was 2620 ± 70.20 / mm^2 in group A and 2625 ± 71.10 / mm^2 in group B. These values have a similarity with the findings of Brightbill who reported that mean endothelial cell count in late adulthood was around 2,500 cells / mm^2 and Indians have slightly lower counts.¹³ In the present study, after 1st postoperative week, endothelial cell loss was 7.63% in group A and 8.19% in group B. After 4th postoperative week, there was further decrease in endothelial cell loss to 3.09% in group A and 2.90% in group B. At 12th postoperative week, there was further decrease in endothelial cell loss by 1.49% in group A and 1.28% in group B. These findings were similar to a study which was done by Li and coworkers who found an average endothelial cell loss of 9.74% in 107 patients of phacoemulsification at 1st postoperative week.¹⁴

Central corneal thickness of all the patients was measured preoperatively and postoperatively after 1st, 4th and 12th weeks.

Mean preoperative values were 530 ± 40.90 micrometer in group A and 532 ± 30.56 micrometer in group B. After 1st, 4th and 12th postoperative week, the central corneal thickness was 545 ± 40.50 micrometer, 535 ± 40.02 micrometer, 532 ± 39.85 micrometer respectively in group A and 547 ± 43.98 micrometer, 537 ± 41.23 micrometer, 533 ± 40.63 micrometer respectively in group B. The similarity of results in these two groups is supported by a study done by Srinivisan et al,¹⁵ who found that there was initial loss of endothelial cell count, increase in central corneal thickness and these values subsequently become normal after 12th weeks of surgery.

Conclusion: The two techniques of nuclear management are equally effective. The endothelial cell loss and central corneal thickness changes were almost equal in these two methods.

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Original Article

Effect of Smoking on Red Blood Cell Parameters: A Cross-sectional Study in a Divisional City of Bangladesh

Shah Abdullah Al Towhid¹, Talha Bin Yousuf², Roushon Ara Begum³

¹Lecturer, Department of Physiology, Sheikh Hasina Medical College, Tangail; ²Associate Professor, Department of Physiology, North Bengal Medical College, Sirajganj; ³

Associate Professor and Head, Department of Biochemistry, Sylhet MAG Osmani Medical College, Syleht, Bangladesh.

Abstract

Background: Several metabolic and biochemical processes, hormone secretion, and the haematological system are all affected by smoking. Numerous studies have found that smoking is associated with higher levels of haemoglobin concentration (Hb%), total red blood cell count (RBC), and red cell distribution width (RDW).

Objectives: To study the RBC parameters in healthy male smokers and non-smokers among adults. **Methodology:** This research was carried out in the Department of Physiology of Sylhet MAG Osmani Medical College, from July, 2021 to June, 2022. A total of 200 participants were included with healthy adult smokers and age-matched healthy adult non-smokers. History and physical examinations were used to evaluate each individual. We measured height and weight, and calculated body mass index of the subjects. Calculations were made on cigarette smoking intensity and duration. Blood was collected to determine RBC parameters, such as total RBC count, haemoglobin level, haematocrit, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and red cell distribution width (RDW) by using Sysmex 500i automatic haematology analyzer (Japan). **Results:** Among the 200 participants, 100 were adult smokers and another 100 age-matched healthy adult non-smokers. The RBC indices were significantly elevated in smokers compared to non-smokers group: mean haemoglobin concentration (g/dl)± standard deviation (SD) were 14.17 ± 2.13 versus 13.27 ± 1.39 respectively with $p < 0.001$, mean haematocrit (HCT) (percent) ± SD were 41.60 ± 6.88 versus 39.13 ± 5.46 respectively with $p = 0.005$, mean corpuscular volume (MCV) (fl) ± SD 91.13 ± 8.86 versus 88.33 ± 5.58 respectively with $p = 0.033$, mean corpuscular hemoglobin (MCH) (pg) ± SD 31.16 ± 3.26 versus 30.05 ± 3.0 respectively with $p = 0.016$ and mean red cell distribution width (RDW) (percent)+ SD 14.74 ± 1.63 versus 14.00 ± 1.57 respectively with $p = 0.001$. However, RBC count ($\times 10^6/\mu\text{l}$) (4.60 ± 0.80 versus 4.46 ± 0.60 ; $p = 0.143$) and mean corpuscular haemoglobin concentration (MCHC) (g/dl) (34.23 ± 2.11 versus 34.11 ± 2.32 ; $p = 0.707$) did not differ significantly between smoker and non-smoker groups. There was no statistical difference between mild, moderate, and severe smokers, according to the study's variables. **Conclusion:** MCV, MCH, RDW, haematocrit, and haemoglobin concentration were all significantly higher in smokers.

Key Words: Smoker, RBC, Haemoglobin, Red cell distribution with, Haematocrit

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Correspondence: Dr. Talha Bin Yousuf, Associate Professor, Department of Physiology, North Bengal Medical College, Sirajganj, Bangladesh. E-mail: talhaysf@gmail.com, Cell: +880 1675 610619.

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Introduction:

The act of smoking involves burning tobacco and inhaling the resulting smoke using various devices, including cigarettes, cigars, biris, and pipes.¹ Smoking is a well-known health risk and one of the leading causes of death. Over 8 million fatalities occur globally each year as a result of tobacco usage.² The World Health Organization (WHO) predicts that tobacco use will cause 10 million deaths annually by the decade 2020–2030, with 70% of these fatalities will occur in the developing world. According to the same document of the WHO, around 2.4 billion individuals worldwide have consumed tobacco through smoking, chewing, snuffing, or dipping.³

A person, who has smoked 100 or more cigarettes in their lifetime and presently smokes every day or occasionally, is considered to be a current smoker if they are 18 years or older. Overall, men were found to smoke more cigarettes currently than the women.⁴

It is assumed that irregularities in blood rheology, infections and inflammation, oxidative stress, and changes to the antithrombotic and fibrinolytic system are responsible for health hazards in smokers.^{5,6}

It has long been proven that smoking has an impact on a number of metabolic and biological processes. Haematological components develop in peripheral blood after starting to grow in the bone marrow. As a result, they are impacted by cigarette smokes' free radicals and peroxides, which harm peripheral blood and bone marrow and contribute to the pathogenesis of a number of illnesses, such as inflammatory processes, atherosclerosis, and carcinomas.^{5,7,8} Moreover, smoking has been found linked to higher levels of haemoglobin concentration (Hb%), total red blood cell (RBC) count, and red cell distribution width (RDW).^{6,7} It has been demonstrated that higher RDW in smokers is a strong predictor of mortality in individuals with coronary artery disease.^{9,10} Smoking tobacco may also alter RBCs' morphology, which lowers the blood's ability to carry oxygen.¹¹

Previous research found that smoking causes pulmonary gaseous exchange abnormalities that result in secondary polycythemia, which is demonstrated by an increase in the number of RBCs, haemoglobin levels, and haematocrit, as well as by low serum erythropoietin levels.¹²

With a slight decrease in daily cigarette use, the negative effects of smoking on haematological parameters improve. A study observed that when chronic smokers stop smoking, the majority of RBC-related indicators quickly revert to baseline.¹³

The purpose of this study was to evaluate the effects of smoking on RBC parameters among healthy smoker and non-smoker males.

Methodology

This study was conducted in the Department of Physiology, Sylhet MAG Osmani Medical College, Sylhet. The study design was a cross-sectional and carried out from July, 2021 to June, 2022. Convenient sampling method was applied for data collection. By using Guilford and Frucher's formula ($n=z^2pq/d^2$),¹⁴ the calculated sample size was 143. But in this study, we took 100 sample in each two groups. Hundreds of them were healthy adult smokers and age-matched another 100 healthy adult non-smokers were selected. Healthy adult individuals of Kajolshah of Sylhet City, Bangladesh, were selected to participate in this study. Informed written consent was obtained from each participant after explaining the purpose of the study. All the participants were assessed through history and physical examination. Height and weight were measured and body mass index (BMI) was calculated. Intensity and duration of cigarette smoking was calculated for smokers by using the following formula: Pack-years = (number of cigarettes smoked per day × number of years smoked)/20.¹⁵

With all aseptic precautions, 5 ml venous blood was collected from each of the cases from the antecubital vein by a plastic disposable syringe with minimum stasis. The blood specimens were stored in an EDTA tube. Study variables were total RBC count, Haemoglobin level, Haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular Haemoglobin (MCH), mean corpuscular Haemoglobin concentration (MCHC) and red cell distribution width (RDW). All RBC indices were measured by using Sysmex 500i Automatic Haematology Analyzer (Biotech limited, Japan) and estimated in the Department of Pathology, Sylhet MAG Osmani Medical College, by the researchers.

Data were collected by using a semi-structured questionnaire designed for the study. After data collection, they were processed and analyzed with the help of Statistical Package for Social Science (SPSS) version 25.0. The comparison was made by using student's unpaired 't' test and ANOVA test. Qualitative data were expressed as frequency and percentage, and comparison was done by using Chi-Square (χ^2) test. The p-value <0.05 was considered as statistically significant.¹⁶

Results

Majority of the participants among smokers (32, 32.0%) and non-smokers (38, 38.0%) were from 21-30 years age group. (Table I)

Table I: Table-1 Distribution of participants by age (N=200)

Age	Study groups		p-value
	Smoker (n=100)	Non-smoker (n=100)	
Up to 20 years	2 (2.0%)	5 (10.0%)	p=0.569*
21 to 30 years	32 (32.0%)	38 (38.0%)	
31 to 40 years	28 (28.0%)	28 (28.0%)	
41 to 50 years	19 (19.0%)	14 (14.0%)	
51 to 60 years	19 (19.0%)	15 (15.0%)	

*Statistical analyses were done by Chi-Square (χ^2) test

The mean \pm standard deviation (SD) body mass index (BMI) was 19.44 ± 1.49 (Kg/m²) in smoker group and 19.07 ± 1.27 (Kg/m²) in non-smoker control group; body mass index did not differ significantly (p=0.569) between two groups. (Figure 1)

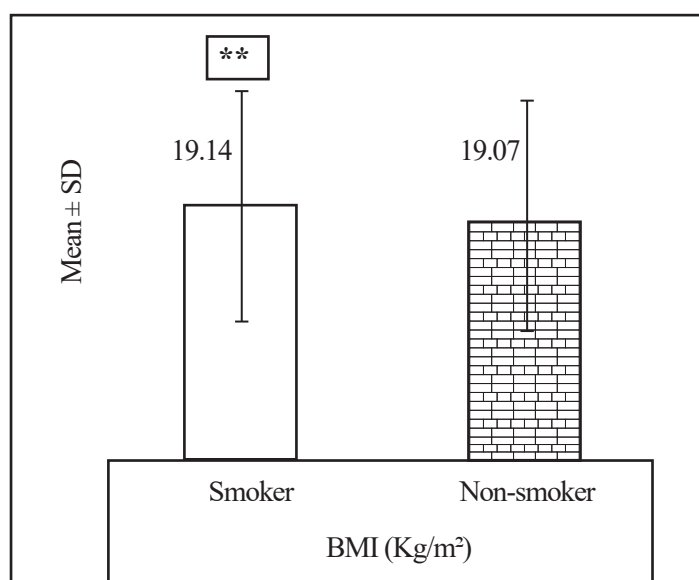


Figure 1: Body Mass Index of the study subjects (n=200)

The mean RBC count \pm SD was $4.60 \pm 0.80 \times 10^6/\mu\text{l}$ in smokers and $4.46 \pm 0.60 \times 10^6/\mu\text{l}$ in non-smokers; difference was not statistically significant (p=0.143). (Figure 2)

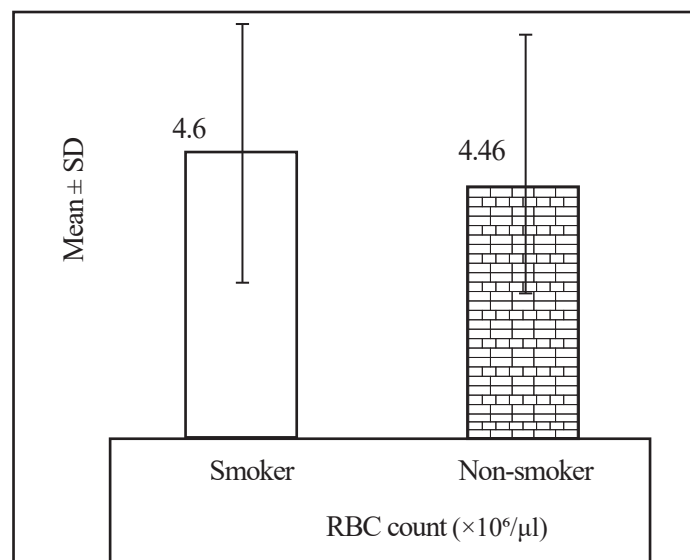


Figure 2: Mean RBC count among smokers and non-smokers

The mean haemoglobin (g/dl) was 14.17 ± 2.13 g/dl in smokers and 13.27 ± 1.39 g/dl in non-smokers; difference was statistically significant (p<0.001) (Figure 3).

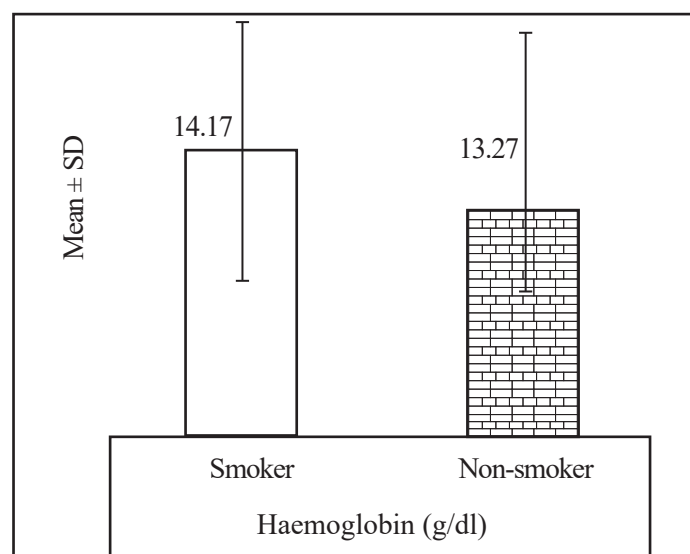


Figure 3: Mean haemoglobin concentration between smokers and non-smokers

The mean HCT was 41.60 ± 6.88 % in smoker and 39.13 ± 5.46 % in non-smoker; difference was significant (p=0.005). The mean MCV was 91.13 ± 8.86 fl in smoker and 88.33 ± 5.58 fl in non-smoker; difference was significant (p=0.033). The mean MCH was 31.16 ± 3.26 pg in smoker and 30.05 ± 3.22 pg in non-smoker; difference was significant (p=0.016). The mean MCHC was 34.23 ± 2.11 g/dl in smoker and 34.11 ± 2.32 g/dl in non-smoker; difference was not significant (p=0.707). The mean RDW was 14.74 ± 1.63 % in smoker group and 14.00 ± 1.57 % in non-smoker control group; difference was significant (p=0.001). (Table II)

Table-II: Comparison of RBC parameters between study groups

RBC parameters	Study groups		p-value
	Smoker (n=100)	Non-smoker (n=100)	
HCT (%)	41.60 ± 6.88	39.13 ± 5.46	p=0.005
MCV (fl)	91.13 ± 8.86	88.33 ± 5.58	p=0.033
MCH (pg)	31.16 ± 3.26	30.05 ± 3.22	p=0.016
MCHC (g/dl)	34.23 ± 2.11	34.11 ± 2.32	p=0.707
RDW (%)	14.74 ± 1.63	14.00 ± 1.57	p=0.001

Independent sample ‘t’ test was used to analyze the data. Haematocrit (HCT); mean corpuscular volume (MCV); mean corpuscular haemoglobin (MCH); mean corpuscular haemoglobin concentration (MCHC) and red cell distribution width (RDW); fl- femtoliter; pg- picogram.

There was no statistically significant difference in the mean RBC count, haemoglobin concentration, HCT, MCV, MCH, MCHC, or RDW amongst mild, moderate, and heavy smokers (p>0.05) (Table 3).

Table 3: Distribution of RBC parameters according to intensity of smoking

RBC parameters	Intensity of smoking			p*-value
	Mild (n=22)	Moderate (n=63)	Severe (n=15)	
RBC count (×10 ⁶ /µl)	4.42 ± 0.83	4.67 ± 0.81	4.56 ± 0.54	p=0.419
Haemoglobin (g/dl)	13.80 ± 1.88	14.37 ± 2.39	13.92 ± 0.99	P=0.501
HCT (%)	41.00 ± 6.69	42.16± 7.28	40.15 ± 5.34	p=0.541
MCV (fl)	94.43 ± 9.68	90.71 ± 8.67	88.08 ± 7.35	p=0.082
MCH (pg)	31.94 ± 3.74	31.00 ± 3.24	30.71 ± 2.49	p=0.431
MCHC (g/dl)	33.82 ± 2.11	34.19 ± 1.89	34.99 ± 2.83	p=0.251
RDW (%)	15.03 ± 1.69	14.81 ± 1.57	13.99 ± 1.67	p=0.147

One way ANOVA* test was used to analyze the data. µl- microliter; Hematocrit (HCT); mean corpuscular volume (MCV); mean corpuscular hemoglobin (MCH); mean corpuscular hemoglobin concentration (MCHC) and red cell distribution width (RDW); fl- femtoliter; pg-pico-gram.

Discussion

Several researches had suggested that smoking has negative consequences on the human body.^{17, 18}

Smoking is one of the risk factors for developing a variety of medical conditions, including cancer, chronic obstructive pulmonary disease, pancreatitis, metabolic

syndro mes, periodontal disease, and gastrointestinal disorders.¹⁹

There was no significant difference in the age groups of the participants between the two study groups (p=0.569). Similar findings were observed in Arbab et al.²⁰ The body mass index (BMI) did not differ significantly between the two groups (p=0.057). This finding was supported by Herath et al⁸ who found that the difference was not significant (p=0.143). This result was consistent with Lakshmi as reported in 2018²¹ Sharma and Agrawal in 2020,²² who observed that smokers' RBC counts were significantly higher than those of non-smokers, and their findings were statistically significant. High RBC levels were reportedly linked to blood viscosity and clotting in smokers. High RBC count is referred to as polycythemia, and extremely high RBC count restrict blood flow and raise the risk of intravascular clotting, coronary vascular resistance, decreased coronary blood flow, and a propensity for thrombosis.²³

There was statistically significant difference between the smoker and non-smokers were observed (p<0.001). This outcome was supported by several studies.²¹⁻²⁴ Carbon monoxide exposure is thought to be the mediator of increased haemoglobin concentration in smokers. A compensating mechanism, according to some investigators, may explain why smokers' blood haemoglobin levels were higher.⁵ When carbon monoxide binds to haemoglobin, carboxyhaemoglobin is produced, an inactive form of haemoglobin that is incapable of transporting oxygen. The ability of haemoglobin to carry oxygen to the tissues is reduced when carboxyhaemoglobin shifts the Hb dissociation curve to the left.²⁵ Smokers maintain higher levels of haemoglobin concentration than non-smokers do in order to compensate the reduced ability of haemoglobin to carry oxygen.²¹

The mean HCT (%) significantly (p=0.005) differed between the smoker and non-smoker groups. This result was concordant with the studies of Lakshmanan and Saravanan 2014²⁴ and Lakshmi.²⁰ Smokers had higher haematocrit levels, and these increases were most likely compensatory for carbon monoxide exposure.

Hypoxia brought on by carboxy-haemoglobin results in enhanced production of erythropoietin, enhancing erythropoiesis can be used to explain an increase in the number of erythrocytes and levels of haematocrit. Moreover, by reflecting a rise in haematocrit value, carbon monoxide lowers plasma volume and, as a result, mimics polycythemia by increasing capillary permeability.²⁶

The mean MCV (fl) values were significantly ($p=0.033$) different between the two groups. Acik et al⁷ and Bashir et al²⁷ had similar findings in their studies. High MCV levels in our study participants suggested that they may have megaloblastic, haemolytic, pernicious, or macrocytic anemia, which is typically brought on by iron and folic acid deficiencies.

The mean MCH (pg) was significantly ($p=0.016$) different between two groups. Asif et al found that MCH did not differ significantly between the smoker group and non-smoker group.²³

The mean MCHC did not differ significantly ($p=0.707$) between the study subjects. This result was consistent with the study of Malenica et al⁵ But Asif et al found that MCHC was significantly higher in the smoker group compared to the non-smoker group.²³

The mean red cell distribution width (RDW) (%) smoker and non-smoker difference was significant ($p=0.001$). This result was supported by the study of Ciftçiler et al.⁶ But Asif et al²³ found that RDW did not differ significantly between the two groups. There was no significant difference in the distribution of RBC parameters according to the intensity of smoking was observed ($p>0.05$).

In this study, haematological parameters were compared also according to status and intensity of smoking in smokers by ANOVA test. The mean RBC count, haemoglobin concentration, HCT, MCV, MCH, MCHC, RDW had no statistically difference among mild, moderate and severe smokers. But Alvi et al found that mean RBC count, haemoglobin concentration, HCT, MCV, MCH and MCHC were increased significantly with the intensity of cigarette smoking.²⁸

Conclusion

The levels of the RBC parameters were found considerably higher in smokers compared with non-smokers. Elevated RBC parameters may develop cardiovascular accidents. For this reason, social awareness should develop and regular checking of these parameters for smokers should ensure.

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Conflict of interest: None

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Original Article

Short-term Clinical Outcomes of COVID-19 Patients Hospitalized with Chronic Obstructive Pulmonary Disease and Asthma in Three Tertiary Level Hospitals in Bangladesh

Md. Ziaul Hoque¹, SM Nahid Hasan², Shah Didar Imam³, SM Moniruzzaman⁴

¹Assistant Professor, Department of Respiratory Medicine; ²Assistant Professor, Department of Internal Medicine; ³Assistant Professor, Department of Neuromedicine; ⁴Associate Professor, Department of Paediatrics, Monno Medical College and Hospital, Gilondo, Manikganj, Bangladesh.

Abstract

Background: Several comorbidities including chronic obstructive pulmonary disease (COPD) or bronchial asthma have been found associated with COVID-19 cases. But it remains unclear which of the comorbidities are associated with worse outcomes of the patients. **Objectives:** This study was carried out to determine the clinical outcomes of hospitalized COVID-19 patients with COPD or asthma. **Methodology:** This prospective study was carried out at Respiratory Medicine unit of Monno Medical College and Hospital, Manikganj, from April 2020 to December 2022. Admitted COVID-19 patients, suffering from COPD or bronchial asthma, were enrolled purposively upon fulfilling the inclusion and exclusion criteria. The patients were divided into two groups with associated comorbidities: Group A suffering from COPD and Group B suffering from Asthma. Data were collected from the patients on variables of interest using a semi-structured questionnaire. **Results:** Among the 144 enrolled patients, 96(66.67%) in group A were suffering from COPD and the other 48 (33.33%) in group B had bronchial asthma. In this study, 41(42.7%) patients in Group A exhibited >25% lung field involvement in the high-resolution computed tomography (CT) chest imaging, compared to only 10(20.8%) in COVID-19 patients in Group B, and this difference in distribution was statistically significant (p=0.026). The COVID-19 patients in Group A were more severe to critically ill (45, 46.9%), compared to patients in Group B (12, 25.0%) with a p value of 0.011. Group A study subjects required intensive care unit (ICU) admission (49, 51.0%) more than the group B participants (16, 33.3%), which was also found statistically significant (p<0.05). Nearly one-fifth (17, 17.7%) of the patients died among the Group A, compared to only 2(4.2%) mortality observed in Group B (p=0.024). The COVID-19 patients with COPD were found significantly associated with the risk of >25% lung field involvement, severe to critical illness, ICU admission, invasive mechanical ventilation, and death (all p values <0.05). **Conclusion:** The comorbidity of COPD was found to increase the risk of disease severity and adverse outcomes in COVID-19 patients significantly. It also heightened the risk of lung field involvement, exceeding 25% more severe disease and increased mortality rates compared to individuals with bronchial asthma.

Key Words: Intensive Care Unit, Chronic Obstructive Pulmonary Disease, COVID-19

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Correspondence: Dr. Md. Ziaul Haque, Assistant Professor, Department of Respiratory Medicine, Monno Medical College and Hospital, Monno City, Gilondo, Manikganj, Bangladesh. E-mail: drziaulhoque1973@gmail.com, Cell: +880 1712 225191.

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Introduction:

The corona virus disease 2019 (COVID-19) is a viral illness caused by the (Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) virus. It has been observed that the clinical outcomes of COVID-19 can vary widely depending on several factors, including age, underlying health conditions, and the severity of the infection. However, it is important to note that information and understanding of COVID-19 are continually evolving, and new research may provide updated insights into short-term clinical outcomes. The World Health Organization (WHO) refers to the SARS CoV-2 illness as COVID-19, or Coronavirus Disease. As of 18 December, 2022, over 649 million confirmed cases and over 6.6 million deaths have been reported globally.¹ Bangladesh reported 49,534 confirmed cases, of which 10,597 had recovered and 672 had passed away as on 23 November, 2020.²

Host demographic factors and preexisting health conditions are involved in determining the outcome of COVID-19.³ Changes in lung structure and muscle atrophy found in the elderly may contribute to physiological modifications such as reduced lung reserve, reduced airway clearance, and a weakened protective barrier.⁴ The sex is another risk factor as a higher prevalence has been seen in men than women.⁵ Clinical outcomes in individuals with COVID-19 have been shown to be more severe when concomitant illnesses such as diabetes mellitus, hypertension, endocrine disorders, and cardiovascular and pulmonary diseases are present.⁶

The most common clinical manifestations are severe acute respiratory illnesses with fever and respiratory symptoms including cough and shortness of breath. However, atypical symptoms, such as people with no respiratory symptoms or just very mild symptoms, are becoming more prevalent globally.⁷ COVID-19 affects the respiratory system, primarily the lungs, and individuals with pre-existing respiratory conditions such as chronic obstructive pulmonary disease (COPD) and asthma may be at higher risk of severe illness from the virus. Severe outcomes of COVID-19 including hospital admission for lung complications like acute respiratory distress syndrome or respiratory failure or death were found associated with older people with preexisting comorbidities.⁸

The SARS-CoV-2 and other respiratory viruses were found to more severely affect asthma patients and were associated with severe asthma outcomes like acute exacerbation.⁹ Although, asthma was not among the most

common clinical conditions in COVID-19 patients.¹⁰

The COPD was reported as the fourth leading cause of death affecting 16 million people in the United States. Although, the association of COPD with adverse outcomes in COVID-19 cases has been controversial, some of the studies with patients of COVID-19 reported COPD as a risk factor with increased hospitalization, intensive care unit (ICU) admission and death.^{4,11}

The association between COPD and adverse outcome from COVID-19 data on Bangladeshi context remains disputed. This study was undertaken to investigate the characteristics of COVID-19 patients with COPD and asthma to determine the health outcomes of COVID-19 hospitalized patients in Bangladesh.

Methodology

Study design

This prospective observational study was conducted on patients diagnosed with COVID-19 between April 2020, and December 2022, who were admitted in departments of Respiratory Medicine at Monno Medical College and Hospital, Manikganj. The enrolled patients were also included from Ibn Sina Medical College and Hospital, Dhaka and Bangladesh Specialized Hospital, Dhaka with history of chronic obstructive pulmonary diseases (COPD) or bronchial asthma. The COVID-19 was identified by a positive laboratory test for SARS-CoV-2. The purpose and procedure of the study were discussed with the patients, and informed written consent was taken from those who agreed to participate in the study. Information regarding demographics as well as clinical and medication history was collected from each of the patients. Inhaled corticosteroid use was defined as having at least 1 prescription in the 12 months preceding the COVID-19 diagnosis. The study protocol was approved by the Institutional Review Board of Monno Medical College. A total of 144 COVID-19 positive patients suffering from COPD or asthma were enrolled purposively upon fulfilling the inclusion and exclusion criteria. Patients suffering from COPD were allocated in group A, and the others with bronchial asthma were included in group B. History taking focused on the clinical presentation of patients upon admission, including information on comorbidities like duration and medications received for comorbidity management. Additionally, a detailed assessment of COVID-19 symptoms and physical examination findings were conducted. Laboratory analysis, including blood

samples, was performed based on the participant's treatment needs, and the cost of laboratory investigations was borne by the participants themselves. Outcome was observed for each of the patients within 30 days of hospital stay from admission. Whether patients with COPD or bronchial asthma required admission to the intensive care unit (ICU) during their hospitalization for COVID-19 was noted. Data on the requirement of High-Flow Nasal Oxygen (HFNO), Invasive Mechanical Ventilation (IMV), and duration of hospital stay were also collected as part of the study. Data were collected from hospital records review, or through face-to-face interview with the patients or their legal guardians. Related data were collected at 2 different time points related to the patients: at admission, and at discharge/death.

Data collection and Statistical analysis

Data entry involved the careful input of collected data into the latest version of Statistical Package for Social Science (SPSS) software, ensuring accuracy and proper coding of variables. Descriptive statistics, such as frequencies, means, and standard deviations, were calculated to summarize the characteristics of the study population. Inferential statistics, such as chi-square tests or t-tests, were used to assess relationships between variables and determine statistical significance. Odds ratio and binary logistic regression were used for examining the associations and predicting outcomes in this study. A 'p' value less than 0.05 was considered significant.

Results

Among the total of 144 COVID-19 patients enrolled, 96(66.67%) were suffering from chronic obstructive pulmonary disease (COPD) in group A and remaining 48(33.33%) had bronchial asthma in group B. Ages of the patients were between 18 to 70 years. Table I shows that there was statistically no significant differences between the Group A and Group B regarding their age, sex, level of education and monthly family income ($p > 0.05$). (Table I)

Table I: Distribution of the respondents according to socio-demographic characteristics by group (group A=96, group B=48)

Socio-demographic characteristics	Group A n (%)	Group B n (%)	Total n (%)	P-value
Age (years)				
≥ 50	44 (45.8)	17 (35.4)	61 (42.4)	0.233 ^a
< 50	52 (54.2)	31 (64.6)	83 (57.6)	
Mean ± SD	40.4 ± 14.25	38.3 ± 14.79		0.402 ^b
Sex				
Male	72 (75.0)	29 (60.4)	101 (70.1)	0.071 ^a
Female	24 (25.0)	19 (39.6)	43 (29.9)	
Educational qualifications				
Illiterate	24 (25.0)	11 (22.9)	35 (24.3)	0.837 ^a
Up to primary	31 (32.3)	18 (37.5)	49 (34.0)	
SSC/equivalent	22 (22.9)	12 (25.0)	34 (23.6)	
HSC and above	19 (19.8)	7 (14.6)	26 (18.1)	
Monthly household income				
≤10,000 Tk.	10 (10.4)	3 (6.3)	13 (9.0)	0.780 ^c
10,001 – 35,000 Tk.	68 (70.8)	35 (72.9)	103 (71.5)	
35,001 – 60,000 Tk.	13 (13.5)	6 (12.5)	19 (13.2)	
>60,000 Tk.	5 (5.2)	4 (8.3)	9 (6.3)	

^aChi-square test was done to measure the level of significance;

^bUnpaired T-test was done to measure the level of significance;

^cFisher's exact test was done to measure the level of significance; Group A- COVID-19 hospitalized patients with COPD; Group B- COVID-19 patients hospitalized with bronchial asthma

Table II demonstrates the differences in the distribution of findings of the respondents' baseline investigations at admission between the COPD and asthma patient groups and all of them were not significant statistically ($p > 0.05$).

Table III shows there was statistically no significant differences in between the Group A and Group B in respect to their oxygen saturation level ($p > 0.05$). Furthermore, 41(42.7%) COPD patients exhibited >25% lung field involvement in the high-resolution computed tomography chest imaging compared to only 10(20.8%) in COVID-19 patients with bronchial asthma, and this difference in distribution was statistically significant. (Table III)

Table II: Distribution of the respondents' baseline investigations findings at admission by group (Group A n=96, Group B n=48)

Baseline investigations	Mean + SD of the findings		P value
	Group A (n=96)	Group B (n=48)	
RBS (mmol/L)	7.5 ± 2.88	7.7 ± 3.06	0.683 ^b
ALT (IU/L)	38.6 ± 9.67	40.4 ± 9.67	0.318 ^b
S. Creatinine (mg/dL)	0.8 ± 0.27	0.8 ± 0.31	0.772 ^b
CBC			
Hb% (gm/dL)	11.3 ± 0.79	11.2 ± 0.77	0.694 ^b
ESR (mm in 1 st hr)	28.9 ± 4.92	29.8 ± 4.42	0.295 ^b
Haematocrit (l/l)	7.7 ± 1.19	7.9 ± 0.99	0.427 ^b
TC- WBC (/cmm ³)	9,856.4 ± 1928.19	9,843.9 ± 2211.53	0.972 ^b
Platelet count (/cmm ³)	296,828.9 ± 55754.1	312,526.9 ± 50460.51	0.103 ^b
TSH (mIU/L)	3.4 ± 0.76	3.6 ± 0.79	0.230 ^b
C-reactive protein (mg/L)	17.6 ± 4.83	18.2 ± 4.49	0.534 ^b
Serum ferritin (ng/mL)	1,193.2 ± 1099.14	1,137.5 ± 1120.0	0.920 ^b
Creatine kinase (units/L)	195.1 ± 75.03	191.4 ± 76.25	0.781 ^b
D-dimer (µ/mL)	1.9 ± 1.49	2.1 ± 1.59	0.681 ^b
LDH (U/L)	252.6 ± 64.83	245.8 ± 67.09	0.560 ^b

^bUnpaired T-test was done to measure the level of significance; Group A- COVID-19 affected hospitalized patients with COPD; Group B- COVID-19 affected hospitalized patients with bronchial asthma.

Table III: Distribution of the respondents' according to percent saturation of oxygen and lung field involvement by groups (Group A, n=96, Group B, n=48)

Parameters	No. (%) of enrolled patients			P value
	Group A	Group B	Total	
SpO₂ (%)				
93-100	49(51.0)	31(64.6)	80(55.6)	0.227 ^a
85-92	25 (26.0)	11 (22.9)	36 (25.0)	
<85	22 (22.9)	6 (12.5)	28 (19.4)	
Lung field involvement (in HR-CT chest)				
<10%	29 (30.2)	23 (47.9)	52 (36.1)	0.026 ^a
10-25%	26 (27.1)	15 (31.3)	41 (28.5)	
>25%	41 (42.7)	10 (20.8)	51 (35.4)	

^aChi-square test was done to measure the level of significance; Group A- COVID-19 hospitalized patients with COPD; Group B- COVID-19 hospitalized patients with bronchial asthma; Within parentheses are percents over column total

Table IV reveals that COVID-19 patients with COPD were more severe to critically ill, compared to patients with bronchial asthma (46.9% vs. 25.0%, respectively), which was statistically significant (p=0.011). Likewise, group A study subjects required ICU admission (51.0%) more than the group B participants (33.3%), which was also found statistically significant (p<0.05).

Table IV: Distribution of the respondents according to severity of disease and requirement of intensive care unit admission by groups (Group A, n=96, Group B, n=48)

Parameters	Group A n (%)	Group B n (%)	Total n (%)	P-value
Severity of COVID-19 disease				
Severe to critically ill	45 (46.9)	12 (25.0)	57 (39.6)	0.011 ^a
Mild to moderate	51 (53.1)	36 (75.0)	87 (60.4)	
ICU admission				
Required	49 (51.0)	16 (33.3)	65 (45.1)	0.044 ^a
Not required	47 (49.0)	32 (66.7)	79 (54.9)	

^aChi-square test was done to measure the level of significance; Group A- COVID-19 affected hospitalized patients with COPD; Group B - COVID-19 affected hospitalized patients with bronchial asthma. Within parenthesis are percentages over column total.

Table V shows, nearly one-fifths (17, 17.7%) of the patients died among the COVID-19 with COPD group compared to only 2(4.2%) mortality observed in patients with bronchial asthma. This difference in distribution was statistically significant (p=0.024). Moreover, there was statistically no significant differences between the Group A and Group B in respect to their duration of hospital stay (p > 0.05).

Table V: Distribution of the respondents according to outcomes by group (Group A with COPD, n=96, Group B with bronchial asthma, n=48)

Parameters	Group A n (%)	Group B n (%)	Total n (%)	P-value
Death	17 (17.7)	2 (4.2)	19 (13.2)	0.024 ^a
Recovered	79 (82.3)	46 (95.8)	125 (86.8)	
Duration of hospital stay (mean ± SD, days)	8.1±3.36	6.9 ± 3.84		0.064 ^b

^aChi-square test was done to measure the level of significance; ^bUnpaired t test was done to measure the level of significance; Group A- COVID-19 affected hospitalized patients with COPD; Group B- COVID-19 affected hospitalized patients with bronchial asthma.

The COVID-19 patients with COPD were found significantly associated with the risk of >25% lung field involvement, severe to critical illness, ICU admission, invasive mechanical ventilation, and death ($p < 0.05$). (Table VI)

Table VI: Clinical outcomes analysis for the presence of COPD among the hospitalized COVID-19 patients by Odd's ration (OR) and 95% confidence interval (CI) (n=144)

Clinical outcome parameters	Odds ratio (OR)	95% CI (upper-lower)	P value
Lung field involvement (>25%)	2.833	1.266-6.339	0.010*
Disease severity (severe to critical)	2.647	1.230-5.697	0.011*
ICU admission (required)	2.085	1.014-4.289	0.044*
Mechanical ventilation (required)	2.376	1.029-5.487	0.039*
Outcome (death)	4.949	1.094-22.395	0.024*

P-value was determined by the chi-square test, * = significant

Discussion

The baseline investigation findings between the hospitalized COVID-19 patients with COPD and asthma in the present study showed statistically no significant difference ($p > 0.05$). Majority of the patients (80, 55.6%) showed oxygen saturation levels within 93-100%. SpO₂ level <85% was observed in 22 (22.9%) COPD patients compared to 6(12.5%) respondents with asthma ($p=0.227$). Lower oxygen saturation levels are indicative of compromised respiratory function and may warrant close monitoring, timely interventions, and appropriate oxygen therapy to prevent further deterioration and improve patient outcomes. A study by Zhang et al conducted in a tertiary care hospital in China found that COVID-19 patients with COPD, had lower oxygen saturation levels compared to those with asthma.¹³ Similarly, a study by Gupta et al conducted in India reported that patients with COPD had significantly lower SpO₂ levels on admission compared to patients with asthma.¹⁴

In the present study, above two-fifths (41, 42.7%) of the patients had >25% lung field involvement in HR-CT chest findings among the COPD patients, while majority (23, 47.9%) of the COVID-19 patients with asthma revealed <10% lung field involvement. The immune response and inflammatory cascade triggered by COVID-19 can be heightened in patients with COPD leading to more pronounced lung inflammation and injury.

This inflammatory response can manifest as a range of radiological findings on HR-CT scans, including ground-glass opacities, consolidations, and interstitial abnormalities, which are often more severe in patients with COPD.¹⁵ More extensive and severe lung involvement observed on HR-CT scans may indicate a higher risk of disease progression, respiratory compromise, and poorer clinical outcomes. Mylona et al¹⁶ observed that 64.7% of the COVID-19 patients requiring ICU admission had the lung field score of 4 (extent of alveolar opacities >75%), compared to 29.9% patients who did not require intensive care unit (ICU) admission had the lung-field score of 0 (none) and 2 (extent of alveolar opacities 25-50%). In their study, COVID-19 patients had a statistically significant association between oxygen level and CT scan severity score (p -value = 0.001) and there was an inverse association between CT severity and oxygen saturation. Current study revealed that COVID-19 patients with COPD were more prone to severe to critical illness compared to patients with bronchial asthma (46.9% vs. 25.0%, respectively), which was statistically significant ($p=0.011$). In a systemic review and metaanalysis, Singh et al identified that COVID-19 patients with COPD had a greater risk of severe disease and death.¹⁷ The incidence of ICU admission was also found higher in patients with COPD compared with those with bronchial asthma (51.0% vs. 33.3%, respectively), with the P-value of 0.044. In a similar study by Sanyaolu et al found that older patients, especially those 65 years and above, who had comorbidities and were infected, had an increased admission rate into the ICU and mortality from the COVID-19 disease.¹⁸

But in regard to mortality rate, nearly one-fifths (17, 17.7%) of the patients died among the COVID-19 with COPD in group A, compared to only 2(4.2%) mortality observed in patients with asthma in group B. The distribution of outcome parameters differed significantly ($p=0.024$). The COVID-19 patients with COPD were found significantly associated with the risk of >25% lung field involvement, severe to critical illness, ICU admission, invasive mechanical ventilation, and death (all p values <0.05). In a retrospective cohort study from China by Zhou et al enumerated that hospitalized patients were predominantly men with a median age of 56 years; 26% required ICU care, and there was a 28% mortality rate.¹⁹ Therefore, the presence of COPD significantly increases the risk of extensive lung involvement, severe to critical illness, ICU admission, invasive mechanical ventilation,

and death. The findings underscore the importance of identifying and managing COPD in COVID-19 patients to mitigate the risk of complications and improve outcomes.

Conclusion

The COPD significantly increases the risk of disease severity and adverse outcomes in COVID-19 patients. Present study findings demonstrated that COVID-19 patients with COPD were significantly associated with a higher risk of invasive mechanical ventilation and death compared to patients with bronchial asthma. The presence of COPD also heightened the risk of lung field involvement exceeding 25%, more severe disease and increased mortality rates compared to individuals with bronchial asthma.

Conflict of interest: None declared.

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Original Article

Forensic Profiling of Road Traffic Accident Victims- A Retrospective Study

Nazmun Nahar Nahida¹, Kishoara Binte Quader², Laila Yesmin³, Alamgir Hossain⁴, Borhan Uddin Ahamed⁵

¹Assistant Professor, Department of Forensic Medicine and Toxicology, Monno Medical College, Manikganj; ²Associate Professor, Department of Forensic Medicine and toxicology, Delta Medical College, Mirpur-1; ³Associate Professor, Department of Forensic Medicine and Toxicology, Khwaja Yunus Ali Medical College, Enayetpur, Sirajganj; ⁴Lecturer, Department of Forensic Medicine and Toxicology, Monno Medical College, Manikganj. ⁵Professor and Head, Department of Forensic Medicine and Toxicology, Monno Medical College, Manikganj.

Abstract

Background: Road traffic accidents (RTAs) have become a significant public health problem that requires a multi-disciplinary strategy to solve. Every year, 1.35 million people die because of RTAs. The effects of a traffic accident not only cause the sufferer to suffer physically, emotionally, and financially, but they also have a deadly impact on the way the entire family functions. **Objectives:** This study's objective was to assess the current RTA situation in Manikganj district, determine the injury pattern, explore the causes and frequency of accidents, and find out the sociodemographic characteristics of the victims. **Methodology:** This retrospective study was carried out in the Manikganj District hospital, Bangladesh, during the period of January, 2019 to December, 2020. **Results:** During the study period, there were 381 postmortems performed, of which 83 (21.78%) instances involved RTA. Of the victims, 49(59.04%) were men and 34(40.96%) women. Incidence of RTA (24, 28.91%) was the highest among people aged 21 to 30 years. The most accidents happened during the daytime (32, 38.55%). All victims sustained many abrasions and bruises (83, 100%), laceration was present in 46(55.42%), fractured ribs in 33(39.75%), fractured hipbones in 32(38.55%), skull bones fractured in 16(19.27%), head injury in 26 (31.32%) and intracranial haemorrhages in 26(31.32%) cases. Most victims (59, 71.08%) were pedestrians, followed by passengers and drivers. In 83 instances, head injuries accounted for most fatalities (22, 26.53%), followed by multiple traumas, haemorrhagic shock, spinal cord damage, septic shock and crush syndrome. **Conclusion:** Strict adherence to traffic laws, public awareness campaigns, and adequate driver training all reduce the likelihood of road accidents and lessen their severity.

Key Words: Forensic profiling; Road Traffic Injuries; Retrospective

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Correspondence: Dr. Nazmun Nahar Nahida, Assistant Professor, Department of Forensic Medicine and Toxicology, Monno Medical College, Monno City, Gilondo, Manikganj, Bangladesh. E-mail: nahidanazmun3@gmail.com, Cell: +880 1791-925583.

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Introduction:

Many people's lives and society overall have been improved by motorization, yet there is a cost associated with these advantages. For most of the world's population, the burden of road traffic injury—in terms of social and economic costs—is rising significantly, even though the number of lives lost in road accidents in high-income nations indicates a declining trend in recent decades.¹

With 165 million inhabitants, Bangladesh is a heavily populated nation. At least 21 fatalities are thought to occur daily in the capital city.²

Road traffic accidents (RTAs), which account for more than 85% of all fatalities and 90% of years lost to disability-adjusted life expectancy, are a significant public health issue in developing nations.¹ The RTA was also found to pose as a larger financial burden on the

community than any other serious illness would. The RTAs were considered as a global health, economic and social catastrophe. It was identified as the 8th leading cause of death and accounted for approximately 1.35 million deaths in 2016 and 20-50 million non-fatal injuries annually globally.³ The RTA was the second leading cause of death in Bangladesh, including both fatal and non-fatal injuries.⁴ The RTAs were the main cause of hospitalization in primary and secondary facilities in Bangladesh.⁵

Bangladesh is a heavily populated nation where individuals from rural areas migrate to the cities due to unemployment and poverty. This highest rate of RTAs in urban locations may be attributed to poorly designed roads and highways, a dysfunctional traffic system, driver and pedestrian infractions of the law, congestion from excessive traffic, irresponsible driving, etc.⁶

Reckless driving, failure to adhere to traffic regulations, overloading of transport vehicles, poor vehicle maintenance, driver fatigue, alcohol use, a lack of awareness among road users, including drivers and pedestrians, poor weather conditions, and a failure to use safety equipment such as seat belts and helmets are some of the causes of the rise in accidents and fatalities.⁷ When a car collides with another car, a person, an animal, a piece of road debris, or another stationary object like a tree or utility pole, a road traffic accident occurs. Pedestrians, cyclists (pedal or motor), and drivers and passengers of vehicles make up the three main categories of people injured in traffic accidents. Among these three major categories, injuries to pedestrians occur most frequently.⁸

This study was conducted to analyze the nature, distribution, and types of injuries sustained after catastrophic road traffic incidents as well as the detailed socio-demographic profile of the unlucky victims to potentially take preventive action.

Methodology

This retrospective cross-sectional study was conducted in Manikganj District Hospital, Bangladesh during the period of January, 2019 to December, 2020. Ethical clearance was duly approved by ethics review committee of Monno Medical College. The material of this study included 83 dead bodies of road traffic accident (RTA), which were brought to Manikganj District Hospital mortuary for postmortem examinations. A thorough, extensive, and meticulous postmortem examination of the dead bodies were carried out at the study place.

Data on gender, age, time, type of road user, pattern of injury and cause of death were collected from inquest reports, challan, autopsy reports, hospital records and case files. These data were then compiled, analyzed by using descriptive statistics and tabulated. Statistical analysis was performed using window-based computer.

Results

Out of 381 post-mortems completed during the study period, 83(21.78%) were Road traffic accident (RTA) cases. Among them, majority (49, 59.04%) were male and 34(40.96%) were female. (Table I)

Table I: Distribution according to sex of the victims (n=83)

Sex	Frequency	Percentage
Male	49	59.04%
Female	34	40.96%
Total	83	100%

The highest incidence of RTA (24, 28.91%) was observed in the age group of 21-30 years, followed by 19 (22.90%) among age group 31-40 years and 41-50 years (11, 13.25%). (Table II)

Table II: Age wise distribution of RTA victims (n=83)

Age group (years)	Frequency	Percentage
0-10	04	4.82%
11-20	11	13.25%
21-30	24	28.91%
31-40	19	22.90%
41-50	11	13.25%
51-60	08	9.64%
>60	06	7.23%
Total	83	100.00%

Most of the accidents happened during daytime 32(38.55%), followed by evening 28(33.73%). (Table III)

Table III: Distribution of time of RTAs (n=83)

Time of accidents	Frequency	Percentage
Morning, 05:01-08:00 hrs	14	16.88%
Day time, 08:01-18:00 hrs	32	38.55%
Evening, 18:01-19:30 hrs	28	33.73%
Night, 19:31-05:00 hrs	09	10.84%
Total	83	100.00%

Regarding the pattern of injuries, we observed that all 83(100.00%) victims had multiple abrasions and bruises all over the body, 46(55.42%) had lacerations in different parts of the body, followed by fracture of lower limbs (52, 62.65%), fracture of upper limbs (48, 57.83%), head injury (26, 31.32%), intracranial haemorrhage (26, 31.32%), injury to abdominal viscera (11, 13.25%) and other fractures on limbs. (Table IV)

Table IV: Distribution of pattern of injury in victims (n=83)

Pattern of injury	Frequency	Percentage
Multiple abrasions	83	100.00%
Multiple bruise	83	100.00%
Laceration	46	55.42%
Fracture of hip bone	32	38.55%
Fracture of ribs	33	39.75%
Fracture of sternum	18	21.68%
Fracture of skull	16	19.27%
Head injury	26	31.32%
Intracranial hemorrhage	26	31.32%
Injury to abdominal viscera	11	13.25%
Fracture of upper limbs	48	57.83%
Fracture of lower limbs	52	62.65%

Regarding the type of victims, the most common victims of RTA were pedestrians (59, 71.08%) followed by passengers (17, 20.48%) and drivers (07, 8.44%). (Table V)

Table V: Distribution according to type of victims (n=83)

Type of victims	Frequency	Percentage
Pedestrian	59	71.08%
Passenger	17	20.48%
Driver	07	8.44%
Total	83	100

Majority of the 83 RTA victims died due to head injury (22, 26.53%), followed by multiple trauma (19, 22.89%), haemorrhagic shock (18, 21.68%), spinal cord injury (12, 14.45%), septic shock (08, 9.63%), and crush syndrome (04, 4.82%). (Table VI)

Table VI: Distribution of RTA victims according to cause of death (n=83)

Cause of death	Frequency	Percentage
Hemorrhagic shock	18	21.68%
Head injury	22	26.53%
Multiple trauma	19	22.89%
Spinal cord injury	12	14.45%
Septic shock	08	9.63%
Crush syndrome	04	4.82%
Total	83	100.00%

Discussion

Out of the 83 victims in this study, majority (49, 59.04%) were men and other 34(40.96%) were women. These findings concur with a study by Karim et al reported in 2011 that found that only 8% of RTA casualties were female and that 47% of victims were men.⁹ This is likely because men in Bangladesh are more exposed to the outdoor activities and are frequently on the go due to their employment, businesses, jobs, or studies, whilst women are frequently confined to their homes and other responsibilities for taking care of household duties.¹⁰ As the primary breadwinner in our society, men are more likely than women to sustain injuries. Additionally, they are more exposed to the traffic and engage in riskier activities than the women- like as rushing to catch a bus, clinging to the side of the vehicle, being impatient and inattentive, and drinking alcohol (in the case of drivers) before operating a motor vehicle.⁶

In this study, the age group of 21 to 30 years had the highest incidence of RTA 24 (28.91%), followed by the age groups of 31 to 40 years (19; 22.90%) and 11 to 20 years (11; 13.25%). This is consistent with other study findings, which state that those aged 15 to 44, who are often the most productive workers, account for more than half of all traffic-related deaths worldwide. Additionally, this age group's handicap burden accounts for 60% of all DALYs lost in road traffic accidents. Other studies from developing nations have revealed similar age distributions of RTA casualties.¹¹⁻¹⁵

Maximum accidents happened during the daytime, when there was a rush of people heading to workplaces, schools, and businesses, with 32 (38.55%) occurring during the day and 28 (33.73%) during the evening. The causes of accidents at night may include drivers' propensity for dozing off at night, poor vision, a lack of luminescent markings on the road, potholes and open manholes, vehicle overtaking, and an increase in the number of cargo vehicles on the road.¹⁶

Considering the patterns of injury in this study, all 83 (100%) individuals had several abrasions and bruises, laceration 46(55.42%). Numerous fractures, including those of the ribs 33 (39.75%), hipbones 32 (38.55%), and skull bones 16 (19.27%), as well as head traumas and intracranial hemorrhages 26 (31.32%) were found, among other injuries to the body. Similar findings were reported by ASMJ Chowdhury published in 2012,¹⁶ who reported that 3(6.38%) RTA victims had pelvic fractures in addition to 56(100%) patients who had various abrasions and bruises, head injuries in 21(44.68%), and other injuries. Due to a fall to the ground and a quick automobile hit, internal damage to the abdominal organs also occurred. Most crush injuries caused by car wheels result in fractures of the upper and lower extremities. Due to a fall to the ground and a sharp impact, there is a fracture and haematoma over the skull. The most frequent type of fracture was linear, which was brought on by RTA, heads being forcibly brought into contact with hard surfaces like roadways.^{16,17}

Pedestrians in the present study made up most RTA victims [59(71.08%)], followed by passengers 17(20.48%) and drivers 07(8.44%). Due to their ignorance of traffic regulations and lack of space in sidewalks, people frequently walk on the pavement, endangering both themselves and cars. Similar research was conducted in India, where it was discovered that out of the 1872 RTA cases, there were 880(47.01%) pedestrian cases and 517(27.61%) vehicle cases, 266(14.20%) driver cases, 196(10.47%) bicycle cases, and 13(0.69%) cases that were undetermined.¹⁸ According to the RTA Report released by the Road Safety Cell of Bangladesh, pedestrians make up 49% of road accident victims in Bangladesh, followed by passengers (37%), and drivers (14%). Studies in Brazil, Mexico, and Uganda indicated that even when such choices increased the risk of injury, pedestrians preferred to cross a risky road rather than make the extra effort to use a pedestrian bridge.¹⁹

The head injury was the most common cause of death for RTA victims, accounting for 22 cases (26.53%), followed by multiple trauma 19 cases (22.89%), haemorrhagic shock 18 cases (21.68%), spinal cord injury 12 cases; (14.45%), septic shock 08 cases (9.63%), and crush syndrome 04 cases (1.54%) out of a total of 83 cases. Similar research from India found that among the 98 cases of RTA victims, most deaths were attributable to head injuries in 46 cases (46.93%), polytrauma in 34 cases

(34.69%), haemorrhagic shock in 14 cases (14.28%), spinal cord damage and complications in 2 cases each, totalling 2.04%.¹⁵

This study has limitations of being conducted at the District Hospital in Manikganj, Bangladesh, that may not reflect the country situation. To find out the overall picture and determinants of road traffic accidents in Bangladesh, a more thorough study is required.

Conclusion

A remarkable portion of the postmortems were due to road traffic accidents (RTA). Deaths of RTA cases occurred due to head injury and other reasonable causes, losing bread-earning members of the families. These losses finally might be responsible for multidimensional miseries in the families. It is possible to lessen this financial burden and protect the most vulnerable groups of people by strictly enforcing traffic laws, promoting efficient patterns of land use, and providing shorter, safer routes for vulnerable pedestrians to reduce their exposure to high roads. A community clinic might be built next to the road to cut down on the number of victims. There should be more traffic police on the road. It is necessary to increase public awareness of traffic accidents and road safety through motivating programs, driver training, removing unsafe vehicles from city streets, mending roads, etc.

Conflict of Interest: None declared.

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Original Article

Comparison of Outcomes of Bell's Palsy Patients Treated with Steroid and Steroid with Antiviral Drug in a Tertiary Care Hospital

Shah Didar Imam¹, Md. Jalal Uddin², ABM Khairul Hasan³, Sajal Kumar Shill⁴, Md. Ziaul Hoque⁵

¹Assistant Professor, Department of Neurology, Monno Medical College & Hospital, Manikganj; ²Professor & Head, Department of Neurology, Mymensingh Medical College and Hospital; ³Associate Professor and Head, Department of Neurology, TMSS Medical College and Hospital, Bogura; ⁴Assistant Professor, Department of Neurology, Kumudini Women's Medical College, Mirzapur, Tangail; ⁵Assistant Professor, Department of Respiratory Medicine, Monno Medical College and Hospital, Gilondo, Manikganj.

Abstract

Background: Bell's palsy is the most common acute mononeuropathy associated with idiopathic unilateral facial weakness, characterized by facial asymmetry. Though steroids have effectiveness in managing Bell's palsy, the use of antiviral is still debatable. **Objective:** To compare the outcome of Bell's palsy with treatment by steroid versus combination of steroid and antiviral drugs. **Methodology:** A prospective analytical study was performed on 84 patients with acute Bell's palsy attending at Neurology outpatient department of Mymensingh Medical College Hospital from July 2014 to June 2016. The patients were divided into two groups purposively after initial assessment as per House-Brackmann grading system (HBS). Group-I patients were treated with oral prednisolone and oral valacyclovir and Group-II patients were treated with oral prednisolone only. Both groups received facial exercises as per demonstration and proper eye care throughout the study period. Follow-up was done after 2 weeks, 4 weeks and 3 months for collection of data about recovery according to reassessment. **Results:** The analysis revealed that recovery rates at all 3 follow-ups were higher in the combination group than that of the prednisolone-only group [29(67.44%) versus 18 (43.90%) at 2nd week follow-up, 35(81.39%) versus 25(60.97%) at 4th week follow-up and 40 (93.02%) versus 30(73.17%) at 3rd month follow-up]. Moreover, the expected recovery rate was higher in severe Bell's palsy patients in the combination group than in steroid-alone group (22, 88.0% complete recovery versus 13, 54.17% complete recovery at the end of 3 months of treatment) [p=0.034]. haemorrhagic shock, spinal cord damage, septic shock and crush syndrome. **Conclusion:** The study showed antiviral (valacyclovir) plus steroid (prednisolone) to be more effective than steroid (prednisolone) alone in the treatment of Bell's palsy. Moreover, outcome was more favorable in combination groups presenting with severe disease. lessen their severity.

Key Words: Bell's palsy, Combination treatment with antiviral and prednisolone, House-Brackmann grading

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Correspondence: Dr. Shah Didar Imam, Associate Professor, Department of Neurology, Monno Medical College and Hospital, Monno City, Gilondo, Manikganj, Bangladesh. E-mail: didarimam@gmail.com, Cell: +880 1711-461587.

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Introduction:

Bell's palsy is the most common acute mononeuropathy associated with idiopathic unilateral facial weakness that occurs in 11.5-53.3 per 100,000 individuals a year across different populations.¹ Although the cause remains elusive, limited evidences suggest that the reactivation of dormant herpes viruses (herpes simplex virus-1, varicella-zoster virus) is known to be one of the causes of Bell's palsy.^{2,3}

For the treatment of Bell's palsy, the use of prednisolone is known to result in high recovery rates and fewer sequelae and there is no doubt that steroid treatment may prevent further damage and is beneficial in most cases.⁴

Although there is consensus that early use of prednisolone is an effective treatment, the use of antiviral agents has led to some researchers who are against the use of antiviral agents, to argue that there is no proof of additional benefit.^{5,6}

However additional use of valacyclovir has been shown to be more effective than steroid treatment alone⁷ and steroid antiviral treatment improves the recovery rate in patients with severe Bell's palsy.^{8,9} These findings have led some to advocate for the use of antiviral agents along with steroids. A systematic review found that treatment with prednisolone reduced the chances of incomplete recovery but using an antiviral drug had an additional benefit.¹⁰ Moderate quality evidence indicated that the combination of antivirals and corticosteroids reduced the sequelae of Bell's palsy compared with corticosteroids alone.¹¹

A randomized prospective study found that a combination of an antiviral and a steroid was more effective in treating severe to complete Bell's palsy than a steroid alone.⁸

Following a literature review, we hypothesized that the additional effect of antiviral drugs would be different according to the severity of the palsy and that, in the case of severe to complete palsy, there would be a difference in recovery according to treatment methods. Therefore, we conducted a prospective analytical study to complete the recovery rate of Bell's palsy with the treatment by steroids versus a combination of steroid and antiviral drugs.

Methodology:

This prospective analytical study was carried out in Mymensingh, Bangladesh from July, 2014 to June, 2016 for a period of two years. Irrespective of age and gender, patients who had Bell's Palsy five (5) days of the attack were included.

Patients who were excluded: (i) patients with Bell's palsy attended after five (05) days of the attack; (ii) facial paralysis other than Bell's palsy with evidence of Ramsay Hunt Syndrome,¹² ontological cause (e.g. chronic suppurative otitis media, acute suppurative otitis media, post mastoidectomy) of facial paralysis, Bell's palsy patient with diabetes mellitus, and Melkersson Rosenthal Syndrome; (iii) history of previous Bell's palsy; and (iv) Bell's Palsy patient with pregnancy.

Considering inclusion and exclusion criteria, 99 cases were selected by purposive sampling and divided into two groups. Group I were prescribed both oral antiviral and oral steroid drugs, and the group II patients were prescribed with oral steroids only. The treatment protocol was: all patients (both Group I and group II) were prescribed oral prednisolone, 1 mg/kg/body weight (usually 40-60 mg daily) for 5 days with a tapering dose over the next 5 days. Moreover, Group 1 patients were also prescribed

valacyclovir (500 mg 12-hourly) for 5 days. For follow-up, all patients were instructed to visit at out patients' department (OPD) at the end of the second week to review and reassess as per House-Brackmann Scale (HBS)¹³ to monitor the improvement of facial weakness. Complete facial muscle recovery was defined as House- Brackmann grade I (HBS I), but weakness remains as per HBS II or more, defined as incomplete recovery.

The data were analyzed by SPSS and a comparison of the efficacy of both regimens of therapy, Mann Whitney and Fischer's exact tests were used, and P values less than 0.05 were considered as significant.

Results:

The combination treatment group (prednisolone plus valacyclovir) comprised 43 patients and the steroid-only treatment group comprised 41 patients. The mean age in years \pm standard deviation of the patients in both groups were: 32.42 \pm 15.19 in group I and 30.27 \pm 12.36 in group II. There was no significant intergroup difference in age, disease severity, or the period between onset and treatment. However, there was a significant difference in complete recovery between the 2 groups. (Table I)

Table I: Characteristics of the enrolled patients

Variables	Number (%) of the patients		P value
	Combination therapy (n=43)	Steroid only (n=41)	
Distribution of disease severity	18 (41.86)		
Mild to moderate (GR-II to GR-IV)	25 (58.14)	17 (41.46)	0.971
Severe (GR-V & GR-VI)		24 (58.54)	
Initiation of treatment	29 (69.44)	20 (48.78)	
Within 72 hours	14 (32.56)	21 (51.22)	0.083
>72 hours- 120 hours			
Recovery rate (%) at 3 months	40(93.02)	30(73.17)	0.015

At the end of 3 months, 40(93.02%) of the prednisolone plus valacyclovir group and 30(73.17%) of the prednisolone-only group had complete recovery (p = 0.015). (Table-II)

Table II: Comparison of the recovery rate of Bell's palsy patients in group I (treated with prednisolone and valacyclovir) and group II (treated with prednisolone only) at different times

Criteria	Time period	No. of patients (%) from treatment groups		P-value
		Valacyclovir Plus Prednisolone (n=43)	Prednisolone only (n=41)	
Accumulative recovery rate	2 nd week	29 (67.44%)	18 (43.90%)	0.030
	4 th week	35 (81.39%)	25 (60.97%)	0.038
	3 rd month	40 (93.02%)	30 (73.17%)	0.015

Improvement of grading of palsy based on House-Brackmann Scale (HBS) after 3-months of treatment was also compared, which shows that initial average HBS of 4.42 came down to 1.12 in the patients treated with antiviral and steroid combination. Whereas, the initial average HBS of 4.41 came down to 1.51 in patients treated with steroid only. The difference between the two treatment groups was found significant (P- value < 0.05). (Table-III)

Table III: Improvement of grading of palsy based on House-Brackmann Score (HBS) from initial stage to follow up at 3-months of treatment

HBS grade status	No. of patients (%) at different grades by HBS initially and at follow up in two treatment groups						P-value
	Anti-viral & steroid (n-43)			Steroid only (n-41)			
	Initial	At 3 months		Initial	At 3 months		
Grades (GR-I to GR-VI) of HBS to show improvement	GR-II	GR-I	GR-II	GR-II	GR-I	GR-II	0.032
	2	2	0	2	2	0	
	(4.65)	(100.00)	(0.00)	(4.88)	(100.00)	(0.00)	
	GR-III	GR-I	GR-II	GR-III	GR-I	GR-II	
	5	5	0	5	5	0	
	(11.63)	(100.00)	(0.00)	(12.20)	(100.00)	(0.00)	
GR-IV	GR-I	≥GR-II	GR-IV	GR-I	≥GR-II		
11	11	0	10	10	0		
(25.58)	(100.00)	(0.00)	(24.39)	(100.00)	(0.00)		
GR-V	GR-I	≥GR-II	GR-V	GR-I	≥GR-II		
23	22	1	22	13	9		
(53.49)	(95.65)	(4.35)	(53.66)	(59.09)	(40.91)		
GR-VI	GR-I	≥GR-II	GR-VI	GR-I	≥GR-II		
2	0	2	2	0	2		
(4.65)	(0.00)	(100.00)	(4.88)	(0.00)	(100.00)		
Average HBS in Groups	4.42	1.12		4.41	1.51		

A comparison of outcomes between two groups of severe Bell's palsy was also analyzed; a significant difference in complete recovery was seen between the two groups in patients presented with severe Bell's palsy (P value <0.05). (Table-IV)

Table IV: Comparison of outcomes between two groups of severe Bell's palsy patients

Treatment group with severe disease	No. (%) of patients showing outcome at Month 3		P-value
	Complete recovery	Incomplete recovery	
Anti -viral & steroid (Group -I) (n=25)	22 (88.00)	3 (12.00)	0.034
Steroid only (Group -II) (n=24)	13 (54.17)	11 (45.83)	

Discussion:

In this study, in the patients treated with anti-viral (valacyclovir) and steroid (prednisolone), the recovery rate was 93.02 %, whereas, in the steroid (prednisolone) only group, it was found to be 73.17 % (p-value = 0.015), revealing the efficacy of combination therapy in the treatment of Bell's palsy.

In many clinical trials, including Hato et al,⁷ Lee et al,⁸ Karthika et al,¹⁴ Shahidullah et al,¹⁵ Kang et al,¹⁶ Yeo et al,¹⁷ Khajeh et al,¹⁸ the combination therapy of steroids and the antiviral drug was compared with steroids alone in the treatment of Bell's palsy. All of these studies show an increased recovery rate of Bell's palsy with antiviral and steroid combination therapy in comparison with steroid treatment alone.

In the randomized control therapy study by Karthika et al,¹⁴ 50 patients were treated with acyclovir (2000 mg/day) plus methylprednisolone (1 mg/kg/day) and 50 patients with methyl-prednisolone alone (1 mg/kg/day). The recovery rate was significantly higher in the steroid and antiviral-treated group (86% versus 82%) with a P value of 0.038, which is consistent with this study.

Another study done in Karachi, Pakistan by Talib et al¹⁹ showed Bell's Palsy treatment with combined antiviral (acyclovir) and prednisolone is found superior in the

recovery rate to prednisolone alone, which is also consistent with this study.

In this study, the initial average House-Brackmann Score (HBS) (Baseline HBS) was 4.42 in Group I and 4.41 in Group II patients. Three months after treatment, the average HBS score came down to 1.12 and 1.51 in Group I patients and Group II patients respectively indicating improvement in average HBS scoring better in the combined group than the prednisolone alone group. A small effect of adding antiviral agents was seen in treating patients with severe Bell's palsy.²⁰

In this study patients, who presented with severe disease (initial HBS V and VI), the complete recovery rate after three months of treatment was 88.00% in the antiviral and steroid treatment group, and 54.17% in steroid only group (P value 0.034). Kim et al study found that combination therapy with steroids and antiviral agents resulted in significantly ($p= 0.02$) higher favourable recovery rates than steroids alone in severe Bell's palsy patients,²¹ which is consistent with this study.

Thus, steroid antiviral combination treatment has more chance of complete recovery than that of steroid-only treatment in patients with severe Bell's palsy, which was consistent with other study findings.^{7,8,16,22} Shahidullah et al¹⁵ have shown 10-fold chance of complete recovery in patients present with severe Bell's palsy if antiviral drugs are added with steroid treatment.

In conclusion, steroid plus antiviral (valacyclovir) treatment is more effective in treating Bell's palsy than steroid treatment only. So, clinicians should consider combination therapy with steroid and antiviral of choice in individuals presenting with Bell's palsy within 5 days of onset.

Conflict of interest: None declared.

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Original Article

Diagnostic Performance of Computed Tomography in Laryngeal Carcinoma and its Extension

Momotaj Begum¹, Sabina Yiasmeen², Sadia Noor Arabi³, Abu Bakar Siddique⁴, Md. Noman Chowdhury⁵

¹Assistant Professor, Department of Radiology and Imaging, Sheikh Russel National Gastroenterology Institute and Hospital, Mohakhali, Dhaka; ²Assistant Professor, Mughda Medical College and Hospital, Dhaka; ³Junior Consultant, National Institute of Traumatology and Orthopaedic Rehabilitation, Dhaka; ⁴Assistant Professor, Department of Radiology and Imaging, Sheikh Russel National Gastroenterology Institute and Hospital, Mohakhali, Dhaka; ⁵Professor and Head, Department of Radiology and Imaging, Dhaka Medical College, Dhaka, Bangladesh.

Abstract

Background: Laryngeal carcinoma is a common malignant neoplasm of the head and neck with high incidence of new malignancies worldwide every year. Several imaging techniques including magnetic resonance imaging (MRI) and computed tomography (CT) scans are widely used to detect laryngeal carcinoma. Of them, CT scan is relatively cheaper, easily available and sensitive in the evaluation of laryngeal carcinoma. **Objective:** To find out the diagnostic performance of CT scan in laryngeal carcinoma and its extensions. **Methodology:** This cross-sectional study was carried out in the department of Radiology and Imaging, Dhaka Medical College Hospital, Dhaka, during the period of July, 2016 to June, 2018 for a period of 2(two) years. A total of 50 samples were included purposively. The enrolled patients were attending outpatient department (OPD) or admitted in indoor and referred to the Radiology and Imaging department for CT scan. All the enrolled cases had laryngectomy and resected tissues were sent for histopathological examination. Data collection was done by the principal investigator and a preformed questionnaire was used during data collection. Following completion of data collection, it was analyzed by SPSS 20.0. **Results:** Age range of the patients was from 18 to 84 years, with the mean age of 61.2 years + 13.4 years standard deviation and a male-female ratio of about 7.3:1. By multidetector CT scan, majority (32, 64.00%) of the tumours were found confined in a specific area with no extension, followed by 12 (24.00%) involving both supraglottic and glottic region. On the other hand, by histopathology, almost all (47, 94.00%) of the cases were found malignant and majority of the malignant cases (31, 65.96%) were found without nodal metastasis. Validity tests of CT in the diagnosis of laryngeal carcinoma revealed sensitivity, specificity, accuracy and positive predictive values of 97.9%, 66.7%, 96% and 97.9% respectively. In case of nodal metastases, the sensitivity, specificity, accuracy and positive predictive value were 93.8%, 97%, 96% and 93.8% respectively. **Conclusion:** Contrast enhanced CT scan has good role in detecting nodal metastases, but had complementary role in detecting laryngeal carcinoma.

Key Words: Laryngeal carcinoma, Computed tomography, Metastasis

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Correspondence: : Dr. Momotaj Begum, Assistant Professor, Department of Radiology and Imaging, Sheikh Russel National Gastroenterology Institute and Hospital, Mohakhali, Dhaka, Bangladesh. E-mail: momotaj1171@gmail.com, Cell: +880 1754-544846.

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Introduction:

The larynx connects the pharynx to trachea of the respiratory tract and is located in the anterior aspect of the neck. It is composed of cartilaginous tissue and plays a

vital role in the respiratory tract by allowing air to passage through it. It is also an organ of phonation. Both benign and malignant conditions can affect the larynx; however, it is the most common site for primary malignant tumour in head and neck regions.¹

Laryngeal carcinoma represent approximately 1-2% of all cancers worldwide.²

The laryngeal carcinoma is usually found in adults with a peak incidence in the 5th to 6th decades of life,³ and is considerably more common in male with a higher male female ratio in the higher incidence area.⁴ No single specific aetiologic factor has been cited for laryngeal carcinoma, but some factors have been found closely associated with increased incidence of carcinoma of larynx. Among the factors, smoking, drinking alcohol, tobacco chewing habits were found as the most important.⁵ A higher incidence of laryngeal cancer has been reported from Asian population. In a study in Dhaka Medical College Hospital, Dhaka, it was seen that 35.32% of all body cancers was in the head and neck region and carcinoma of the larynx was the commonest (31.58%).¹

Carcinoma of the larynx interferes with most vital functions in the sufferers like voice, respiration and swallowing by virtue of its anatomical location, local infiltration and direct extension.⁶ There is a tendency for squamous cell carcinoma of larynx to metastasize to cervical lymph nodes via embolization. Supraglottic area of larynx has rich lymphatics and so are associated with early metastasis to cervical lymph nodes. Common levels of neck nodes are jugulodigastric (level II) and mid jugular (level III) lymph nodes.⁷ While this is less common with glottic/subglottic tumours.

In laryngeal carcinoma, computed tomography (CT) scanning in combination with clinical examination has been shown to give a better representation of disease extent than clinical examination alone when compared with a pathologic specimen.⁸

Beiler et al⁹ offers a careful retrospective clinicopathologic analysis of the accuracy of pretreatment CT scanning to predict cartilage invasion and extra-laryngeal cancer spread. The capability of CT scan for evaluating deep laryngeal areas, submucosal tissues, laryngeal cartilages and lymph nodes makes it a valuable preoperative diagnostic technique in evaluating patients with laryngeal carcinomas. Correlations of CT signs and histopathologic findings were determined.

The diagnostic accuracy of CT in laryngeal carcinoma observed with sensitivity and specificity for supraglottic mucosa, glottic mucosa and subglottic mucosa were 100%, 100% and 100% respectively for sensitivity, and 83%, 85% and 86% respectively for specificity.¹⁰ In case of cartilage destruction, sensitivity and specificity was found as 89%

and 80% respectively, and in case of peri-epiglottic space (PES) involvement, sensitivity and specificity were 100% and 53%.

The clinical implications of findings of Du et al¹¹ are critically important, since they showed that multidetector CT scan had a positive predictive value of 78% and a negative predictive value of 100% for detection of invasion through cartilage, with sensitivity being 100% and specificity 96%.

The objective of this study was to determine the diagnostic accuracy, including sensitivity, specificity, positive predictive value and negative predictive value of CT in evaluation of laryngeal carcinoma.

Methodology:

It was a cross-sectional study, carried out in the department of Radiology and Imaging, Dhaka Medical College Hospital (DMCH), Dhaka, from July 2016 to June 2018 for a period of 2 years. A total of 50 patients with suspected laryngeal carcinoma, attending department of ENT and Head-Neck Surgery, and referred to the department of Radiology and Imaging, DMCH for computed tomography (CT) scan of neck were included. All the patients underwent laryngectomies, after which laryngeal tissues were sent to department of Pathology for histopathological evaluation of laryngeal carcinoma and the reports were collected and compiled in data sheet. The patients were evaluated by CT findings and histopathological examination reports.

Multidetector CT (MDCT) scan was performed in the department of Radiology and Imaging with HITACHI 128 slice CT scanner. Both pre- and post-contrast scan was obtained with the patients in supine position during breath hold. The area included from base of the skull to the arch of aorta using 2.5 mm collimation, 1.5 mm pitch, 120 kvp, 150 mAS. Scans were obtained using 4 mm thick axial section. In selected cases, such as glottis tumours, 2 mm sections were obtained for further definition of the lesion present. The CT examination was interpreted on hard copy. Axial, coronal and sagittal images of soft tissue and bone window images were obtained. Injectable contrast (Iopamidol- 370 mg/ml strength as a 100ml bolus infusion) was used to facilitate detection of metastatic lymph nodes. Validity of the MDCT scan was detected considering histopathology results as gold standard and calculated using the standard formulae for sensitivity, specificity, positive predictive and negative predictive values.

Results:

Ages of the enrolled patients were from 18 to 84 years with the mean age of 61.2 years ± 13.4 years standard deviation. Male female ratio was 7.3:1.

By computed tomography (CT) scan, about two-thirds of the cases (32/50, 64.00%) were suspected as carcinoma of larynx without lymphadenopathy and additional 15(30.00%) as carcinoma with lymphadenopathy. The remaining 3(6.00%) were suspected as benign lesions. (Table I)

Table I: Diagnosis of the laryngeal tumours by computed tomography (CT) scan (n=50)

CT diagnosis	Frequency	Percentage (%)
Suspected carcinoma without lymphadenopathy	32	64.00
Suspected carcinoma with lymphadenopathy	15	30.00
Suspected benign	3	6.00

Considering histopathological findings of the cases, almost all (47, 94.00%) of the suspicions were diagnosed as carcinoma of larynx and remaining 3(6.00%) as benign lesions. Among the carcinoma larynx cases, majority (31, 65.96%) had no nodal metastasis and about one-third (16, 34.04%) were found having nodal metastases. (Table II)

Table II: Diagnosis of laryngeal tumours by histopathology (n=50)

Histopathological diagnosis	Frequency	Percentage (%)
Carcinoma of larynx	47	94.00
Carcinoma without nodal metastasis	31	65.96
Carcinoma with nodal metastasis	16	34.04
Benign	3	6.00

By computed tomography (CT) scan, majority of the cases (32/50, 64.00%) were found confined in a specific area with no extension, while 12(24.00%) cases were found involving both supraglottic and glottic regions and only 4(8.00%) cases had extensions in all three areas of the larynx. (Table III, Figure 1, Figure 2)

Table III: Extension of the lesions of suspected Laryngeal carcinoma cases to the surrounding structures by computed tomography (CT) scan (n=50)

Type of extension found by CT scan	Frequency	Percent
No extension of lesion	32	64.00
Supraglottic & glottic	12	24.00
Transglottic	4	8.00
Glottic & subglottic	2	2.00



Figure 1: Axial NECT scan of neck showing mixed density mass involving left vocal cord compressing the air column

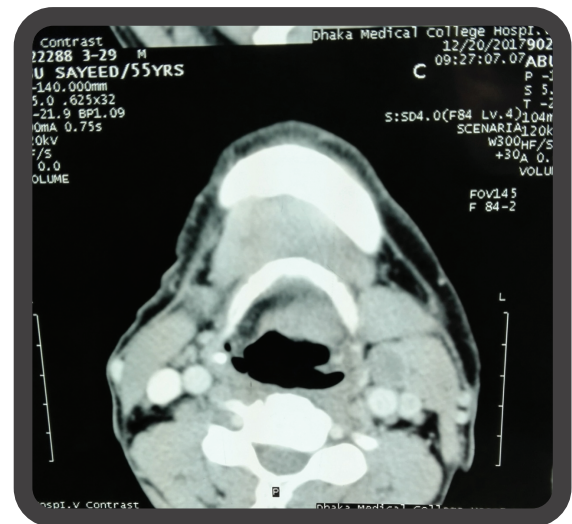


Figure 2 : Axial CECT scan of neck showing left sided cervical lymphadenopathy

Considering histopathology as gold standard, there was 46(97.87%) true positive identifications for carcinoma larynx with 1(2.13%) false positive, and 2(66.67%) true negatives with 1(33.33%) false negative result by multidetector CT (MDCT) scan. (Table IV)

Table IV: Relationship between histopathology and multidetector CT (MDCT) scan results

Histopathology results	MDCT scan results for malignancy	
	Positive	Negative
Malignant (n=47)	46 (97.87%)	1(2.13%)
Non-malignant (n=3)	1(33.33%)	2(66.67%)

Validity tests of MDCT diagnosis revealed sensitivity of 97.9% and specificity of 66.7% with 96.0% accuracy and 97.9% positive predictive value. (Table V)

Table V: Diagnostic accuracy of multidetector computed tomography (MDCT) in assessing laryngeal carcinoma

Validity tests	Percentage (%)
Sensitivity (TP/TP+FN)	97.9
Specificity (TN/TN+FP)	66.7
Accuracy (TP+TN/TP+TN+FP+FN)	96.0
Positive predictive value (TP/TP+FP)	97.9
Negative predictive value (TN/FN+TN)	66.7

TP=true positive, FP=false positive, TN=true negative, FN=false negative

Histopathology detected 34(68.00%) patients had no nodal involvement and remaining only 16(32.00%) had nodal involvement. Comparing with histopathology results, MDCT showed 15(93.75%) true positive cases of laryngeal carcinoma with nodal involvement and 33 (97.06%) true negatives. Only 1(2.94%) case was false positive and 1(6.25%) yielded false negative result. (Table VI)

Table VI: Relation between CT scan and histopathology results for nodal involvement

Histopathology results showing nodal involvement	Multidetector CT scan showing nodal extension	
	Present	Absent
Yes (n=16)	15 (93.75%)	1 (6.25%)
No (n=34)	1 (2.94%)	33 (97.06%)

Taking histopathology results as gold standard, the sensitivity and specificity of MDCT to detect nodal extension were 93.8% and 97.0% respectively with 96.0% accuracy.

Table VII: Diagnostic accuracy of multidetector computed tomography in assessing nodal extension of the laryngeal carcinoma cases

Validity tests	Percentage (%)
Sensitivity (TP/TP+FN)	93.75
Specificity (TN/TN+FP)	97.0
Accuracy (TP+TN/TP+TN+FP+FN)	96.0
Positive predictive value (TP/TP+FP)	93.8
Negative predictive value (TN/TN+FN)	97.0

TP=true positive, TN= true negative, FP=false positive, FN=false negative

Discussion

In this study, it was observed that mean age of the included patients was 61.2 years \pm 13.4 years standard deviation and age ranges from 18 years to 84 years. In one study in Bangladesh by Mahfuz et al¹² found the age of the patients ranged from 30 to 79 years (54 \pm 10.49).

Regarding the extension of the lesion, it was observed that majority (32, 64.00%) of the tumours were confined in a specific area with no extensions, while 12 cases (24.00%) involved both supraglottic and glottic region and only 8.00% had extension in all three areas of larynx. Kazkayasi et al¹³ showed that tumour extension between laryngeal mucosal surfaces and its cartilaginous framework and invasion to the extra-laryngeal tissue planes was most important for classification of a lesion and for decision making about treatment choice.

Among the suspected 50 cases, 47(94.00%) were diagnosed as laryngeal carcinoma with only 3(6.00%) as benign tumours. Among the laryngeal carcinoma cases, majority (31, 65.96%) were found having no nodal metastasis and remaining 16(32.00%) had nodal metastases. Diagnostic accuracy of MDCT for sensitivity, specificity, accuracy, positive predictive value and negative predictive value were 97.9%, 66.7%, 96.0%, 97.9% and 66.7% respectively. Comparing with histopathology findings, MDCT scan detected 15(93.75%) cases with nodal extension. In a study in China, Li et al¹⁴ found almost similar findings of majority of patients (85.0%) having laryngeal cancer.

Using histology as the gold standard, Li et al¹⁴ determined that the multidetector CT (MDCT) scan had a positive predictive value (PPV) of 78% and negative predictive value (NPV) of 100% for invasion into surrounding tissues. Atlanoglu et al¹⁵ observed sensitivities of CT assessment for supraglottic mucosa, glottic mucosa and subglottic mucosa of 100%, 100% and 100% respectively with corresponding specificities of 83%, 85% and 86% respectively.

In the current study, it was observed that majority (34, 68.0%) patients had no nodal involvement and only 16(32.00%) patients were found having nodal involvement. In Bangladesh, Mahfuz et al¹² found that nodal involvement was 38.71% in cases of supraglottic carcinoma. Raitiola et al¹⁶ observed nodal involvement as 52.53% in supraglottic carcinoma. In another study by Thabet et al¹⁷ found only 6.0% patients demonstrated histological evidence of paratracheal nodal metastases (larynx, 20%, postericoid/cervical oesophageal region, 43%), which are comparable with the current study. Chu et al¹⁸ found approximately 30%

of all laryngeal cancers arose in the supraglottic region. Lymph node metastases were common and affected the pre- and para-tracheal nodes. The sensitivity and specificity of CT to detect nodal disease using these criteria were 90% and 75% respectively.¹³ In our study, the sensitivity and specificity of CT to detect nodal disease were 93.8% and 97% respectively with 96% accuracy and 93.8% positive predictive value, which matches previous studies mentioned above.

A large study including countrywide specimen can overcome the limitations of the present study including a small number of cases at one institution.

Conclusion:

The current study revealed high sensitivity, accuracy and positive predictive value of computed tomography in the diagnosis of laryngeal carcinoma in pre-operative discrimination and subsequent. From the present study findings, it could be concluded that computed tomography is a useful modality in the diagnosis of laryngeal carcinoma and its extension.

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Original Article

Incidence of Benzodiazepine Use and Misuse Among Adults in Selected Areas of Bangladesh

Munira Afrin,¹ Fatema Zerine Khan,² Shompa Sharmin Rasna,³ Tasneema Juaira,⁴ Nahida Nazmun⁵

¹Professor and Head, Department of Pharmacology and Therapeutics, Monno Medical College, Gilondo, Manikganj; ²Associate Professor and Head, Department of Pharmacology and Therapeutics, Armed Forces Medical College, Dhaka; ³Assistant Professor, Department of Pharmacology and Therapeutics; ⁴Associate Professor, Department of Physiology; ⁵Assistant Professor, Department of Forensic Medicine and Toxicology, Monno Medical College, Gilondo, Manikganj, Bangladesh.

Abstract

Background: Benzodiazepines (BDZ) are widely prescribed for anxiety and insomnia in Bangladesh, but their misuse has become a major public health concern. **Objective:** The aim of this study was to identify the incidence and patterns of use and misuse of BDZ in Bangladesh, and to explore the factors contributing to their misuse. **Methodology:** A cross-sectional study, including 368 current BDZ users, was conducted in the department of Pharmacology, Monno Medical College, Manikganj, during January, 2021 to December, 2022. The participants were selected randomly. Structured questionnaires were used to include participants' personal information, drug use characteristics, physiological and psychological effects of drugs usage. Verbal consent was taken from each of the respondents. **Results:** In this study, 268(72.83%) of the participants were male, where 157(42.66%) were from the age group 31-40 years and 139(37.77%) were single. Among the study population, 51(13.86%) were students, 79(21.47%) had monthly family income above 50,000 Bangladeshi taka. Many of the participants reported that they used BDZs to relieve stress/pressure (108, 29.35%), followed by 95(25.82%) to manage insomnia, 79(21.47%) for relieving anxiety, depression and to get pleasure and others. The mostly used drug was clonazepam (112, 30.43%), followed by diazepam (108, 29.35%) and others. Most of the users were influenced by friends (115, 31.25%). The common side effects of using BDZs were confusion (47, 12.77%), fatigue (45, 12.22%), drowsiness (37, 10.05%), and others. The mostly experienced withdrawal effect was headache (86, 23.28%), followed by insomnia (59, 16.25%), confusion (50, 13.48%) and others. **Conclusion:** BDZs were widely used in selected areas of Bangladesh with high incidence of misuse. The most common reason of misuse was self-medication. Increasing awareness program should be taken for safe and effective use of the drug.

Key Words: Benzodiazepines (BDZ), Drug misuse, Side effects, Withdrawal effects

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Correspondence: Professor Dr. Munira Afrin, Professor, Department of Pharmacology and Therapeutics, Monno Medical College, Monno City, Gilondo, Manikganj, Bangladesh. E-mail: mafrin79@gmail.com, Cell: +880 1711-950598.

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Introduction:

Benzodiazepines (BDZs) are a class of drugs commonly used to treat anxiety, insomnia, and other mental health conditions. However, their misuse has become a growing concern in many countries, including Bangladesh and which is related to public health issue.¹ The second most common class of drug; benzodiazepines are the reason for death induced by drugs in Australia.² Non-medical use of

Benzodiazepines in Australia as sleeping pills, among males, the majority of benzodiazepine related ambulance attendances in 2019 were female.³ International Centre for Diarrhoeal Disease Research, Bangladesh (icddr) conducted a study shows that 79.4% of the drug users were male in Dhaka city, 64.8% of the drug users were unmarried, 56.1% were either students or unemployed, and 95.4% are smokers and among them, 85.7% get into

consuming drugs under the influence of friends in Bangladesh.⁴

The people using non-prescribed benzodiazepines may be consuming these substances and they are thinking those are genuine pharmaceutical products.⁵ These counterfeit benzodiazepines may have no known medical uses and can cause unexpected and serious adverse effects.⁶

Factors contributing to misuse include easy availability, lack of awareness about risks, and inadequate regulation.⁷ Understanding the extent and reasons for benzodiazepine misuse in Bangladesh is crucial for developing effective prevention and intervention strategies.

Methodology

Study Design and Study Population

A cross-sectional study was completed among the benzodiazepine (BDZ) users. Data was collected through face-to-face interviews with a structured questionnaire. The target population was all those who used non-prescription BDZ alone or with other drugs. A total number of 368 participants, who were living in different areas of Dhaka city, were included in this study with the age range of 22-60 years. The duration of collecting data was 2 years (from January, 2021 to December, 2022). Participants were selected by simple random sampling from drug sellers, doctors and those attending drug dispensaries.

Data collection method

The structured questionnaire had different segments and accordingly interviewed to participants. The respondents were giving the detail information regarding socio-demographic profile with smoking habit. Then collected information about participants' chronic disease, frequency and duration of drug use, purpose of the drug use, name of the drug use, history of multiple drug use and recommended by whom etc. Respondents also informed among problems (physical and psychological) faced in current context after taking the drug, and withdrawal effect.

This paper consisted of multiple choice and open answer question. After explaining the purpose of the study to the respondents individually and observed about their willingness to respondents and the researcher interviewed all the respondents by asking questions in Bengali and completing the question paper in English.

Statistical Analysis

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 20.0 for Windows

(SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages.

Ethical considerations

All procedures of the present study were carried out in accordance with ethical guidelines of the Institutional Ethical Review Board. Participants in the study were informed about the procedure and purpose of the study and confidentiality of information provided. All participants consented willingly to be a part of the study during the data collection periods. All data were collected anonymously and were analyzed using the coding system.

Results:

Sociodemographic profile of respondent

Out of 368 respondents, 268(72.83%) were male and 100(27.17%) were female. Most of the respondents were coming from the age group 31-40 years (157, 42.66%), followed by 41-50 years (141, 38.32%) and others. Majority of the respondents were married (220, 59.78%), other 139(37.77%) were single and only 9(2.45%) were divorcee. The educational qualification of the respondents was in maximum cases at university level (169, 45.92%), then 107(29.08%) completed the higher secondary level, a few others completed only primary and secondary levels, while only 5(1.36%) were illiterate. Considering occupation of the participants, majority were service holders (135, 36.68%), some 81(22.01%) were businessmen, 51(13.86%) were students and others of different occupation, while some 36(9.78%) were unemployed. Monthly family income of most of the respondents (100, 27.17%) was in between 20,000-35,000 Bangladeshi taka (BDT), followed by 82(22.28%) having 25,000-50,000 (BDT) and 79(21.47%) having above 50,000 BDT. More than half (211, 57.34%) of the drug users were smokers and among them, majority (108, 48.82%) were chain smokers. (Table I)

Drug use characteristics of the respondents

Most of the respondents (108/368, 29.35%) taken drug to get relieve from stress/pressure, followed by 95(25.82%) to have relieve from insomnia, 79(21.47%) for relieving anxiety, depression and to get pleasure, 58(15.75%) to get sound sleep and remaining 28(7.61%) taken BDZs for migraine- headache and to increase the working capacity. (Figure 1)

Table I: Socio-demographic profile and smoking habit of the respondents (n=368)

Different Variables	Frequency	Percentage (%)
Gender		
Male	268	72.83
Female	100	27.17
Age Group (Years)		
22-30	45	12.23
31-40	157	42.66
41-50	141	38.32
51-60	25	6.79
Marital Status		
Single	139	37.77
Married	220	59.78
Divorced	9	2.45
Level of Education		
Primary	26	7.07
Secondary	61	16.58
Higher secondary	107	29.08
University	169	45.92
Illiterate	5	1.36
Occupation		
Student	51	13.86
Service	135	36.68
Business	81	22.01
Garment worker	45	12.23
Unemployed	36	9.78
Housewife	20	5.43
Monthly Family Income (Bangladeshi taka)		
Below 10,000	40	10.87
10,000-20,000	67	18.21
20,001-35,000	100	27.17
35,001-50,000	82	22.28
Above 50,000	79	21.47
Smoking		
Non-smoker	157	42.66
Smokers	211	57.34
Regular Smoker	103	48.81
Chain-smoker	108	48.82

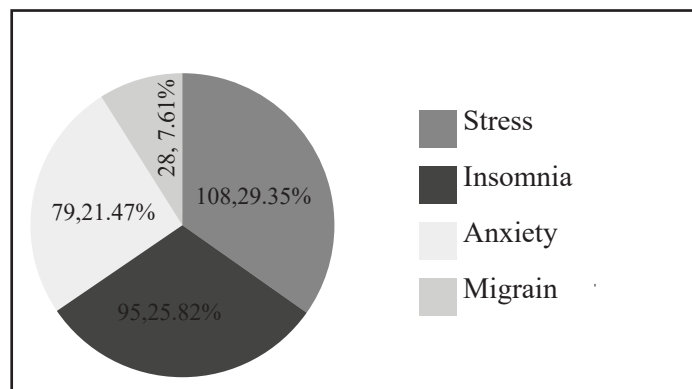


Figure 1: Use of drug for different participant (n=368)

Majority of the respondents taken clonazepam (112, 30.43%), followed by diazepam (108, 29.35%), bromazepam (92, 25.00%) and clobazam (56, 15.21%). (Figure 2)



Figure 2: Use of different Benzodiazepines by the respondents

Considering frequency of drug use, it was found that majority (111, 30.16%) taken drug according to their necessity, while 96(26.08%) of them taken drugs daily, 81(22.01%) taken almost daily and another 80(21.73%) of the respondents taken drugs irregularly with no fixed schedule. (Table II)

Table II: Frequency of drug use by the participants (n=368)

Frequency of drug use	Number of respondents	Percent (%)
According to needs	111	30.16
Daily	96	26.08
Almost daily	81	22.01
No fixed time	80	21.73

Most of the drug users were influenced by their friends (115/368, 31.25%), followed by recommendations by doctors (34, 9.24%), verbal advice from medicine seller/pharmacist (88, 23.91%), by their colleague (31, 8.42%) and by their family members (15, 4.08%). Many of the respondents (85, 23.09%) also taken drugs by self-medication. (Table III)

Table III: Influencers of drug use among the respondents (n=368)

Variables	Frequency	Percentages (%)
Friends	115	31.25
Doctors	34	9.24
Seller	88	23.91
Colleague	31	8.42
Family Members	15	4.08
Self	85	23.09

Physiological, psychological effects and related dependence

Some of the respondents reported experiences of having some problems after taking drugs including development of confusion (47/368, 12.77%), fatigue (45, 12.22%), daytime drowsiness (37, 10.05%), anxiety (35, 9.51%) and others. Although, majority (134, 36.41%) of the respondents did not experience any problem. (Figure 4)

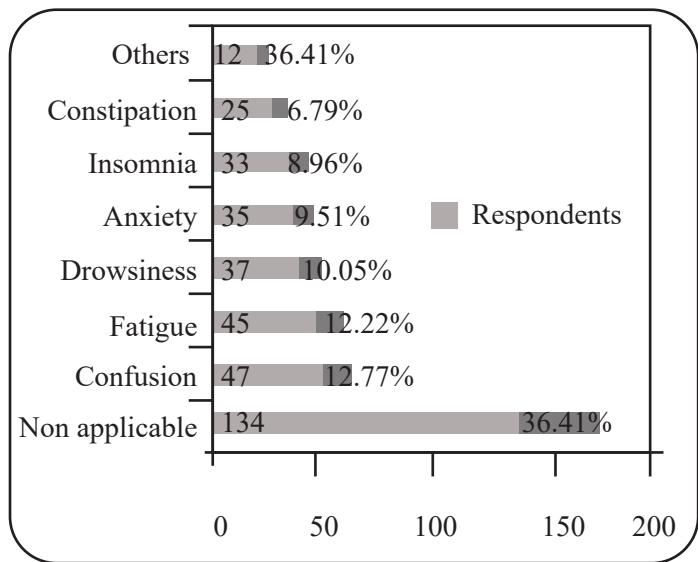


Figure 4: Different side effects experienced by the respondents (n=368)

Among 368 participants with BDZs usage, 336(91.08%) tried to stop taking the drug and remaining 32(8.92%) never tried to do so. Most of the participants (241, 71.73%) trying to stop the drugs faced some withdrawal effects. The most common withdrawal effect among the BDZs users was headache (86, 35.68%). Others faced insomnia (59, 24.48%), confusion (50, 20.75%) and restlessness 46(19.09%). (Table IV)

Table IV: Withdrawal effects of the respondents (n=241)

Withdrawal effect	Frequency	Percentages (%)
Headache	86	35.68
Insomnia	59	24.48
Confusion	50	20.75
Restlessness	46	19.09
Total	241	100.00

Discussion

In the analysis of current survey data, incidence of benzodiazepine (BDZ) use shows 9.24% only prescription followers and predominantly were males (72.83%).

Ojha et al⁷ found in their study that almost all of the respondents were males (91%) and only 9% were female that is similar with the current study. By age, the highest rate of overall benzodiazepine use was among adults aged 31-40 years.

Two different studies reported in Bangladesh shows majority drug users from age group 22-25 years,⁸ and 64.6% between ages 20-24 years.⁹ These findings are very much close to the age group of current study. Again, another study in Bangladesh found almost half (48.0%) of the participants in the age group 30-39 years,¹⁰ with a completely different result.

In 2004, Mahbubur et al found 85.7% respondents get into consuming the drugs under the influence of friends.³ Mahbuba Naznin in 2010 found that 38.75% respondents were influenced by friends in her study.¹¹ Abul Hashem et al mentioned 42.6% respondents were influenced by their peer group or friends.⁹ All the findings strongly support the current research, because the majority (31.25%) of respondents in this study was influenced by their friends.

The most common type of misuse included drugs use without a prescription, although this was more common among younger adults; older adults were more likely to use their benzodiazepine more often than prescribed. Neilsen et al found almost 70% participants used BDZ as a non-prescription drug and the most commonly used drugs were diazepam (55%) and alprazolam (30%) in Queensland, Tasmania, Western Australia and Victoria.¹² But another study from Australia reported 13% respondents used prescribed BDZ.¹³ Misuse of BDZ was reported in 57.2% because of their workload and increasing of patients' stress by Thai doctors.¹⁴ This study reveals only 9.24% respondents taken BDZ based on doctors' prescription in Dhaka city.

Reasons of drug intake were almost common in all studies. Kevin WC et al shows in a survey that the main reasons for using BDZ without a prescription were curiosity (46%), relieving tension or anxiety (41%) and for feeling good (37%).¹ Among the Lebanese BDZ users, 44.4% were taking for relieving anxiety, for insomnia (22.5%) and for depression (16%).¹⁵ Only 17.0% medical students used sedative drugs at some time because of significant psychological stress in King Saud University College of Medicine in 2011.¹⁶ Among all the self-reported BDZ users, 11% tried and 29% had no interest to stop taking drug.¹ Whereas, according to the current study, 91.08% tried to stop uses the BDZ, which is a good sign for future

generation and also for the policy makers. The withdrawal effects were rebound insomnia, anxiety, drowsiness, restlessness, BDZ dependence, etc, which occurred even when doses of drugs were low and consumed over a short period of time as mentioned in two different studies.¹⁷⁻¹⁸

Prescription drug monitoring programs were an important tool to understand misusing of other medications and would thus be at high risk of benzodiazepine misuse.

More studies with large samples should be included to find out the causes of misuse of drug without prescription.

Conclusion:

Benzodiazepines were widely used in a selected area in Bangladesh, with high incidences of misuse. The most common reasons for misuse were self-medication. Strategies for promoting safe and effective use of benzodiazepines should be increasing awareness about the risk associated with their use, improving regulation of their availability and use, and providing education about withdrawal effects.

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Original Article

Knowledge and Experiences of Diseases with Associated Factors among Agricultural Workers in Manikganj District

Afsana Mahjabin,¹ Khondoker Mohammad Ali,² Md. Jahangir Alam,³ Md. Salahuddin Emdad,⁴ Faizun Nahar Nabila,⁵ Kazi AKM Sohel,⁶ Anabil Digarna⁷

¹Associate Professor, Department of Community Medicine, Monno Medical College, Manikganj, Bangladesh; ²Professor, Department of Community Medicine, Monno Medical College, Manikganj, Bangladesh; ³ Professor, Department of Community Medicine, Monno Medical College, Manikganj, Bangladesh; ⁴Lecturer, Department of Community Medicine, Monno Medical College, Manikganj, Bangladesh; ⁵Lecturer, Department of Community Medicine, Monno Medical College, Manikganj, Bangladesh; ⁶Lecturer, Department of Community Medicine, Monno Medical College, Manikganj, Bangladesh; ⁷Lecturer, Department of Community Medicine, Monno Medical College, Manikganj, Bangladesh.

Abstract

Background: Farmers are generally the people of poor segment of the society and agricultural workers are prone to develop different types of health problems. **Objectives:** The study was conducted with a view to finding out the pattern of health problems of the agricultural workers in a rural area of Manikganj district. **Methodology:** This was a descriptive type of cross-sectional study carried out in Koshunda village of Manikganj district during the period of November, 2021 to April, 2022 in the Department of Community Medicine, Monno Medical College, Manikganj. For finding out pattern of diseases, knowledge and practice of the study subjects were determined by using pretested questionnaire. **Results:** Among the 300 cases, majority (124, 41.33%) of the respondents belonged to the age group 36-50 years. Most of the respondents (239, 79.67%) were male, being literate (195, 65.00%) had monthly family income of 10,001 or more BDT (139, 46.33%). Regarding cultivators' knowledge of health problems during cultivation, majority (230, 76.67%) expressed occurring cut injury, followed by 206(68.67%) temperature injury, 85(24.08%) insect bite and others. Responding to question regarding injuries caused by tools and machineries of or animals involved in cultivation, majority (134, 44.67%) told that they are injured by hand tools, followed by 51(17.00%) due to cattle's kick, 46(15.33%) due to tractors and other machineries, and others-whereas, majority of them (199, 66.33%) also reported that the injuries occur in hands, followed by 192(64.00%) in legs and others. Diseases experienced by the respondents during agricultural works included temperature-related injury (165, 55.00%), cut injury (96, 32.00%), skin problems (34, 11.33%) and others. Regarding the knowledge of the respondents' choice of physician, majority (125, 41.67%) preferred MBBS Doctors, followed by rural medical practitioners (121, 40.33%), homeopathic doctors (67, 22.33%) and others. **Conclusion:** Most of the farmers shared their knowledge of suffering from different types of diseases with choice of treatment by MBBS doctors.

Key Words: Disease pattern, Agricultural workers, Manikganj, Bangladesh

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Correspondence: Dr. Afsana Mahjabin, Associate Professor, Department of Community Medicine, Monno Medical College, Monno City, Gilondo, Manikganj, Bangladesh. E-mail: afsana.aqsa@gmail.com, Cell: +880 1768-677154.

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Introduction:

In developing countries agriculture is the vital source of income. But it may lead to poor health as it is associated with infection, injuries and increased occupational diseases to the agricultural workers.¹ One of the riskiest jobs for workers

has always been agriculture.^{2,3} The danger of injury has increased with heavy machinery use.⁴ About 22% of the injuries those occur during agricultural work were greater than or equivalent to an AIS 2 (Abbreviated Injury Scale), even though the majority of the injuries were not serious.⁵

Agriculture is the largest employment sector all over the world. It is also the most hazardous occupation among all the other occupations.⁶ The people engaged in agricultural work are prone to developing multitude of health problems but this is often overlooked due to misconception or neglect of the policy makers of this sector.⁷ The people working in agricultural sector are exposed to many risk factors such as sunlight, cold, pesticide & inorganic dusts etc.⁶ This may cause physical injury to the people & repeated injury may result in permanent disability of the farmers. Generally agricultural workers remain in the workplace for almost 42 hours per week. This long duration makes the workers vulnerable to developing injury. If it happens so, then this can lead them towards extreme poverty specially the families where the agricultural worker is the only earning member.⁵ But this is a fact that most agriculture related diseases can be prevented if proper measures are taken. In order to support the relevant authorities (policy makers) in addressing this worsening situation in agriculture, this study was conducted to identify the pattern of health problems and the factors that are linked to them.

Methodology

This study was carried out in the department of Community Medicine of Monno Medical College for a period of six-months among 300 agricultural labourers in Koshunda village, of Baliakhora union, and Ghior upazila of Manikganj. This was a descriptive type of cross-sectional study using purposive sampling strategy and performed between November 1, 2021, and April 30, 2022.

The institutional Ethical Review Board of the Monno Medical College granted the ethical approval. The inclusion requirements of the study included adult participants of 18 years of age or older, engaged in agriculture as farmers and able to offer informed written consent. The farmers with critical disease condition and with psychological disorders were excluded.

All related information were collected by face-to-face interviews using pre-tested, semi-structured questionnaires. The data were calculated and interpreted after proper editing and cleaning using the statistical software SPSS version 23.0.

Results

In this study, among 300 respondents, majority (124,

41.33%) belonged to the age group 36-50 years with the mean age + standard deviation (SD) of 43.58±3.489 years. A total of 239(79.67%) were male and 195(65.00%) were literate. Among the literate cultivators, majority (101, 51.80%) had primary level of education. Most of the cases were Muslims (278, 92.67%). Monthly family income of majority of the respondents (129, 43.00%) was 5,001-10,000 Bangladeshi taka. (Table I)

Table I: Socio-demographics characteristics of the respondents (n=300)

Socio-demographic characteristics	Frequency	Percentage
Age (years)		
18-35	89	29.67
36-50	124	41.33
51-65	61	20.33
Above 65	26	8.67
Total	300	100.00
Mean±SD= 43.58±3.489 years		
Sex		
Male	239	79.67
Female	61	20.33
Total	300	100.00
Education		
Illiterate	105	35.00
Literate	195	65.00
Primary education	101	51.80
Secondary (up to SSC*) education	50	25.64
HSC**and above	44	22.56
*SSC- secondary school certificate, **HSC-higher secondary school certificate		
Religion		
Islam	278	92.67
Hinduism	22	7.33
Family Income (Taka)		
<5,000	32	10.67
5,001-10,000	129	43.00
10,001-15,000	90	30.00
> 15,000	49	16.33

The study reflected that majority (230, 76.67%) respondents mentioned cut injury as the health problem observed during cultivation, followed by 206(68.67%) of temperature-related injury, insect bite (85, 28.33%), skin disorders (75, 25.00%), respiratory diseases (73, 24.33%) and others. (Table II)

In connection with the mechanical injuries caused by tools and machineries of or animals involved in cultivation, majority told that injuries occur due to hand tools (134, 44.7%), followed 51(17.00%) due to cattle's kick, 46(15.33%) due to tractors and other machineries and others. (Table III)

Table II: Multiple response knowledge of the respondents about the common health problems during cultivation (n=300)

Diseases	Frequency	Percentage
Cut injury	96	32.00
Temperature-related Injury	165	55.00
Skin problems	34	11.33
Insect bite	28	9.33
Snake bite	20	6.67
Helminthic diseases	24	8.00
Others	43	14.33
Respiratory diseases	25	8.33

Table III: Multiple response of the farmers regarding injuries due to tools and machineries of or animals involved in cultivation (n=300)

Tools & machineries/ Animals of injury	Frequency	Percentage
Hand tools	134	44.67
Tractors and other machineries	46	15.33
Animal kick	51	17.00
Others	22	7.33

In this study, considering injuries due to tools and machineries of or animals involved in cultivation, most of the respondents (199, 66.33%) said that injuries occur in hands, followed by 192(64.00%) in legs and others. Only 67(22.33%) respondents said that injuries may occur in any site of the body. (Figure 1)

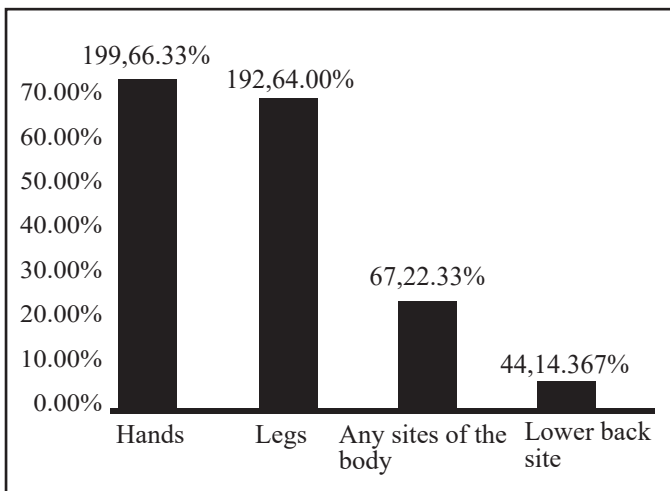


Figure 1. Multiple response of the agricultural workers regarding common sites of injury due to tools and machineries of or animals involved in cultivation (n=300)

The study reflected that majority (165, 55.00%) of the farmers faced temperature-related injury during agricultural works, followed by 96(32.00%) farmers affected by cut injury, 34(11.33%) affected by skin problems, 25(8.33%) suffered from respiratory diseases and others. (Table IV)

Table IV: Multiple response of the participants regarding diseases experienced during agricultural works (n=300)

Diseases	Frequency	Percentage
Cut injury	230	76.67
Temperature related injury	206	68.67
Skin disorders	75	25.00
Insecticide poisoning	51	17.00
Insect bite	85	28.33
Snake bite	77	25.66
Helminthic Diseases	14	4.66
Respiratory Diseases	73	24.33
Others	32	10.66

In relation to choose physicians for treatment of the diseases, majority of the respondents in their multiple responses mentioned about MBBS doctors (125, 41.67%), followed by Rural Medical Practitioners (121, 40.33%), Homeopathic doctors (67, 22.33%) and others. (Figure 2)

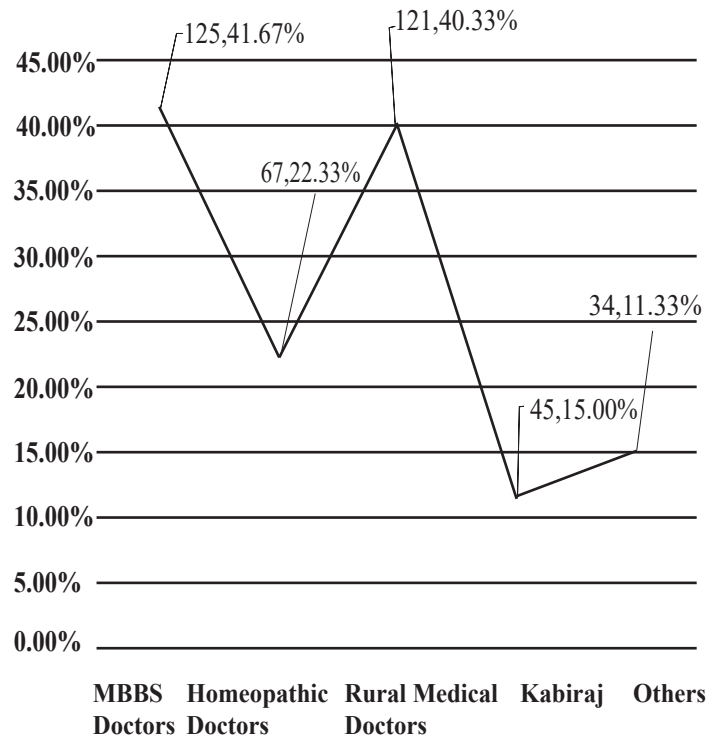


Figure 2. Multiple responses of the agricultural workers regarding choice of physicians for treatment of their illnesses

Discussion

According to the survey, out of 300 respondents, the majority (124, 41.33%) were between the ages of 36 and 50 years, the highest number of respondents (239, 79.67%) were men, and the majority of respondents (105, 35.00%) were illiterate. In contrast to the findings of this study, a comparable study carried out in Thailand⁸ shows that the majority of respondents (60.00%) were female and that the highest percentage of respondents (74.00%) had completed primary school.

Regarding knowledge of the participants about diseases that could arise when working in agriculture, the majority of respondents (230, 76.67%) agreed that physical or cut injuries could occur, while 206(68.67%) agreed that temperature-related injuries could occur. In this survey, 75 (25.00%) of participants reported having concerns about skin conditions, while 73(24.33%) noted respiratory illnesses. A study carried out in Vietnam⁹ reveals that 55.1% of participants reported experiencing damage related to temperature, which is nearly identical to the findings of this study. This could be because both countries' weather patterns are similar. This finding is comparable with another study done in Nepal,¹⁰ which found that 79.7% of people were aware of cut injuries.

In connection with the common sources of injury, majority (134, 44.67%) has mentioned that injuries occurred due to hand tools, followed by 46(15.33%) due to tractors and machineries. However, the study conducted by Parvez et al⁵ reflects that 67.00% of injuries occurred by hand tools and 33.00% were due to machineries and other sources, which is inconsistent with this study. Another study conducted in India¹¹ shows that 64.7% injuries occurred due to hand tools, followed by 29.1% due to machineries, showing dissimilarities with the result of this study.

In relation to knowledge of the participants regarding common organs of injury, majority (199, 66.33%) reported that injuries may occur in hands, 192(64.00%) mentioned in legs. Only 44(14.67%) reported that injuries may occur in lower back site. A study conducted in Nepal¹⁰ to find out knowledge of the participants shows that 67.00% participants mentioned injury may occur in hands, which is consistent with the result of this study. Another study conducted by Keawduangdee et al¹² exploring knowledge reveals that 83.1% participants mentioned injuries could occur in Lower back site, which is dissimilar with the result of this study.

The current study reflects that 96 (32.00%) farmers were affected during agricultural work by physical injury, mostly due to cut or lacerated type, 165(55.00%) faced temperature-related injury, 34(11.33%) suffered from skin diseases and another 25(8.33%) from respiratory diseases. However, another study conducted among the agricultural workers of Mymensingh district¹³ reveals that 16.0% workers suffered from respiratory illness and 10% from skin diseases, which is inconsistent with this study.

Regarding the prescribers for treatment of injuries, majority (125, 41.67%) of the farmers reported MBBS doctors, followed by 121(40.33%) by Rural Medical Practitioners and 67(22.33%) by homeopathic doctors. A study conducted Kulkarni et al¹⁴ reflects that 76.8% informed MBBS doctors as prescribers, which shows dissimilarity with this study.

This was a small study, carried out in a conveniently chosen area in Manikganj. Additionally, the sample size was limited, thus it might not accurately represent Bangladesh.

Conclusion

The majority of participants in this study were aware that cuts might occur during agricultural work, followed by temperature-related injuries. When considering knowledge about weapons or animals that injure farmers, most of them mentioned that hand tools were the main causes of injuries, while tractors and other machineries were following. The majority of respondents listed hands as the most common organ injured, followed by legs. According to this survey, half of the farmers experienced heat-related injuries, and one-third had cuts. The majority of respondents preferred MBBS doctors as their treatment providers, followed by rural medical professionals. To safeguard farmers against accidents, a vast geographic area should be the focus of a thorough study aimed at determining the true pattern of health problems.

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Fever of Unknown Origin in Children

Mahmud Hossain

Professor and Head, Department of Paediatrics, Monno Medical College and Hospital, Monno City, Gilondo, Manikganj

Summary:

Fever is a common symptom in children and fever of unknown origin (FUO) is not uncommon in paediatric age group. The FUO remains a challenging clinical problem and is an important cause of morbidity and mortality in children. These undifferentiated prolonged fevers need step-wise approach for diagnosis. Details and proper history taking, thorough serial physical examination, critical analysis of sign-symptoms diary and investigation reports are crucial to get a clue that led to the diagnosis. Though in some aspect more concerned with developing countries data, this article is based on reviewing of published papers from both developed and developing countries. Worldwide infection remains the most common cause of FUO in children, followed by collagen vascular diseases, neoplasm, miscellaneous diseases and undiagnosed illnesses. Indiscriminate use of antimicrobials and other medications may mask the real diagnosis. Awareness of primary-level healthcare providers about the cause and logical management approach of pediatric FUO is important for better outcome.

Introduction:

Fever is one of the most common reasons for which children need to visit a doctor. Although in majority of the cases in children, fever is a symptom of self-limited viral infection, in some cases, it could be a sign of a serious illness related to a life-threatening infection or malignancy. Rarely, the fever is prolonged or recurrent and the aetiology is not readily apparent. The differential diagnosis of these unexplained fevers is broad, and the evaluation of such children requires a step-wise approach.¹

Fever and Fever of Unknown Origin (FUO)

Children are considered to have fever if their body temperature (axillary) is above 99.5°F.² American College of Emergency Physicians (ACEP) chooses a rectal temperature of >38°C (100.4°F) as the most widely used definition of fever.³

Based on expert opinion and literature review, Marcy et al suggested that fever is the endogenous elevation of at least one measured body temperature of $\geq 38^{\circ}\text{C}$ (100.4°F), regardless of the intrinsic and extrinsic factors- in other words, at any anatomic site, using any device, at any age, and under all environmental condition.⁴

Most children who present with fever have additional signs and symptoms that leads to a specific diagnosis. Fever without a source may need further evaluation that includes laboratory tests or imaging. Rarely, the fever is more prolonged, requires more intensive evaluation, and falls in the category of fever of unknown origin (FUO).⁵

The FUO concept in adults was introduced by Petersdorf and Beeson in 1961⁶ but was not addressed in children until the 1970s. Some important articles about FUO were published previously, as retrospective case series and each used a different definition of fever on unknown origin (FUO).⁷⁻¹¹

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Correspondence: Dr. Mahmud Hossain, Professor (current charge), Department of Paediatrics, Monno Medical College and Hospital, Gilondo, Manikganj, Bangladesh.
E-mail: mahmudhossain1962@gmail.com, Cell: +880 1712-209260.

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Definition of FUO in children is still controversial. McClung as well as Lohr and Hendeley both defined pediatric FUO as an illness marked by 3 weeks of intermittent fever $\geq 39.0^{\circ}\text{C}$ despite aggressive outpatient evaluation, or 1 week of intensive inpatient evaluation.⁷

More recent investigators have shortened the time requirement necessary for a febrile illness to qualify as a FUO. Pizzo defined PUO in children as a temperature $\geq 38.5^{\circ}\text{C}$ on ≥ 4 occasions for at least 2 weeks.⁸ Lorin and Feigin have defined FUO as a febrile illness of at least 8 days in duration in which no diagnosis is apparent after an initial evaluation either in the hospital or as an outpatient.¹² Recently, the definition has been altered to three visits without a diagnosis being reached in outpatients.¹³

Causes of FUO in children¹⁴⁻²²

The causes of prolonged FUO may be classified into 5 categories: (1) infectious diseases, (2) collagen-vascular diseases, (3) neoplasms, (4) miscellaneous diseases and (5) undiagnosed illnesses.

1. Infection:

The common infections reported from the developing countries include Tuberculosis, Enteric Fever, Urinary Tract Infection (UTI), Malaria, Rickettsial Disease, Infectious mononucleosis, Cytomegalovirus, Hepatitis A, B, and C, Meningitis, Leishmaniasis, Bacterial Endocarditis, Abscess (Hepatic, Gluteal, Abdominal, Pelvic, Brain, Epidural, Dental, Paraspinal, Perinephric, Rectal, Subphrenic, Psoas), Septic Joint, Osteomyelitis, Pneumonia, Sinusitis, Brucellosis, Human immune deficiency virus.

2. Collagen vascular disease:

Juvenile idiopathic arthritis, systemic lupus erythematosus, Kawasaki disease, Atypical Kawasaki, Polyarteritis nodosa, Dermatomyositis, Rheumatic Fever, Behcet's disease, Vasculitis of unknown origin.

3. Neoplasms:

Leukaemia, Lymphoma, Neuroblastoma, Langerhans cell histiocytosis, Hemophagocytic Syndrome, Hepatocellular Carcinoma.

4. Miscellaneous Diseases:

Drug fever, Diabetes Insipidus, Periodic fever, Inflammatory bowel disease, Familial dysautonomia, Factitious fever, Kikuchi fujimoto disease, Addison disease, Pancreatitis, Thyrotoxicosis, Thyroiditis.

5. Undiagnosed illnesses.

Most of the undiagnosed FUO cases appear to be benign and many of them were found to resolve spontaneously

without a confirmed cause. These cases possibly consist of prolonged viral syndromes or difficult-to-confirm atypical bacterial infections.

Among infectious causes, there is variations between developed and developing countries. In developing countries, common infectious causes include tuberculosis, typhoid fever, malaria, and Leishmaniasis. While in developed countries, common infectious causes include lyme disease, cat scratch disease, cytomegalovirus (CMV) infection and brucellosis. Similarly, the rate of vaccine preventable diseases is higher in developing compared to developed countries.

One study in Turkey found that second most common cause of FUO in children is immune deficiency diseases such as Di-George syndrome, immotile cilia syndrome, selective IgA deficiency and transient hypogammaglobulinemia in infancy, which is an unusual finding compared with other studies.

Geographical and socio-economic factors, age distribution and time of study are all known to influence the etiology of FUO in a given population. In addition, the native population, their characteristic traits and the flora and fauna also influence local disease patterns and epidemiology. Local referral patterns and hospital settings further modify the diagnosis. Study findings of FUO conducted in developed countries and those from developing countries are different, because of limited availability of expensive serological and other tests in later settings.

Evaluation of FUO:

A. History and physical examination:

Evaluation of FUO should be systematic and logically guided by history and physical examination findings. A thorough physical examination along with detailed history and a critical analysis of the laboratory tests already performed are important.

The first step in evaluating FUO is documentation of fever, because the perception of the reporting parents regarding fever often varies from the medical definition. It is useful to determine what the parent defines as fever and whether this varies from the medical definition of 38.0°C (100.4°F). Parents frequently report tactile or subjective fevers without actually measuring the patient's temperature with an instrument.

A detailed description of the patient's fever pattern as intermittent (tuberculosis, malaria), recurrent (periodic fever disorders), relapsing [Lymphoma, brucellosis, rat bite fever), remittent (typhoid, endocarditis, juvenile idiopathic

arthritis (JIA)], or sustained (pyogenic abscess, lobar pneumonia) can sometimes narrow the differential diagnosis.^{23, 24} Information on the frequency and timing of fevers can be helpful in determining the fever curve and ability to document the fever in the medical setting. Though some researchers suggest that the pattern, magnitude and duration of fever are not useful in diagnosis of the causes of FUO.²⁵

Fever can be the initial presentation of certain immunodeficiency syndromes, but many affected patients have a history of repeated infections, diarrhea, or abnormal physical findings, such as a rash. A history of atopy or autoimmune disease increases the likelihood of an autoimmune or rheumatologic cause. Furthermore, neutropenic fever in certain situations can be a medical emergency, and the presence of neutropenia may broaden the potential infectious sources.²⁶

Travel history is critical in the evaluation of FUO (e.g., hilly area is endemic for malaria in Bangladesh). Exposure to animals, unusual foods, insect bites, and sick contacts are also important.

Drug history should also be asked, some antibiotics, anticonvulsants, neuroleptics, antiarrhythmic, vasodilators including others can cause prolonged fever. History of immunization against vaccine preventable diseases should be taken, although all vaccine does not have high protective value and vaccine failure is not uncommon. History of close contact with active tuberculosis is very important in Bangladesh and other developing countries in particular.²⁷

One of the important aspects of evaluation for FUO is repeated history taking and encouraging the patient and family to report any new, different, or unusual signs or symptoms appeared. Serial physical examinations should be performed, and observation in a controlled inpatient setting may be beneficial because up to 25% of significant physical findings may be absent at the time of presentation.²³

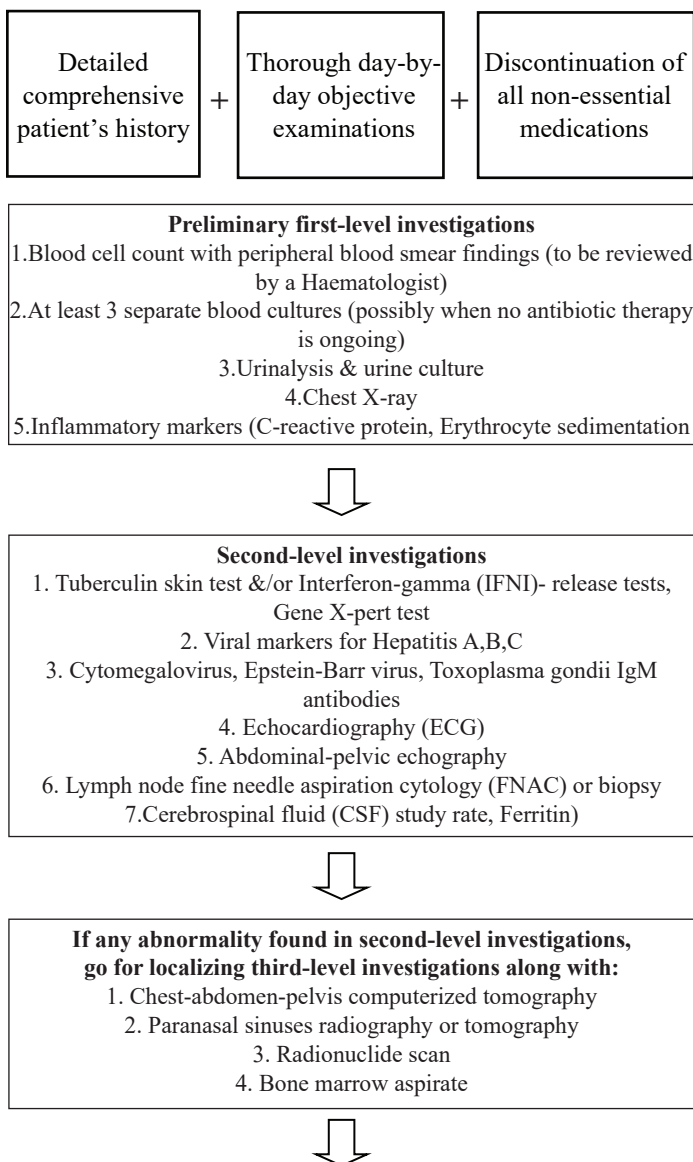
Table 1. Physical findings and associated Fever of Unknown Origin diagnoses⁵

Finding	Associated Illness
Hepatomegaly	Typhoid fever, malaria, lymphoma, leukemia, metastatic carcinoma, relapsing fever, granulomatous hepatitis, hemophagocytic lymphohistiocytosis (HLH), viral infections, brucellosis, bartonellosis, endocarditis
Splenomegaly	Leukemia, lymphoma, tuberculosis, typhoid fever, rickettsial disease, brucellosis, infective endocarditis, cytomegalovirus, HLH), Epstein-Barr virus, psittacosis, relapsing fever, Kikuchi-Fujimoto disease
Liver edge tenderness	Liver abscess, Bartonellosis
Splenic abscess	Infective endocarditis, brucellosis, enteric fever
Murmur	Infective endocarditis, atrial myxoma
Relative bradycardia	Typhoid fever, malaria, leptospirosis, psittacosis, central fever, drug fever
Abnormal funduscopic examination findings	Miliary tuberculosis, toxoplasmosis, vasculitis
Conjunctivitis	Epstein-Barr virus, leptospirosis, Kawasaki disease (limbic sparing), tuberculosis, systemic lupus erythematosus, bartonellosis, chlamydial infection, histoplasmosis, tumor necrosis factor receptor associated periodic syndrome, familial cold autoinflammatory syndrome
Decreased pupillary constriction	Hypothalamic or autonomic dysfunction
Dry eyes	Systemic lupus, Familial dysautonomia, erythematosus, polyarteritis nodosa, Sjögren syndrome
Ischemic retinopathy	Polyarteritis nodosa
Periorbital edema	Tumor necrosis factor receptor-associated periodic syndrome
Subconjunctival hemorrhage	Endocarditis, trichinosis
Uveal tract involvement	Tuberculosis, juvenile idiopathic arthritis, toxoplasmosis, sarcoidosis, systemic lupus erythematosus
Lymphadenopathy	Lymphoma, tuberculosis, leukemia, bartonellosis, lymphogranuloma venereum, cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus, toxoplasmosis, juvenile idiopathic arthritis, brucellosis, Kikuchi-Fujimoto disease, tularemia, viral infections, hyperimmunoglobulin D syndrome, familial cold autoinflammatory syndrome

B. Diagnostic Workup:

A number of basic laboratory studies may be used to determine the source of FUO. A complete blood cell count (CBC) with differential count and smear can suggest an infectious or oncologic cause. Blood and urine cultures are recommended, with the understanding that repeat cultures may be needed. If the patient has neurologic symptoms, cerebrospinal fluid (CSF) studies are also indicated. Whenever possible, cultures should be obtained before initiating antibiotics to avoid ambiguity and contamination of results. Abnormalities in serum electrolytes or liver enzymes may indicate viral, atypical bacterial or hematologic causes.²⁸ For all these purposes, the following flow-chart can be followed to evaluate the patient.

Flowchart of diagnostic workup for investigations of children with fever of unknown origin (FUO).¹⁹



Third-level investigations:
(depending on history and physical suggestive clues)

1. Protein electrophoresis
2. Anti-nuclear antibodies
3. Anti-dsDNA antibodies
4. Anti-neutrophil cytoplasmic antibodies
5. Complements C3 & C4
6. Specific test for bacteria, viruses (including HIV), spirochaetes, rickettsiae, parasites & fungi

Testing for acute-phase reactants, such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and ferritin, is common in the evaluation of FUO. These test results are non-specific and not diagnostic of any particular disorder. On the other hand, elevated acute-phase reactants should encourage the physician to proceed with further appropriate evaluation. Although, normal acute-phase reactant results do not exclude serious causes of FUO.

The CRP can be pathologically elevated in a wide variety of disease processes, including inflammatory, infectious, and autoimmune. There has been much interest in CRP as a predictor of serious bacterial infection and current evidence suggests that a markedly elevated CRP is required for specificity for bacterial infection. When evaluating the FUO, particularly in the hospital setting, mildly elevated CRP values should not be used to rule in or out a particular disease process. Trending CRP values are a more valuable diagnostic tool and can be used to evaluate treatment response and direct treatment modalities.²⁹

The ESR is useful in determining chronic inflammation or infection. Ferritin is another acute-phase reactant. Elevated ferritin (in the absence of increased iron) may indicate an infectious, autoimmune, oncologic, or inflammatory process.³⁰ Some investigators have suggested that serum ferritin may be helpful in evaluation of FUO to distinguish between infectious and noninfectious causes. A serum ferritin value greater than 10,000 mg/mL is 90% sensitive and 96% specific for haemophagocytic lymphohistiocytosis (HLH).³¹

Chest radiographs should be performed if pulmonary symptoms are present or if there is concern for atypical bacterial infection, HIV, tuberculosis, or oncologic processes. Additional imaging techniques, particularly computed tomography (CT) scan and magnetic resonance imaging (MRI) are associated with various risks and should be performed cautiously. The CT scans are known to increase the risk of leukaemia and brain tumours, particularly in the paediatric population and MRI is

time-consuming and often requires sedation in young children.³²

Specific molecular testing for HIV, tuberculosis, or atypical bacterial pathogens and viral serologies are expensive and final results can be delayed days to weeks. These tests should be performed based on specific risk factors or suggestive physical findings.

A 2010 review also suggested a comprehensive metabolic profile including uric acid and lactate dehydrogenase and quantitative serum immunoglobulins.³³

If fever persists and laboratory studies and imaging fail to reveal the underlying cause, invasive procedures may be necessary. Bone marrow biopsy can be performed to evaluate for oncologic or haematologic aetiologies. Thoracentesis, joint aspiration, or biopsies may also be indicated to obtain fluid or tissue for analysis.

Management:

The ultimate treatment of FUO is tailored to the underlying diagnosis.

Fever and infection in children are not synonymous, and antimicrobial agents should only be used when there is evidence of infection, with avoidance of empirical trials of medication. An exception may be the use of anti-tuberculous treatment in critically ill children with suspected disseminated tuberculosis. Empirical trials of other antimicrobial agents may be dangerous and can obscure the diagnosis of infective endocarditis, meningitis, para-meningeal infection, or osteomyelitis.

After a complete evaluation, antipyretics may be indicated to control fever associated with adverse symptoms.³⁴

Outcome:

The outcome of FUO in children is determined by the underlying disease and to a lesser extent, by the rapidity of diagnosis. Diagnostic delay often results from failure to recognize helpful clues in a patient's history, although the mortality risk would seem uninfluenced, with the only exceptions of intra-abdominal abscesses, miliary tuberculosis, and disseminated fungal infections. However, when all diagnostic approaches are failing and the child's condition is stable, a careful ambulatory follow up might be a correct strategy to manage unresolved cases of FUO. For these paediatric patients, there is a general trend to consider their outcomes as favourable, with fever disappearing after 4-5 weeks and no sequels.¹⁹

Symptomatic treatment of FUO and significant organ/system dysfunction at the time of admission to the tertiary-care centre were the main risk factors leading to

poor outcome. In contrast, careful, repeated clinical evaluation and the use of specific laboratory examinations or imaging, when new symptoms occur were found crucial for the favourable out-come of childhood FUO.¹⁵

In many cases, no diagnosis can be established and fever abates spontaneously. In as many as 25% of children in whom fever persists, the cause of the fever remains unclear, even after thorough evaluation.³⁴

Conclusion:

Though fever is the most common presentation in childhood illness, in many cases, it becomes a difficult issue of handling, particularly, when it is prolonged in duration and undifferentiated in nature.

Even in today's high-tech era of medicine, FUO is one of those conditions in which the art of medicine is critical. Good communication between the clinician and the family and patient is often the key to success, and repeated history taking and physical examination by the old-fashioned diagnostician frequently becomes helpful.³⁵

Education about the indiscriminate use of antibiotics for any febrile presentation and familiarizing primary care physicians about the common causes of FUO is important in improving the diagnosis and management of FUO in developing countries.

Further review is needed to determine the aetiology, mortality and overall outcomes associated with pediatric FUO particularly in Bangladesh context.

Conflict of interest: none declared.

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- x. Units of measurement-** Measurements of length, height, weight and volume should be in metric units (meter, kilogram or litre) or their decimal multiples. Temperatures should be in Celsius. Blood pressures should be in millimeters of Mercury.
- xi. Abbreviations and symbols-** Use only standard abbreviations. Avoid abbreviations in the ‘Title’ of the manuscript. The spelled-out abbreviation followed by the abbreviation in parenthesis should be used on first mention, unless the abbreviation is a standard unit of measurement.

B.2.2. For Case Reports- Limit within 2,500 words including up to 30 references and up to 4 tables and figures- corresponding a maximum of 3 printed pages of the JMoMC. Divide text into an abstract, an introduction, the case presentation, discussion and conclusion. For using identifiable pictures of patients, provide patient’s informed consent for this publication, which includes his/her awareness of possible consequences after publication.

B.2.3. For Reviews- Limit within 6,000 words including up to 110 references and up to 6 tables and figures. Divide text into an abstract, an introduction that outlines the main themes, brief subheadings and/or an outline of important unresolved questions.

B.2.4. For Letters to Editor- Limit within 1,000 words including up to 5 references and up to 2 tables and figures- that corresponds to 1 printed page of the JMoMC.

C. Manuscripts management for JMoMC

C.1. Manuscript receive and management: Manuscripts are received throughout the year and a submitted manuscript is usually published and posted to the author within a highest of 9-months of submission. However, this timeline may be prolonged in cases of: (a) bad submission time (3-months before publication dateline, unless requested); (b) bad preparation (not followed appropriately the JMoMC requirements), (c) bad responses (failing to respond within set timeline and response is inadequate).

C.2. Stages and timelines of Management

C.2.1. Stage 1: Editorial Scanning (usually completed in 1st month of submission)

- a. Received papers are entered into receive register giving an ID and acknowledged;
- b. Editorial scanning- checked for appropriateness, integrity and plagiarism;
- c. Primary author response- sent to corresponding author for primary response.

C.2.2. Stage 2: Peer Review (usually completed in 2nd month of submission)

- a. Processed for Peer reviews (select Peer(s), sent to reviewers with timeline);
- b. Sent to corresponding author for responses with a timeline;
- c. Cross-check by Editorial staff for accommodation of the review comments.

C.2.3. Stage 3: Decision of Acceptance/ Rejection (usually completed within 3rd month of submission)

- a. Information of 'Acceptance'/ 'Rejection' communicated with the corresponding author;
- b. Accepted papers are processed for Pre-Press version and submitted to Printing Press;
- c. Decisions of rejections of the submissions are made in cases of serious violation of publication ethics including plagiarism, allegations of misconduct pre- and post-publication, authorship dispute, undisclosed conflict(s) of interest, research misconduct (fabricated study and data falsification), unethical practice during research, and duplicate publication.

(2) Stage 4: Publication (usually within 6th month of submission)

- a. Printed hard copies are distributed soon after publication (in no cost currently) to the faculty members of MoMC, Libraries of the BMDC-registered Medical/ Dental institutions in Bangladesh and the authors of the publications;
- b. **Usually 3-copies** of the published issue are sent for the authors of a publication to the address of communication of the corresponding author.

