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Author Guidelines

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A running title of less than 100 characters should be provided. In addition to the title of the article, the title page should include the names of the author(s) and the name and address of the institution or laboratory where the work was conducted. The complete address of the primary author or the author for correspondence to whom proofs will be delivered should be provided, along with the author's email account number.

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The abstract should not exceed 300 words and convey simply what was accomplished, the primary findings, and how the work was interpreted. The structure of the abstract should include context, objectives, materials and methods, results, and a conclusion. Case reports and review paper abstracts may not be structured. Three to five keywords pertinent to the topic should be listed beneath the abstract.

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- Conclude with a concise summary of the main purpose of the task and an evaluation of whether or not it was accomplished.

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Articles in journals

1. Hou WR, Hou YL, Wu GF, Song Y, Su XL, Sun B, et al. cDNA, genomic sequence cloning and overexpression of ribosomal protein gene L9 (rpL9) of the giant panda (Ailuropoda melanoleuca). Genet Mol Res. 2011;10: 1576-1588.
2. Devaraju P, Gulati R, Antony PT, Mithun CB, Negi VS. Susceptibility to SLE in South Indian Tamils may be influenced by genetic selection pressure on TLR2 and TLR9 genes. Mol Immunol. 2014 Nov 22. pii: S0161-5890(14)00313-7. doi: 10.1016/j.molimm.2014.11.005.

Chapter in a book

1. Hansen B. New York City epidemics and history for the public. In: Harden VA, Risse GB, editors. AIDS and the historian. Bethesda: National Institutes of Health; 1991. pp. 21-28.

Book

1. Thomas SHL, White J. Poisoning. In: Colledge NR, Walker BR, Ralston SH. Davidson's principles & practice of medicine. 22nd edn. London: Churchill Livingstone, 2014: 205-230.
2. Bates B. Bargaining for life: A social history of tuberculosis. 1st ed. Philadelphia: University of Pennsylvania Press; 1992.

Internet

1. Frontier Medical College Abbottabad, Pakistan. Available at: http://www.fmc.edu.pk/aboutus.php. Accessed October 2011.
2. Ferro JM, Canhao P. Etiology, clinical features, and diagnosis of cerebral venous thrombosis. Available at: https://wwwuptodate.com. Accessed August 2018.

Thesis/Dissertation

1. Wells A. Exploring the development of the independent, electronic, scholarly journal. M.Sc. Thesis, The University of Sheffield. 1999. Available from: http://cumincad.scix-.net/cgi-bin/works/Show?2e09

Scientific or technical report

1. Akutsu T. Total heart replacement device. Bethesda MD: National Institutes of Health, National Heart and Lung Institute; 1974 Apr Report No: NIH-NHLI-69-2185-4.

Accepted unpublished material

1. Khan MAH, Majumder I, Hoque MM, Fariduddin M, Mollah FH, Arslan MI. Lipid profile in hypothyroid patients: A cross-sectional study. Medicine Today. In press.

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EDITORIAL

Upcoming Challenges in Physiology in Bangladesh

By any measure, Bangladesh is at a physiological crossroads. The country is transitioning from a dominantly infectious-disease profile to the "double burden" of noncommunicable and climate-sensitive illnesses—while medical education, laboratories, and research funding race to keep up. For physiologists—teachers, researchers, and clinicians alike—the next decade will be defined by how effectively we align training and research with these shifting realities.

1) From pathogens to pressure: redefining priority systems

Noncommunicable diseases (NCDs) now shape morbidity, mortality, and household economics, demanding deeper emphasis on cardiovascular, respiratory, metabolic, neuro-endocrine, and renal physiology in both curricula and research. Recent analyses underscore how NCDs strain families with long-term medication costs and productivity losses, amplifying inequity.

At the same time, vector-borne diseases remain volatile. Large dengue waves and off-season transmission patterns require applied work on host–vector–environment interactions, endothelial permeability, hemodynamic instability, and immune kinetics—areas where physiologists should lead translational studies with public health partners.

2) Heat, humidity, and the climate physiology agenda

Pre-monsoon and urban heat events are becoming hotter and more frequent across South Asia, with Bangladesh among the most exposed. This translates into real-world physiology: thermoregulation failure, dehydration, renal stress, pregnancy risks, and performance limits for outdoor workers. We need locally grounded research on heat tolerance thresholds, hydration/ electrolyte strategies, cardiorespiratory load, and early-warning biomarkers—plus integration of heat-health into MBBS and allied health training.

3) Curriculum is evolving—practice must catch up

Bangladesh has adopted a community-oriented, competency-based MBBS curriculum with detailed learning objectives for physiology. The challenge now is implementation: reliable lab time, case-based integration across organ systems, and assessment that rewards reasoning over recall. Simulation, bedside physiology, and point-of-care measurement literacy (e.g., spirometry, ABG interpretation, autonomic testing) should become routine, not enrichment.

4) Labs, logistics, and the research squeeze

Sustained physiology research needs animal ethics capacity, cell and tissue culture, electrophysiology, and biostatistics support. Yet Bangladesh's gross R&D spending remains low by global standards—recent official estimates place GERD at roughly 0.30% of GDP—and universities face tight operating budgets. Competitive UGC grants and new oversight efforts are welcome, but program continuity, mentorship pipelines, and

shared core facilities will matter more than one-off projects.

5) Data deserts and the measurement problem

Physiology thrives on measurement. However, national science statistics (e.g., researchers per million, field-specific outputs) remain patchy, complicating planning for human resources and equipment. Bangladesh needs a transparent, regularly updated STI dashboard—linking UGC, BMDC, DGHS, and universities—so curriculum seats, lab investments, and postgraduate positions are driven by evidence rather than guesswork.

6) Antimicrobial resistance and diagnostic physiology

Strengthening AMR surveillance and laboratory capacity is now a WHO-flagged priority. Physiologists can add value beyond microbiology: host–pathogen interaction, fever regulation, drug pharmacodynamics in altered physiology (e.g., sepsis), and the cardiopulmonary consequences of severe infections—all critical to rational therapy and clinical trials.

7) Talent density and brain-gain strategies

The sheer number of medical colleges and MBBS seats has grown rapidly, but faculty depth in core physiological sciences hasn't kept pace. Nationally coordinated fellowships, protected time for research-active teachers, and international co-supervision models can improve both teaching quality and output—especially if linked to centers of excellence and shared instrumentation hubs.

8) Digital, AI, and point-of-care physiology

Bangladesh should leapfrog with low-cost digital labs and AI-assisted tools—virtual frog muscles are cheaper than chronic equipment outages. Priorities: (i) affordable data-acquisition kits for teaching labs; (ii) standardized repositories of normal values in Bangladeshi populations; (iii) clinical decision support that embeds physiological reasoning (e.g., shock pathways, acid–base). This is feasible if procurement and maintenance are centralized, and if faculty development includes coding, statistics, and open-science practices.

What to do next—five concrete steps

1. Name the agenda. Establish a national "Physiology for Bangladesh 2030" roadmap that ties curriculum, research themes (heat–work–heart; NCD integrative physiology; infection–immunity), and funding.
2. Back the basics. Ring-fence a portion of UGC/ministerial grants for core physiology labs, shared facilities, and technical staff across universities and medical colleges.
3. Measure what matters. Publish annual indicators: physiology faculty-to-student ratios, lab uptime, funded projects, and outputs—linked to incentives.
4. Teach at the bedside. Mandate integrated physiology "immersion weeks" with medicine/surgery/OBGYN to connect mechanisms to patients.
5. Climate-proof health. Build a national heat-health physiology consortium with DGHS and city corporations to translate lab findings into workplace and school protections.

Bangladesh has already modernized its curriculum and expanded medical training capacity. If we now invest in measurement, mentorship, and mission-driven labs, physiology can move from lecture halls to leading roles in the country's health transition.

References

1. Islam MT, et al. BMC Health Services Research (2025): Utilization patterns for NCD care in Bangladesh, highlighting system strain.

2. Chowdhury NMRA, et al. Exploring the effects of catastrophic health expenditure due to NCDs in Bangladesh (2025).

3. DGHS Dengue Dashboard (accessed Aug 31, 2025).

4. Outbreak News Today. “Bangladesh dengue cases top 30,000 for 2025” (Aug 2025).

5. Patwary MM, et al. Urban heat stress and perceived health impacts in Bangladesh (2025).

6. World Weather Attribution via AP News: Asia heatwave attribution findings (2024).

7. Bangladesh Medical & Dental Council—MBBS Curriculum (Front matter, 2020/21 update).

8. BMDC Physiology Syllabus PDF (Curriculum 2021).

9. Bangladesh Bureau of Statistics via The Business Standard: GERD 0.30% of GDP (FY2020–21) (May 27, 2024).

10. New Age: Public university budget and research line updates (FY2024–25).

11. Dhaka Tribune: UGC steps to monitor research funds at private universities (2025).

12. The Daily Star: Growth in medical colleges and MBBS seats (2024).

13. WHO Country profile, Bangladesh (2024–25): AMR/lab capacity priorities.

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ORIGINAL ARTICLE

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Variation in Number, Position, and Direction of Nutrient Foramen of Clavicle and Their Relationship with Side and Gender in Bangladesh

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Abstract

Background: *The clavicle is an atypical long bone of the pectoral girdle. The shaft of the clavicle usually presents one nutrient foramen for the passage of the nutrient artery which is the main source of artery supply of clavicle. The position, number, and direction of the nutrient foramen of the clavicle are not constant.* ***Objectives:*** *This study aimed to determine the variation in the number, position, and direction of the clavicle and their relationship with side and gender.* ***Methods:*** *This cross-sectional type of descriptive study was conducted over 1 year from January 2022 to December 2022 in the Department of Anatomy, Rajshahi Medical College, Rajshahi. This study was performed on 350 dry adult human clavicles (225 were male and 125 were female clavicles) which were collected from the students of the Department of Anatomy, Rajshahi Medical College, Rajshahi as well as other Medical Colleges after fulfilling the inclusion criteria. Data were collected purposively with the help of a semi-structured questionnaire. All the measurements were performed using a magnifying lens, guide wire, and 24-hypodermic needle (0.56 mm in diameter). Data were analyzed by SPSS software, version 24.0, and a p-value < 0.05 was considered statistically significant for all tests.* ***Results:*** *The study revealed that among 350 dry adult clavicles, 196 (56%) were right-sided and 154 (44%) were left-sided. 251 (71.70%) of the clavicles showed single foramen, 85 (24.30%) double, and 8 (2.30%) triple nutrient foramen. 359 (80.67%) of the nutrient foramina were on the posterior surface, 79 (17.75%) on the inferior surface, 5 (1.12%) on the superior surface, and only 2 (0.45%) on the anterior surface of the dry adult clavicles. All the nutrient foramina was directed towards the acromial end. The relationship of the position and number of neurovascular foramina between the right and left-sided and between the male and female adult human clavicles were found statistically non-significant (p > 0.05).* ***Conclusion:*** *Information about the nutrient foramen is of great clinical importance, especially in surgical procedures like microvascularised bone transplantation and bone grafting.*

Keywords: number, position, and direction of nutrient foramen.

Introduction

The clavicle or collarbone is the only long bone that lies more or less in the horizontal plane. It differs from the other long bones as it has no medullary cavity (1). The clavicle is an atypical long bone of the pectoral girdle and is subcutaneous throughout its length. It transmits the weight of the body from the appendicular skeleton to the axial skeleton. Most of the parts of the clavicle develop by intra-membranous ossification. Its lateral or acromial end forms the acromioclavicular joint so that the arm can swing easily away from the trunk (2). The bone has a cylindrical part called the shaft, with two ends, lateral and medial. The shaft is divided into the medial two-thirds and the lateral one-third (3). The medial two-thirds of the shaft is almost rounded and has four surfaces. The anterior surface is convex forward, and the posterior surface is smooth. The superior surface is rough in its medial part and the inferior surface has a rough oval impression at the medial end. The lateral half of the inferior surface has a longitudinal subclavian groove for insertion into the subclavius muscle. The nutrient foramen lies at the lateral end of the subclavian groove. The medial or sternal end articulates with the clavicular notch of the manubrium sterni to form the sternoclavicular joint. The articular surface of the medial end extends to the inferior aspect for articulation with the first costal cartilage (3).

The lateral third is flattened from above downward and has two surfaces, superior and inferior, limited by the anterior and posterior border. Close to the posterior border, at the junction of the lateral fourth with the rest of the bone, there is a prominent conoid tubercle which gives attachment to the conoid part of the coracoclavicular ligament (4). Lateral end bears a facet that articulates with the acromion process of the scapula to form the acromioclavicular joint.

Usually, the clavicle contains one nutrient foramen for the entry of the nutrient artery present in the shaft (5). The nutrient foramen is directed away from the growing end as a rule that is towards the acromial end of the clavicle. The nutrient artery is the key source of blood supply to a long bone which enters the shaft of the bone along with the nerves through the nutrient foramen during its growth period. The nutrient foramen develops naturally during the growth of the fetus. The nutrient artery originates from the clavicular branch of a suprascapular artery or acromiothoracic artery (6). In one study it was published that the clavicle is supplied by the periosteal arteries and is devoid of nutrient artery (7).

Moreover, it has great clinical importance as the clavicle is commonly fractured at the junction of the medial two-thirds and lateral one-third by falling on the outstretched hand. Nutrient artery is commonly originated from the artery which participates in the early invasion of the ossifying bone, in such a manner that the nutrient foramen is found at the actual center of ossification (8).

So, the nutrient artery is particularly vital during the active growth period and at the early phases of ossification. The position of the nutrient foramen and the direction of the nutrient canal in mammalian bones are variable and may alter during growth. Though there are variations in positions, number, and direction of nutrient foramina in clavicles there are limited studies on it in Bangladesh. This study aimed to determine the morphological and morphometric variations of neurovascular foramina of adult human clavicles in Bangladesh.

Methods

This cross-sectional descriptive study was conducted in the Department of Anatomy, Rajshahi Medical College over one year from January 2022 to December 2022. This study was performed on dry adult human clavicle bones which were collected from the students of the Department of Anatomy of Rajshahi Medical College as well as from the different Medical Colleges of Bangladesh after fulfilling the inclusion criteria. Howev-

er, damaged bones, malformed bones, and bones with congenital anomalies were excluded from the study. A total of 350 clavicles were included in the study by purposive sampling technique. Data were collected by a semi-structured questionnaire and the sex of clavicles was determined by observation of different sex determination variables. The number and position of nutrient foramen were determined by observation and their direction was measured by a guide wire and 24-hypodermic needle (0.56 mm in diameter). Independent samples t-test was used to determine the relationship of the position and number of neurovascular foramina between the right and left side and between the male and female adult human clavicles. A p-value less than 0.05 was found statistically significant for all tests.

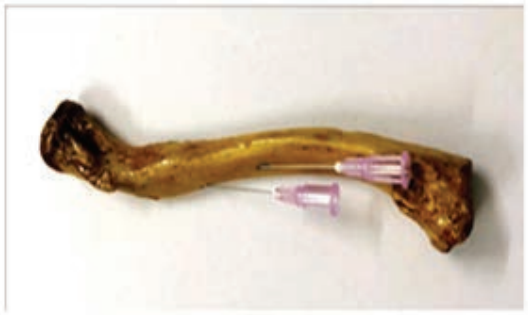


Fig 1: Double nutrient foramina.

Fig 2: Triple nutrient foramina.

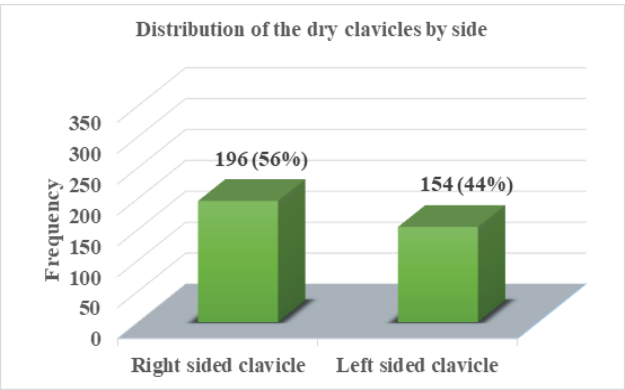
Fig 3: Nutrient foramina at the inferior surface.

Fig 4: Nutrient foramen at the posterior surface.

Results

Out of 350 dry adult clavicles, 196 (56%) were from the right side and 154 (44%) were from the left side (Figure I).

Figure I: Distribution of the dry clavicles according to side (n=350).



The position of the nutrient foramina of the clavicles revealed that 359 (80.70%) of the nutrient foramina were on the posterior surface, 79 (17.80%) on the inferior surface, 5 (1.10%) on the superior surface and 2 (0.40%) on the anterior surface (Table 1).

Table 1: Position of the nutrient foramina on the surface of clavicles (number of nutrient foramina=445).

Positions of the nutrient foramina	Frequency	Percentage
Posterior surface	359	80.70%
Inferior surface	79	17.80%
Superior surface	5	1.10%
Anterior surface	2	0.40%
Total	445	100%

Number of the nutrient foramina of the clavicles revealed that 251 (71.70%) clavicles contained single nutrient foramen, 85 (24.30%) double, 8 (2.30%) triple foramina and 6 (1.70%) were none (Table 2).

Table 2: Number of the nutrient foramina of the clavicles (n=350).

Number of the nutrient foramina	Frequency	Percentage
None	6	1.70%
Single nutrient foramen	251	71.70%
Double nutrient foramina	85	24.30%
Triple nutrient foramina	8	2.30%
Total	350	100%

All the nutrient foramina were directed toward the acromial end, and none was directed toward the sternal end of the dry adult human clavicles (Table 3).

Table 3: Direction of the nutrient foramen of the clavicles (number of nutrient foramina=445).

Direction of nutrient foramen	Frequency	Percentage
Acromial end	445	100%
Sternal end	0	0%
Total	445	100%

The difference in position of the neurovascular foramina between the right & left-sided adult human clavicles was found statistically non-significant ($p > 0.05$).

Table 4: Relationship of the position of the neurovascular foramina between the right & left-sided adult human clavicles (number of nutrient foramina=445).

Position of nutrient foramina	Right	Left	Total
	Frequency (%)		
Posterior surface	198 (55.15%)	161 (44.85%)	359 (80.70%)
Inferior surface	47 (59.49%)	32 (40.51%)	79 (17.80%)
Superior surface	3 (60%)	2 (40%)	5 (1.10%)
Anterior surface	1 (50%)	1 (50%)	2 (0.40%)
Total	249 (55.96%)	196 (44.04%)	445 (100.00%)

$\chi 2=0.56$, df=3, $p > 0.05$

The difference in the number of neurovascular foramina between the right & left-sided adult human clavicles was not statistically significant ($p > 0.05$).

Table 5: Relationship of the number of neurovascular foramina between the right & left-sided adult human clavicles (n=350).

Number	Right	Left	Total
	Frequency (%)		
None	2 (33.30%)	4 (66.70%)	6 (1.70%)
Single foramen	142 (56.60%)	109 (43.40%)	251 (71.70%)
Double foramina	49 (57.60%)	36 (42.40%)	85 (24.30%)
Triple foramina		5 (62.50%)	8 (2.30%)
Total	196 (56%)	154 (44%)	350 (100.00%)

The difference in position of the neurovascular foramina between the right & left-sided adult human clavicles was found statistically non-significant ($p > 0.05$).

Table 6: Relationship of the position of the neurovascular foramina between the male & female adult human clavicles (number of nutrient foramina=445).

Position of nutrient foramina	Male	Female	Total
	Frequency (%)		
Posterior surface	228 (63.50%)	131 (36.50%)	359 (80.70%)
Inferior surface	50 (63.29%)	29 (36.71%)	79 (17.80%)
Superior surface	4 (80.00%)	1 (20.00%)	5 (1.10%)
Anterior surface	2 (100.00%)	0 (0%)	2 (0.40%)
Total	284 (63.82%)	161 (36.18%)	445 (100.00%)

$\chi 2=1.73$, df=3, $p > 0.05$

The difference in number of the neurovascular foramina between the male & female adult human clavicles was not statistically significant ($p > 0.05$).

Table 7: Relationship of the number of neurovascular foramina between the male & female adult human clavicles (n=350).

Number	Male	Female	Total
	Frequency (%)		
None	3 (50.00%)	3 (50.00%)	6 (1.70%)
Single foramen	165 (65.70%)	86 (34.30%)	251 (71.70%)
Double foramina	52 (61.20%)	33 (38.80%)	85 (24.30%)
Triple foramina	5 (62.50%)	3 (37.50%)	8 (2.30%)
Total	225 (64.30%)	125 (35.70%)	350 (100.00%)

$\chi 2=1.12$, df=3, $p > 0.05$

Discussion

The clavicle is an atypical long bone characterized by many unique embryologic features. It is the first bone to ossify and its most part is intramembranous in origin. The clavicle possesses larger or smaller foramina (openings) for the entrance of blood vessels and nerves. The objective of this study was to assess the morphological and morphometric variations of neurovascular foramina of adult human clavicles in Bangladesh.

This study revealed that among 350 dry adult clavicles, 225 (64.30%) were male and 125 (35.70%) were female. In the distribution of the sides of the clavicles, 196 (56%) were from the right side and 154 (44%) were from the left side.

The position of nutrient foramina on the surface of clavicles showed by the present study that 359 (80.70%) of the nutrient foramina were on the posterior surface, 79 (17.80%) on the inferior surface, 5 (1.10%) on the superior surface and 2 (0.40%) on the anterior surface of the clavicles. Studies done by Tanna (3), Kumar et al. (9), Sowmiya and Sundarapandian (10), Sahu and Meher (11), and Joshi and Mathu (12) showed similar findings. Murlimanju et al. (1) where the foramen was found on the inferior surface of 29 (55.8%) clavicles, on the posterior surface of 36 (69.2%), and on the superior surface only 1 (1.9%) which was not consistent with this study.

In the present study, 251 (71.70%) clavicles showed single nutrient foramen, 85 (24.30%) double and 8 (2.30%) triple. On 6 (1.70%) clavicles no nutrient foramen was found. Nearly similar findings were seen in a research done by Keche et al. (13) where out of 67 clavicles, 44 (65.67%) showed single foramen and 22 (32.84 %) double. The study done by Joshi and Mathur (12) where out of 50 clavicles, 34 (68%) presented a single foramen and 16 (32%) double foramina which was consistent with the current study.

Furthermore, a study done by Murlimanju et al. (1) in India showed that the neurovascular foramina were observed in 50 (96.1%) clavicles and absent in 2 (3.9%). Single foramen was seen in 20 (38.5%) clavicles, double in 23 (44.2%), and triple in 7 (13.4%). Rai et al. (5), Tanna and Tanna (3), and Sahu and Meher (11)

reported that nutrient foramina were present in all of their study clavicles but the present study revealed that the nutrient foramina were found in 344 (98.30%) clavicles. Rai et al. (5), Tanna and Tanna (3), and Sahu and Meher (11) also observed that double foramina were found in more than 50% of clavicles which was nearly similar to this study.

Moreover, clavicles are supplied by the periosteal vessels when there is an absence of nutrient foramina (7) and the periosteal vessels become the sole source of blood supply where the nutrient foramen was absent.

All nutrient foramina were directed towards the acromial end, and none was directed to the sternal end of the dry adult human clavicles revealed by the present study. These findings were in accordance with the study done by Keche et al. (13) where all the nutrient foramina were directed towards the acromial end. Murlimanju et al. (1) showed that in 48 (96%) clavicles, the foramina were directed toward the acromial end, and in 2 (4%) clavicles, the foramina were directed towards the sternal end which was nearly similar to this study. Similar findings were also found in the studies done by several researchers (Rai et al. (5), Tanna and Tanna (3), Sahu et al. (11), Joshi and Mathur (12), Fischer and Carret (14), Havet et al. (15) and Kumar et al. (16)). Sowmiya and Sundarapandian (10) and Rekha et al. (17) found 4.8% and 4.79% of nutrient foramina directed towards the sternal end respectively which were not similar with the present study.

The middle third region of the clavicle is most involved in any type of injury and accounts for 5–10% of all fractures in adults. Havet et al. (15) described the arterial supply of the clavicle to clarify the pathological mechanism and the surgical procedure of non-unions. The periosteal vessel was always present on the superior surface and anterior border of the clavicle but never on the inferior surface or posterior border. The periosteal vessels located between the muscular insertions could be compromised in case of displacements or fractures.

So, the relationship of the position of the neurovascular foramina between the right & left-sided adult human clavicles was found statistically not-significant ($p > 0.05$). Keche et al. (13) also reported similar findings where the position of nutrient foramina on the surfaces of both sides was found statistically not significant ($p > 0.05$).

So, the relationship of the number of neurovascular foramina between the right & left-sided adult human clavicles was not statistically significant ($p > 0.05$). Similar findings were reported by Keche et al. (13) where the number of nutrient foramina on both sides was found statistically not significant ($p > 0.05$).

The information about the position, number, and direction of nutrient foramina is useful for surgeons performing surgical procedures like internal fixation, coracoclavicular ligament repair, transplant techniques, and bone grafting. The clinical knowledge of the nutrient foramina and its variations is important, as microvascular bone transfer is becoming more popular.

Conclusion

The clinical knowledge of the nutrient foramina and its variations are important, as microvascular bone transfer is becoming more popular where preservation of the circulation of the affected bone is of vital importance for facilitating graft healing in the recipient.

Limitations of the study

Limitations were data were collected from 6 medical colleges, a purposive sampling technique was selected and the sample size was only 350 which was small.

References

1. Murlimanju BV, Prabhu LV, Pai MM, Yadav A, Dhananjaya KVN, Prashanth KU. Neurovascular foramina of the human clavicle and their clinical significance. Surg Radiol Anat. 2011; 33 (8): 679–682.

2. Champatyray S, Nayak SR, Mishra T. Study of Neurovascular Foramina of the Human Clavicle and Their Clinical Significance. Annals of the Romanian

Society for Cell Biology. 2012; 25 (4): 14534-14541.

3. Tanna N, Tanna V. Anatomical variation in position, direction, and number of nutrient foramina in clavicles. Int J Med Sci Public Health. 2015; 4 (3): 357.

4. Standring, S.ed., 2016. Gray's Anatomy: The Anatomical Basis of Clinical Practice. 41st ed. London: Elsevier.

5. Rai R, Shrestha S, Kavitha B. Morphological and topographical anatomy of nutrient foramina in human clavicles and their clinical importance. IOSR-JDMS. 2014; 13 (1): 37-40.

6. Patel HG, Babariya D, Pensi CA. Nutrient foramina of dry human clavicle and their clinical significance. IJSR. 2014; 3 (11): 324-325.

7. Knudsen FW, Andersen M, Krag C. The arterial supply of the clavicle. Surg Radiol Anat. 1989; 11 (3): 211–214.

8. Malukar O, Joshi H. Diaphysial nutrient foramina in long bones and miniature long bones. Lateral. 2011; 2 (2): 23-26.

9. Kumar D, Raichandani L, K Kataria S, Singh J. Variation in number and position of nutrient foramen of clavicle – A morphological study in western Rajasthan. IJASHNB. 2019; 5 (3): 67–71.

10. Sowmiya G, Sundarapandian S. Neurovascular foramina of the human clavicle and their clinical significance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2016; 7 (6): 2634-2640.

11. Sahu S, Meher D. Morphological and topographical anatomy of nutrient foramina in human clavicles of Eastern Odisha. International Journal of Applied Research. 2017; 3 (4): 521-523.

12. Joshi P, Mathur S. A comprehensive study of nutrient foramina in human lower limb long bones of the Indian population in Rajasthan state. … Journal of Health Sciences and Research. 2018; 3 (3): 36-42.

13. Keche HA, Thute PP, Fulmali DG, Keche AS. Morphometric study of nutrient foramina in dry human clavicles in central India. jemds. 2021;10 (28): 2099–2103.

14. Fischer LP, Carret JP. [Arterial vascularization of human bones]. Bull Assoc Anat (Nancy). 1978; 62 (179): 419–452.

15. Havet E, Duparc F, Tobenas-Dujardin AC. Vascular anatomical basis of clavicular non-union. Surgical and Radiological Anatomy. 2008; 30 (1): 23-28.

16. Kumar R, Madewell JE, Swischuk LE, Lindell MM, David R. The clavicle: normal and abnormal. Radiographics. 1989; 9 (4): 677–706.

17. Rekha S. Morphometric study of nutrient foramen in dry human clavicle bones of Jammu Region. International Journal of Research and Analytical Reviews. 2019; 6 (1): 413x-416x.

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Pattern of Histological Types of Breast cancer in Bangladeshi women

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Abstract

Background: *Carcinoma of breast has become the major public health problem among females in developing as well as developed countries.* ***Objective:*** *Because of the lack of awareness in Bangladeshi population and inadequate access to health care, most patients are diagnosed at an advanced stage of the disease. Early detection has a crucial impact on overall treatment outcomes.* ***Materials and methods:*** *This cross-sectional descriptive study was carried out in the Department of Biochemistry of DMC in collaboration with the department of oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU) and department of radiology of Dhaka medical college and hospital from January 2022 to December 2022 after getting formal approval from the Institutional Review Board (IRB) of DMC.* ***Result:*** *In this study among 68 patients, 64 (94.11%) patients were diagnosed with invasive ductal carcinoma.* ***Conclusions:*** *Regarding the investigation of this study, significant and insignificant factor's parallel visualization with breast cancer will be supportive to increase awareness, screening and early detection of breast cancer among Bangladeshi women as well as all over the world. This preventive strategy could be a model for other resource-limited developing countries.*

Keywords: *Breast cancer, awareness, invasive ductal carcinoma, developing country.*

Introduction

Breast cancer is the most common malignancy in women around the world and its incidence is rising particularly in developing countries. According to GLOBOCAN, it is the most common cancer in women, accounting for 25.1% of all cancers (1). Worldwide, it is estimated that more than one million women are diagnosed with breast cancer every year and more than 400,000 will die from the disease (2). The significance of breast cancer as a disease is with high incidence and death rate is really bold in developing countries. It is estimated that 45% of the 1.35 million new cases diagnosed each year and more than 55% of breast cancer related deaths, occur in low and middle income countries (2). In low- and middle-income countries, the infrastructure and resources for routine screening mammography are often unreachable. In such countries, breast cancer is usually diagnosed at late stages and due to insufficient resources, women with breast cancer may receive inadequate treatment or palliative care. So it's necessary to increase the doctors and awareness among all population both rural and urban areas in Bangladesh. The awareness can be increased to provide the proper knowledge about factors those are associated with breast cancer (3).

In Bangladesh, none of the breast cancer cases is discovered by organized screening. Almost all breast cancer cases are detected clinically. Breast cancer can be detected at earlier stages by simple self-examination of the breasts (4), but most of the patients (more than 90%) seek medical attention at advanced stages: i.e., stages III and IV (5, 6) in Bangladesh and over 63% of the patients (n = 987) had grade III tumors (7). The objective of this study was to identify histological variations in Bangladeshi female patients with breast cancer, thus it will help to understand the histological type of breast cancer among Bangladeshi female patients and will create a social awareness among the population.

Materials and Methods

This was a cross-sectional study, the sampling technique was convenient and carried out in the Medicine OPD, Ad-din Akij Medical College Hospital, and Khulna from January 2022 to June 2022. We included those who reported having diabetes for 6 months or more regardless of taking oral hypoglycemic agents or insulin. Patients were diagnosed as type 2 diabetic by their primary physicians. We excluded subjects with other chronic illnesses like hypertension, chronic kidney and liver disease, those who were pregnant, and anyone taking lipid-lowering drugs. In this way, a total number of 220 patients were enrolled at first. After fulfilling inclusion and exclusion criteria finally, 110 patients aged 30 years or above were taken as the study population. Blood samples were collected and the serum lipid profile was estimated by Autoanalyzer. SPSS, Microsoft Excel, and Microsoft Word were used in this study.

Both male and female patients aged over 30 years and have a diagnosis of type 2 DM were included in the study. A written consent was obtained from each patient, using an informed consent form. The research was conducted in full compliance with ethical principles.

Results

In this study among 68 patients, 64 (94.11%) patients were diagnosed with invasive ductal carcinoma followed by 2 patients were diagnosed with ductal carcinoma in situ & 2 patients were diagnosed with metastatic carcinoma. Most of patients had positive family history of breast cancer (94%) as well as oral contraception (47.1%).

TABLE I: Age and BMI distribution of the study subjects (N=68)

Variables	Mean ± SD
Age (years)	43.71 ± 9.84
BMI (kg/m^2)	23.95 ± 3.38

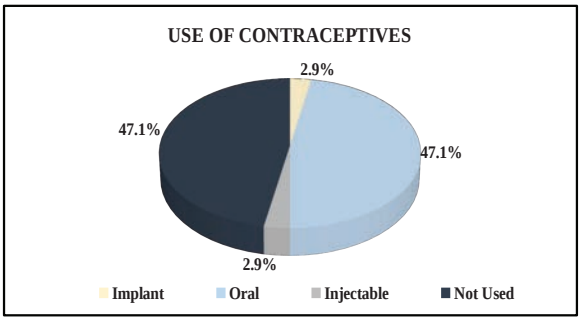

Figure 1: Pie diagram showing different types of Contraceptives used by the study subjects and their respective percentage (%).

Table II: Family history of breast cancer of the study subjects (N=68)

Family history of breast cancer	Frequency (n)	Percentage (%)
Yes	4	6
No	64	94

Table III: Incidence of various histologic types of breast neoplasm

Type of neoplasm	Number of cases	Percentages
Invasive ductal carcinoma	64	94.11%
Ductal carcinoma in situ	2	2.94%
Metaplastic carcinoma	2	2.94%

Discussion

The report of World Health Organization (WHO) is also published that the death rate of breast cancer in Bangladesh is high and ranked in 2nd position all over the world (3). A maternal health survey estimated that cancer was responsible for 21% of all women's deaths in the reproductive age range (8). Another verbal autopsy study showed that 62% of all deaths associated with breast cancer were in women under 50 years old (9). In our study, invasive ductal carcinoma was the most commonly observed histological type of breast cancer with 64 cases (Table III). This was similar to another study conducted, where majority cases (75%) were invasive ductal carcinoma (10). Another study conducted in china, where 94.79% cases were invasive ductal carcinoma (11). In Bangladesh, approximately 95% of all breast cancers are invasive ductal carcinomas (12) which is also supportive to our study result and over 63% of the patients (n = 987) had grade III tumors (12).

In the present study, the mean± SD age of the study group was 43.71 ± 9.84 years. Similar study was conducted by Duzkale and Kandemir, 2021 where the age of diagnosis of the patient group was 40.86 ± 10.28 years (13). In the present study, there was 64 patients, who had no family of breast cancer and only 4 patients had been found positive for family history of breast cancer. Another study found only 4.34% of breast cancer patients with positive family history in the Bangladeshi population (14). The frequency of positive family history had been found low in the studies of Bangladesh. One hypothesis could be made for the low frequency of positive family history in the present study is that they might be unaware of the presence of cancer in their family members as the disease remained undiagnosed. In this study the percentage of oral contraceptive use was 47.1 % and the percent-

ages of patients who had never use any contraception was 47.1 %, which is consistent with the study of Phipps et al. (15) they reported oral contraceptive use were not associated with some specific subtype of breast cancer. Asian countries, the life expectancy of Bangladeshi women has increased significantly in recent years from 59 years in 1990 to 70 years in 2011 (9). The emergence of a tumor or apparent sore during the early stages of breast cancer is often disregarded because of the low level of awareness among the general public. In addition, there may be other barriers that prevent women from seeking medical attention, such as the high cost of care, the agony of societal stigmatization, poor diagnostic facilities, and a lack of confidence in the current healthcare systems. Families and communities need healthy women to be well.

Although Bangladesh has made enormous progress in the healthcare sector – especially related to infectious diseases, as recently highlighted by Lancet (16). Bangladesh, burdened with a huge population, is facing a severe shortage of human resources for health. No national health insurance system exists in Bangladesh. While over 70% of the population live in rural areas (17), most of the secondary and tertiary healthcare facilities are centered in urban areas. Community hospitals are generally overcrowded and lack elementary resources, including equipment and essential drugs. In contrast, private clinics and hospitals are relatively well equipped, but these are financially out of reach for most Bangladeshis. In the case of Bangladesh, the existing country-wide network of community-based primary healthcare infrastructure would be very beneficial for raising breast cancer awareness and early detection.

Conclusion

Despite of some limitations such as the purposefully chosen institution and relatively small sample size, this study has given us a foundational understanding that invasive ductal carcinoma is the most common histological type of breast cancer.

References

1. Ghoncheh M, Pournamdar Z, Salehiniya H. Incidence and mortality and epidemiology of breast cancer in the world. Asian Pacific journal of cancer prevention. 2016; 17(S3):43-6.

2. Tfayli A, Temraz S, Abou Mrad R, Shamseddine A. Breast cancer in low-and middle- income countries: an emerging and challenging epidemic. Journal of oncology. 2010; 2010:1-5.

3. Ahmed K, Asaduzzaman S, Bashar MI, Hossain G, Bhuiyan T. Association assessment among risk factors and breast cancer in a low income country: Bangladesh. Asian Pacific Journal of Cancer Prevention. 2015; 16(17):7507-12.

4. Özaras G, Durualp E, Civelek FE, Gül B, Ünsal M. Analysis of breast self-examination training efficiency in women between 20–60 years of age in Turkey. Asian Pac J Cancer Prev. 2010; 11(3):799-802.

5. Mohiuddin M, Gafur MA, Karim MR, Khan SA, Hoque MM, Islam MS, Ali MS. Clinicopathological stages of carcinoma breast patient. Mymensingh medical journal: MMJ. 2012; 21(2):238-45.

6. Story HL, Love RR, Salim R, Roberto AJ, Krieger JL, Ginsburg OM. Improving outcomes from breast cancer in a low-income country: lessons from Bangladesh. International journal of breast cancer. 2012; 2012: 1-9.

7. Mostafa MG, Larsen MT, Love RR. Estrogen receptor, progesterone receptor, and Her- 2/neu oncogene expression in breast cancers among Bangladeshi women. Journal of Bangladesh College of Physicians & Surgeons. 2010; 28(3):157.

8. National Institute of Population Research, Training (Bangladesh), Mitra and Associates (Firm), Macro International. Institute for Resource Development. Demographic, Health Surveys. Bangladesh demographic and health survey. National Institute of Population Research and Training (NIPORT). 2011; 3(1): 43-53

9. Hossain MS, Ferdous S, Karim-Kos HE. Breast cancer in South Asia: a Bangladeshi perspective. Cancer epidemiology. 2014; 38(5):465-70.

10. Pathak R, Jha A, Neupane PR, Chalise S, Basnyat AS. Histopathological evaluation of carcinoma of breast. Journal of pathology of Nepal. 2016; 6: 922-927.

11. Han Y, Wang J, Xu B. Clinicopathological characteristics and prognosis of breast cancer with special histological types: a surveillance, epidemiology, and end results database analysis. The Breast. 2020; 54:114-20.

12. Mostafa MG, Larsen MT, Love RR. Estrogen receptor, progesterone receptor, and Her-2/neu oncogene expression in breast cancers among Bangladeshi women. Journal of Bangladesh College of Physicians & Surgeons. 2010; 28(3):157.

13. Duzkale N, Kandemir O. The Relationship of Mutation Carriage of BRCA1/2 and Family History in Triple-Negative Breast Cancer: Experience from a Diagnostic Center in Turkey. European Journal of Breast Health. 2021; 17(2):137.

14. Bhattacharjee A, Hossain AF, Yeasmin S, Akter T. Incidence, epidemiology and clinico-pathological status of different molecular subtypes of breast cancer in NICRH, Dhaka. Delta Med Col J. 2018; 6:9-17.

15. Phipps AI, Chlebowski RT, Prentice R, McTiernan A, Wactawski-Wende J, Kuller LH, Adams-Campbell LL, Lane D, Stefanick ML, Vitolins M, Kabat GC. Reproductive history and oral contraceptive use in relation to risk of triple-negative breast cancer. Journal of the National Cancer Institute. 2011; 103(6):470-7.

16. Das P, Horton R. Bangladesh: innovating for health. The Lancet. 2013; 382(9906):1681-2.

17. CIA. The world factbook; 2014, https://wwwciagov/library/publications/theworld- factbook/geos/bgh

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Screening of Accompanying First Degree Relatives of Patients with Primary Open Angle Glaucoma

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Abstract

Introduction: *Glaucoma is one of the common causes of blindness worldwide, and the leading cause of irreversible blindness. First-degree relatives of POAG patients have 4–16% risk of developing POAG. Though poorly understood, primary open angle glaucoma (POAG) is believed to have a genetic or familial component that may occur through polygenic or multifactorial transmission.* ***Objective:*** *To assess the screening of accompanying first degree relatives of patients with primary open angle glaucoma.* ***Methods:*** *The authors performed a hospital-based cross- sectional study at a Department of Ophthalmology, Ad-din Akij Medical College, Khulna & Bangladesh Eye Hospital, Khulna, Bangladesh from July to December 2022. A total of 60 first degree relatives of POAG patients were included in the study. All first-degree family members of POAG patients who accompanied them to the glaucoma clinic underwent a full ophthalmic examination. The optic disc was evaluated and intraocular pressure (IOP) was measured. POAG and glaucoma suspect were defined as per ISGEO classification.* ***Results:*** *60 first degree relatives of 52 glaucoma patients were examined. The mean age was 30.67 years (±12.71). 54 (90.0%) of 60 of accompanying first degree relatives were off springs, 6 (10.0%) were siblings. 5 out of 60 (8.3%) were diagnosed as glaucoma and started on anti-glaucoma medication. 14 (23.3%) were glaucoma suspects. 41 (68.4%) of the participants had no sign of glaucoma.* ***Conclusion:*** *Ocular examination of the first-degree relatives accompanying POAG patients helped to identify a remarkable number of individuals with glaucoma and thus might be used as an effective and viable tool for screening glaucoma in a hospital setting. Awareness regarding glaucoma is very low even among the first degree relatives of glaucoma patients.*

Keywords: Awareness, Glaucoma, POAG, Relatives.

Introduction

Glaucoma is one of the common causes of blindness worldwide, and the leading cause of irreversible blindness (1). First-degree relatives of POAG patients have 4–16% risk of developing POAG. Given the circumstances and the prevalence of POAG in first degree relatives of POAG patients, screening the first degree relative/s accompanying the patient to the hospital can be a cost effective and viable tool for glaucoma screening that will not add any extra cost of travel and accommodation. An estimated 57.5 million people worldwide are affected by open angle glaucoma with a global prevalence of 2.2% (2). Primary OAG is a chronic optic neuropathy, which occurs with an open angle in the absence of other explanatory causes. Primary open-angle glaucoma (POAG) has a genetic or familial component. It is believed that the genetic influence occurs through polygenic or multifactorial transmission. Reportedly, 5–50% of cases of POAG are hereditary, with the best estimate being 20–25%. The risk of developing POAG in first-degree relatives is 4–16% (3-5). The disease has a hereditary component and becomes more prevalent with age. POAG progresses very slowly and is usually asymptomatic until late in its course, so affected individuals can develop severe damage before they seek professional help. POAG has been shown to be more prevalent in first-degree relatives, so their screening for glaucoma is important. Various studies have reported different prevalence depending on the population sampled, the age of the individuals studied, the techniques of examination, and the definitions of glaucoma used. Although there is no standard definition, current criteria require the presence of visual field and optic disc damage, regardless of intraocular pressure (IOP) (6). Though poorly understood, POAG has genetic of familial component that may occur through polygenic or multifactorial transmission (7, 8). Reportedly, 5–50% of cases of POAG are hereditary, with the best estimate being 20–25% and the risk of developing POAG in first-degree relatives is 4–16% (9-11). Likewise, the relative risk of developing POAG in a population with a positive family history is 9.2 (12). Many studies suggest that approximately 5% of POAG results from mutations in the myocilin (MYOC) gene, and thus individuals predisposed to the development of POAG can be identified to some extent (9,13,14). However routine genetic screening for the mutation is not feasible in a developing country like ours. Given the circumstances and the prevalence of POAG in first degree relatives of POAG patients, screening the first degree relatives can be a cost effective way of diagnosing the disease in its early stage. We performed this study to investigate whether screening the first degree relative accompanying the glaucoma patient to the hospital may be a viable tool for glaucoma screening.

Materials and Methods

The authors performed a hospital-based cross- sectional study at a Department of Ophthalmology, Ad-din Akij Medical College, Khulna & Bangladesh Eye Hospital, Khulna, Bangladesh from July to December 2022. A total of 60 first degree relatives of POAG patients were included in the study. All first-degree family members of POAG patients who accompanied them to the glaucoma clinic underwent a full ophthalmic examination. The optic disc was evaluated and intraocular pressure (IOP) was measured. POAG and glaucoma suspect were defined as per ISGEO classification. Data entry and statistical analysis was done using Statistical Package for the Social Sciences (SPSS version 21).

All the people who were accompanying POAG patients to the glaucoma department were asked about their relationship with the patients and only the first degree relatives were included in the study after their consent. Ophthalmic history was obtained from the participants who accompanied the glaucoma patients to the glaucoma clinic. They were asked if they had heard about glaucoma. An answer of "yes" indicated that the subject was "aware" of glaucoma. Participants were interviewed regarding past history of any ocular examination and any history of examination related to glaucoma and its treatment. They then underwent a full ophthalmologic examination. The study excluded relatives of patients with closed or narrow angles and secondary glaucoma. Slit lamp biomicroscopy with a Volk's 90 D lens was used to examine the optic disc, and Goldmann applanation tonometry was used to assess the intraocular pressure (IOP). Cases with IOP under 21 mmHg without medication and absence of typical glaucomatous optic disc changes were classified as normal (N) and advised for annual follow up. Participants having IOP more than or equal to 21 mmHg in either eye, or CDR asymmetry of more than 0.2, or having CDR ≥0.6 without typical glaucomatous optic disc damage or visual field change were referred for visual field test (Sita Standard automated static perimetry 24-2 program on the Humphrey Visual Field Analyzer [Zeiss- Humphrey Systems, Dublin, CA]). Visual field results were analysed by three experienced Glaucoma specialist for the presence of any glaucomatous visual field changes. POAG and glaucoma suspect was defined as per ISGEO classification.

Results

A total of 60 first degree relatives of POAG patients were included in the study, among which 28 (46.6%) were female and 32 (53.4%) were male. The mean age of the cases was 30.67±12.71years. The mean age in case of females was 32.86 ±14.52 years, while that in case of male was 28.82 ± 10.84 years. 54 (90.0%) out of 60 accompanying first degree relatives were off springs and 6 (10.0%) were siblings. Out of 60 participants only 20 (33.3%) had their eyes checked up in the past and among which 2 (3.3%) had their eyes evaluated for glaucoma and also had their IOP measured with GAT. None of the participants were diagnosed with cases of glaucoma and thus none of them were under any type of anti-glaucoma medication. Out of 60 participants only 8 (13.33%) were aware of glaucoma. Among all the participants, 5 (8.2%, 3 female and 2 male) cases had optic disc and visual field changes supportive of glaucomatous damage and were diagnosed as glaucoma and started on glaucoma medication. Out of these 5 cases, 3 were offsprings and 2 were siblings. 13 participants (21.6%, 6 female and 7 male) were diagnosed as glaucoma suspects, among which, 12 were offsprings. 40 participants (66.6%) had no signs of glaucoma.

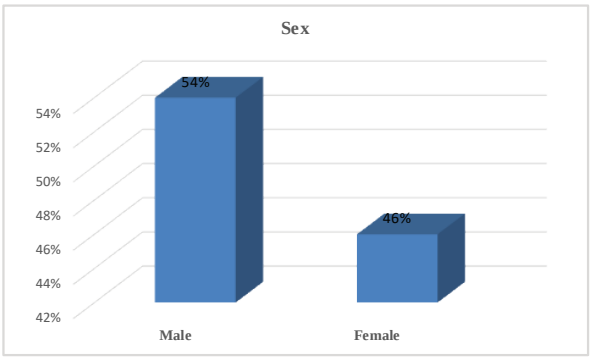

Fig-1: Sex distribution of the patients.

Table-1: Subjects already diagnosed as glaucoma and glaucoma suspects.

participants	N	%
First Degree	50	83.4%
Siblings	10	16.6%

Table-2: Glaucoma and glaucoma suspects their eyes checked.

IOP measured with GAT	N	%
Past IOP	20	33.3%
GAT	02	3.3%

Discussion

Family history is one of the important risk factors for the development of POAG [9, 10]. Since the visual field loss from glaucoma is irreversible, early detection and treatment is the only way to limit the damage from the disease. However, there is no proven feasible community based screening for detecting glaucoma established till date. Thus, this study was focused on screening a target population that comprised the first degree relatives of POAG patients who accompanied them to the glaucoma clinic. In our study, 8.25% of the participants had glaucoma, which is much higher than the prevalence (1.24%) of open angle glaucoma reported in the Bhaktapur glaucoma study Thapa et al. (15). This may be due to the inclusion of only first degree relatives of POAG patients in our study while the Bhaktapur glaucoma study was a population based study. The mean age of the participants in our study was 30.67 years (±12.71%), while that in the Bhaktapur glaucoma study was 55.4 ±12.3 years. Despite their young age, the Barbados family study revealed that about a quarter of the relatives had OAG or suspected OAG Leske et al. (10). In our study, it was found that 35.8% of patients diagnosed with POAG before the age of 50 years had positive family history as compared to only 11.7% in patients older than 70 years (16). Findings from these studies are consistent with our finding, suggesting that screening first degree relatives might help in early diagnosis of glaucoma. Vegini et al. (11) reported the prevalence of glaucoma in first degree relative as 16.8%. The Glaucoma inheritance study from Tasmania included 442 relatives of glaucoma patients and reported the prevalence as 18% McNaught et al (9). Likewise in another study Kong et al. (17) of 531 first-degree relatives, 67 (12.62%) were identified to have POAG, a rate eight times higher than that of the control group (8 of 526, 1.52%). All of these studies showed a higher prevalence of glaucoma than our study that may be attributed to the higher mean age of the participants in these studies; which was: 54 years McNaught et al. (9) 48.2 years old (±11.15) Vegini et al. (11) and 58.53 (±13.70) Kong et al. (17). In our study 23% of the participants were classified as glaucoma suspects, which is similar to the findings (30%) by Gupta P et al. (18). The higher prevalence of glaucoma suspects in first degree relatives suggests future risk of developing POAG in the participants. In our study among 5 (8.2%, 3 female and 2 male) cases had optic disc and visual field changes supportive of glaucomatous damage and were diagnosed as glaucoma and started on glaucoma medication. Despite accompanying a glaucoma patient to the glaucoma clinic, only 14.75% of the participants were aware of glaucoma in our study. Thus, relatives of glaucoma patients are more likely to be aware of glaucoma than the general population in Bangladesh, however, this percentage is still much lesser compared to the findings of other studies done in developed countries. Studies done in developed countries observed much higher awareness in relatives of glaucoma patients, 79% in the general population Livingston, McCarty and Taylor et al. (19) and 82% in the relatives Celebi AR et al. (20), which was attributed to higher levels of education. The lower observed awareness level in our study may be due to the

lower level of education in our society. The level of education however was not analysed in this study. This suggests that the family members of the glaucoma patients still lack awareness regarding glaucoma and the importance of glaucoma evaluation among them. Our study has few limitations. We included only accompanying first degree relatives, thus a large number of relatives might have been left out. We also did not study other risk factors except for being a first degree relative in the study. The reasons why not all first-degree relatives could be included were: migration of relatives to different cities, inability to come to the hospital for examination, and lack of interest for the examination. This again projects the difficulty in screening all first-degree relatives of glaucoma patients. Furthermore, we compared our results mostly with non-Asian countries, which may also account for a difference in prevalence rates. This shows the lack of awareness about increased hereditary risk of glaucoma among the general population. Although the subjects were aware of the fact that their relative had glaucoma, they did not know that they were at increased risk and needed to undergo glaucoma screening. Our study emphasizes the need for screening first-degree relatives of patients with POAG/NTG. Selective screening of first-degree relatives of POAG/NTG patients helps in early disease diagnosis. We also need a large population-based study to find out the prevalence rates of glaucoma in relatives of glaucoma patients among the Bangladeshi population.

Conclusion

Ocular examination of the first-degree relatives accompanying POAG patients helped to identify a significant percentage of individuals with glaucoma and thus might be used as an effective and viable tool for screening glaucoma in a hospital setting. Awareness regarding glaucoma is very low even among the first degree relatives of glaucoma patients.

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References

1. Flaxman SR. Global causes of blindness and distance vision impairment 1990–2020: a systematic review and meta-analysis. The Lancet Global Health. 2017; 5(12):1221–1234. doi: 10.1016/S2214-109X (17)30393-5.

2. Wiggs JL and Pasquale LR. Genetics of glaucoma. Human Molecular Genetics. 2017; 26(1):21–27. doi: 10.1093/hmg/ddx184.

3. McNaught AI, Allen JG, Healey DL. Accuracy and Implications of a Reported Family History of Glaucoma: Experience from the Glaucoma Inheritance Study in Tasmania. Arch Ophthalmol. 2000;118(7): 900-904.

4. Leske MC, Nemesure B, He Q, Wu SY, Fielding Hejtmancik J, Hennis A. Patterns of open- angle glaucoma in the Barbados Family Study. Ophthalmology. 2001;108(6):1015-1022.

5. Vegini F, Figueiroa Filho N, Lenci RF, Garcia Neto D, Susanna Junior R. Prevalence of open angle glaucoma in accompanying first degree relatives of patients with glaucoma. Clinics (Sao Paulo). 2008;63(3):329-332 doi: 10.15900/S1807-59322008000300007.

6. Foster PJ. The definition and classification of glaucoma in prevalence surveys. The British Journal of Ophthalmology. 2002; 86(2): 238–242. doi: 10.1136/bjo.86.2.238.

7. Lichter PR. Genetic clues to glaucoma's secrets. The L Edward Jackson Memorial Lecture. Part 2. American Journal of Ophthalmology. 1994; 117(6): 706–727. doi:

10.1016/s0002-9394(14)70314-9.

8. Quigley HA. The search for glaucoma genes--implications for pathogenesis and disease detection. The New England Journal of Medicine. 1998; 338(15):1063–1064. doi: 10.1056/NEJM199804093381511.

9. McNaught AI. Accuracy and implications of a reported family history of glaucoma: experience from the Glaucoma Inheritance Study in Tasmania'. Archives of Ophthalmology. 2000; 118(7):900–904.

10. Leske, MC. Patterns of open-angle glaucoma in the Barbados Family Study. Ophthalmology. 2001; 108(6):1015–1022. doi: 10.1016/s0161-6420(01)00566-8.

11. Vegini F. Prevalence of open angle glaucoma in accompanying first degree relatives of patients with glaucoma. Clinics. 2008; 63(3):329–332. doi: 10.1590/S1807-59322008000300007.

12. Wu J. Disease severity of familial glaucoma compared with sporadic glaucoma', Archives of Ophthalmology. 2006; 124(7):950–954. doi: 10.1001/archopht.124. 7.950.

13. Wiggs JL. Prevalence of mutations in TIGR/Myocilin in patients with adult and juvenile primary open-angle glaucoma. American Journal of Human Genetics. 1998; 63(5):1549–1552. doi: 10.1086/302098.

14. Frezzotti R, Renieri A, & Frezzotti P. Adult-onset primary glaucoma and molecular genetics: a review. European journal of ophthalmology. 2004; 14(3): 220–225. doi: 10.1177/112067210401400306

15. Thapa SS. Results of the Bhaktapur Glaucoma Study, Nepal', Nepalese journal of ophthalmology: a biannual peer-reviewed academic journal of the Nepal Ophthalmic Society: NEPJOPH. 2013; 5(1):81–93. doi: 10.3126/nepjoph. v5i1.7832.

16. Budde WM and Jonas JB. Family history of glaucoma in the primary and secondary open-angle glaucomas', Graefe's Archive for Clinical and Experimental Ophthalmology. 1999; 237(7):554–557. doi: 10.1007/ s004170050278.

17. Kong, X. Familial aggregation of primary open angle glaucoma in Shanghai, China. Molecular Vision. 2013; 19:1859–1865.

18. Gupta P. Prevalence of glaucoma in first-degree relatives of patients with primary open-angle glaucoma and normal-tension glaucoma. Asian Journal of Ophthalmology. 2018; 16(2):95–100. doi: 10.35119/asjoo. v16i2.374.

19. Livingston PM, McCarty CA and Taylor HR. Knowledge, attitudes, and self-care practices associated with age related eye disease in Australia. The British Journal of Ophthalmology. 1998;82(7):780–785. doi: 10.1136/ bjo.82.7.780.

20. Celebi A R C. Knowledge and Awareness of Glaucoma in Subjects with Glaucoma and their Normal First- Degree Relatives. Medical Hypothesis, Discovery and Innovation in Ophthalmology. 2018;7(1):40–47.

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Outcome of Cholecystectomy in AAMCH

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Abstract

Introduction: *Laparoscopic cholecystectomy is the gold standard treatment of Gall stone disease. It is the most used surgical procedure worldwide. The aim of the study was to analyze the outcome of the patients who had undergone cholecystectomy in AAMCH.* ***Materials and Methods:*** *This is a retrospective study which was conducted at Ad-din Akij Medical College, Khulna from August 2022 up to July 2023. This study analyzed among 381 patients 20-65 years old diagnosed with gallstone disease undergone laparoscopic cholecystectomy , open cholecystectomy and laparoscopic cholecystectomy converted to open cholecystectomy. This study was focused on the number of patients who were operated each month and their postoperative complications, duration of hospital stay, co-morbidities and prevalence of age and sex.* ***Result:*** *We analyzed total number of 381 patients among them 321(83.7%) undergone laparoscopic cholecystectomy, 52(13.5%) of them undergone open cholecystectomy and 10(2.9%) of them undergone laparoscopic cholecystectomy converted to open cholecystectomy. Most of the patients were female 217(56.9%). Highest number of patients 53(12.9%) were operated in July, 2023. lowest number of patients 13(3.4%) were recorded in the month of April, 2023. Patients' comorbidities were hypertension (15%), Diabetes mellitus (5%), hypothyroidism (1.5%), asthma (1%). Laparoscopic cholecystectomy resulted in less postoperative complication (2.3%) than open cholecystectomy (3.2%). Average duration of postoperative hospital stay in laparoscopic cholecystectomy was 3-4 days and 5-7 days in open cholecystectomy.* ***Conclusion:*** *Most of the patients of Gall stone disease had undergone Laparoscopic cholecystectomy. Majority of the patient were operated during warmer months and lowest recorded number of patients was in the Holy month of RAMADAN(April,2023). Laparoscopic cholecystectomy showed less complication, shorter hospital stay and earlier feeding compared to open cholecystectomy.*

Keywords: Cholecystectomy, Laparoscopy, postoperative complication.

Introduction

Gallstone disease is the most common biliary pathology which affects 10-15% population worldwide. The treatment of choice for the patients with symptomatic gallstone disease is cholecystectomy and the laparoscopic cholecystectomy is the gold standard treatment for Gallstone disease but laparoscopic cholecystectomy is still reported as having a higher complication rate about 9-17% in some published series (1) .Laparoscopic cholecystectomy is considered to be unsafe and technically difficult to perform in case of acute cholecystitis (2,3).The broad range of complication and conversion rate should be kept in mind because they depend on variables such as patient age, emergency intervention, acute inflammation (empyema, gangrene, perforation of GB), patient comorbidities (4).With increasing experience in laparoscopic surgery many surgical services have reported on the use of laparoscopic cholecystectomy for acute cholecystitis suggesting that it is technically feasible but at the expense of a higher conversion rate of 4.9% worldwide (5,6) and common bile duct lesions (7). Routine use of open cholecystectomy might enable more patients to have the operation during the acute phase because most surgeons prefers this approach but the impact of morbidity and hospital stay should also be considered. There is the expectation that open operation is associated with more pain longer duration with hospital stay and delayed postoperative oral feeding (8,9) . In some trials successful laparoscopic cholecystectomy is associated with an earlier recovery and shorter hospital stay and early postoperative oral feeding compared to open cholecystectomy (10). The Aim of the study was to analyze the patients who were undergone cholecystectomy in AAMCH and number of operation in each month, complications of the operations, comorbidities of the patients, hospital stay and cost effectiveness.

Aim

To study the outcome of cholecystectomy in AAMCH.

Materials and Methods

All the patients having cholecystectomy in AAMCH, Khulna from August 2022 to July 2023 were retrospectively registered in this study. The operations were performed by consultants of surgery and subordinate doctors participated in surgery under supervision. Patients were eligible to participate in the trail comparing conventional open cholecystectomy and laparoscopic cholecystectomy according to exclusion and inclusion criteria.

We analyzed 381 patients aged 20-65 years diagnosed with gall stone disease randomly assigned to laparoscopic cholecystectomy or open cholecystectomy. Excluded where those with confirmed choledocholithiasis and underwent concomitant surgeries, patients with liver chirrosis, pregnant women and malignant tumor. Demographic data such as age, sex, elective or emergency procedure, duration of surgery, surgical risks, use of prophylactic heparin, intercurrent diseases and use of prophylactic antibiotics were computed. Surgical site infection, respiratory complications (pneumonia, bronchopneumonia, pleural effusion, and pulmonary embolism), urinary infections, deep vein thrombosis and other complications were recorded from the immediate post operative period until the time of hospital discharge. We evaluated the time to oral feeding ambulation, length of postoperative hospital stay and clinical conditions at time of discharge in AAMCH.

Results

Of the 381 patients 319 (83.7%) underwent laparoscopic surgery, 52 (13.5%) open cholecystectomy, 10 (2.9%) Laparoscopic cholecystectomy converted to open cholecystectomy.

Table 1. Types of cholecystectomy performed in AAMCH.

Type of cholecystectomy	Number	Percentage
Laparoscopic Cholecystectomy	319	83.7%
Open Cholecystectomy	52	13.5%
Laparoscopic converted to Open Cholecystectomy	10	2.9%

There was relation between the numbers of operation each month with the environmental condition. Most of the patients were operated during the warmer months and the number of patients decreased during cold weather mainly in December, January, and February. But the lowest number of patients (3.1%) was operated in the month of April.

Table 2. Number of patient undergone cholecystectomy in each month

Month	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul
Laparoscopic Cholecystectomy	37	25	28	34	19	18	17	21	12	29	26	42
Open Cholecystectomy	8	4	5	5	4	3	8	4	0	7	8	7
Laparoscopic Cholecystectomy to Open Cholecystectomy	1	0	1	2	1	0	1	0	0	1	1	2
Total	46	29	34	41	24	21	26	25	12	37	35	51
Percentage	12%	7.9%	8.9%	10.2	6.5%	5.6%	6.8%	6.6%	3.1%	9.7%	9.3%	13.4%

Analyzing our data we have found a relation with the previous mentioned type of cholecystectomy by gender and age as shown below in table 2.We have found a relationship man to woman.

Table 3. Prevalence of age and sex

Type of cholecystectomy	Age	Male	Female	M:F Ratio	Total
Laparoscopic	45±11	137	182	1:1.33	319
Open	47±10	22	30	1:1.36	52
Converted	50±10	4	6	1:1.5	10
Total	46.5±10.5	163	218	1:1.33	381

Many of the patients had co-morbidities such as hypertension, Diabetes mellitus, Hypothyroidism, Asthma.

Table 4. Co-morbidities.

Disease	Laparoscopic	Open	Converted	Total
Hypertension	24	12	2	37(9.7%)
Diabetes	13	9	1	23(6%)
Asthma	6	2	0	8(2%)
Hypothyroidism	3	1	1	5(1.3%)

There was no difference in median time to onset of post operative oral feeding. It was earlier in laparoscopic cholecystectomy where most of the patient received oral diet introduced in first 12 hours while in open surgery oral intake was introduced in most of the patients after 24 hours..

Table 5. : Time of postoperative oral feeding.

Operation	5-6hr	12hr	24hr	48hr	72hr
Laparoscopic	10	298	19	2	0
Open	0	7	35	9	2
Converted	0	2	6	1	1

Most of the patients with laparoscopic cholecystectomy leave the hospital within 3-4 days. Patients with open cholecystectomy leave the hospital on 5-7 days.

Table 6. : Duration of hospital stay.

Operation	1-2days	2-3days	3-4days	5-6days	6-7days
Laparoscopic	2	297	13	5	3
Open	0	0	5	38	9
Converted	0	0	3	5	2

Post operative complications resulting in from laparoscopic cholecystectomy occurred in 2.5% patients whereas postoperative complications in open cholecystectomy occurred in 5.8% patients.

Table 7. : Post-operative complications occurring in patients undergoing cholecystectomy

Complication	Laparoscopic Cholecystectomy	Open Cholecystectomy
Wound infection	1	2
Urinary infection	0	0
Bile duct injury	3	0
Internal hemorrhage	1	0
Port site hemorrhage	1	0
Deep vein thrombosis	0	0
Respiratory Infection	1	1
Subcutaneous emphysema	0	0
Total	8(2.5%)	3(5.8%)

Discussion

In AAMCH Laparoscopic cholecystectomy surpassed open cholecystectomy. This is because the benefits of Laparoscopic cholecystectomy in respect of shorter duration of post operative hospital stay, early recovery, having less complications etc. Most of the patients were operated during warmer months of the year from the month of March to November. The number of patients decreased in the colder month of December to February. The lowest number of patients 3.9% was operated in April because it was the holy month of Ramadan. In this study the duration of post operative hospital stay for laparoscopic surgery was 3-4 days and in open cholecystectomy was 5-7 days. The hospital stay was more in open cholecystectomy than in laparoscopic cholecystectomy. Other study showed the mean postoperative stay for an open cholecystectomy has been 8 days compared with the three days recorded for laparoscopy (11).Both preoperative and postoperative complications are thoroughly dealt with in most studies that have compared open and laparoscopic cholecystectomy (12, 13). Usually the complications are classified as bile duct injury, vascular, bowel injury, residual stone, wound, urinary tract infection, urinary retention and ileus (14). Bile duct injury has been more common after laparoscopic cholecystectomy (15). In this present study we had three cases of bile duct injury. Patients were reported and the injury was successfully treated. The conversion rate of laparoscopic cholecystectomy in to open is 4.9% worldwide (16).Conversion rate in AAMCH is 2.9%. It is due to better patient selection criteria and satisfactory investigation reports.

Conclusion

Majority of the cholecystectomy in AAMCH was done laparoscopically. Laparoscopic cholecystectomy offers the greatest benefits to patients; it was associated with the lower rate of post operative complications, feeding earlier, shorter hospital stay than open cholecystectomy. Although the cost of laparoscopic cholecystectomy is higher than open cholecystectomy but considering duration of hospital stay, cost of medicine and the duration by which patient can return to work, laparoscopic cholecystectomy has shown more cost effectiveness than that of open cholecystectomy.

Conflict of interest: None.

References

1. Navez B, Mutter D, Russier Y. Safety of laparoscopic approach for acute cholecystitis: retrospective study of 609 cases. World J Surg. 2001; 25:1352-6. https://-doi.org/10.1007/s00268-001-0122-4 PMid: 11596902

2. Schafer M, Krähenbühl L, Büchler MW. Predictive A factors for the type of surgery in acute cholecystitis. Am J Surg. 2001; 182: 291-7. https://doi.org/10.1016/S0002-9610(01)00702-4

3. Rai R, Sinha A, Rai S. Randomized clinical trial of open versus laparoscopic cholecystectomy in the treatment of acute cholecystitis. Br J Surg. 2005; 92:44-49. https://doi.org/10.1002/bjs.4836 PMid: 15584058

4. Nuzzo G, Giuliante F, Persiani R.The risk of biliary ductal injury during laparoscopic cholecystectomy. J Chir (Paris). 2004; 141:343-53. https://doi.org/10.1016/S0021-7697(04)95358-6

5. Johansson M, Thune A, Nelvin L, Stiernstam M, West- man B, Lundell L. Randomized clinical trial of open versus laparoscopic cholecystectomy in the treatment of acute cholecystitis. Br J Surg. 2005; 92:44-9. https://doi.org/10.1002/bjs.4836PMid: 15584058

6. Asoglu O, Ozmen V, Karanlik H, Igei A, Kecer M, Parlak M,et al. Does the complication rate increase inlaparoscopic cholecystectomy for acute cholecystitis? J Laparoendosc AdvSurg Tech. A 2004; 14:81-6. https://doi.org/10.1089/109264204322973844 PMid:15107216

8. Chau CH, Tang CN, Siu WT, Ha JP, Li MK. Laparo- scopic cholecystectomy versus open cholecystectomy in elderly patients with acute cholecystitis: retrospective study. Hong Kong Med J. 2002; 8:394-9.

9. Pessaux P, Regenet N, Tuech JJ, Rouge C, Bergamaschi R, Arnaud JP A prospective commparative rudy in the elderly with acute cholecystitis. SurgLaparoscEndoscPer- cutan Tech. 2001; 11:252-5.https://doi.org/10.1097/00129689-200108000-00005 PMid:11525370

10. Glavic Z, Begic L, Simlesa D, Rukavina A. Treatment of acute cholecystitis. A comparison of open vs laparoscop- ic cholecystectomy. SurgEndosc. 2001; 15:398-401.https://doi.org/10.1007/s004640000333PMid: 11395823

11. Nilsson E, Ros A, Rahmqvist M, Bäckman K, Carlsson P. Cholecystectomy: costs and health-related quality of life: a comparison of two techniques. Int J Qual Health Care. 2004; 16:473-82. https://doi.org/10.1093/intqhc/mzh077PMid: 15557357

12. Kesteloot K, Penninckx F. The costs and effects of open versus laparoscopic cholecystectomies. Health Economics. 1993; 2: 303-312. https://doi.org/10.1002/hec.4730020403PMid:8142992

13. De Pouvourville G, Ribet-Reinhart N, Fendrick M, Houry S, Testas P, Huguier M. A prospective comparison of costs and morbidity of laparoscopic versus open chole- cystectomy. Hepatogastroenterology. 1997; 44: 35-9.

14. Ponsky JL. Complications of laparoscopic cholecystec- tomy. Am J Surg. 1991; 161: 393-395. https://doi.org/10.1016/0002-9610(91)90605-D

15. Deziel DJ, Millikan KW, Economou SG, Doolas A, KoS-T, Airan MC. Complications of laparoscopic cholecystec- tomy: a national survey of 4,292 hospitals and an analysis of 77,604 cases. Am J Surg. 1993; 165: 9-14. https://doi.org/10.1016/S0002-9610(05)80397-6

16. Tang B, Cuschieri A. Conversions during laparoscopic cholecystectomy: risk factors and effects on patient outcome. J Gastrointest Surg. 2006; 10: 1081–1091 [PubMed] [Google Scholar]

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Immunohistochemical Expression of p16 in Colorectal Carcinoma in Bangladeshi people.

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Abstract

Background: *Worldwide, colorectal cancer is one of the major cancer burdens, being the third most common in men and the second most common in women. Treatment of colorectal cancer in advanced disease stage is challenging. Thus, early diagnosis in primary stages using sensitive molecular markers seems to be necessary. P16 acts as a tumor suppressor gene by binding to CDK4/6 and ultimately slows down the cell cycle by inhibiting progression from phase G1 to phase S. Colorectal carcinoma developed by inactivation of p16 gene by DNA methylation. Newer targeted therapy drugs like palbociclib have a promising role in inactivated p16 gene by DNA methylation. The aim of the study is to determine the expression of p16 in colorectal carcinoma in our population.* ***Objectives:*** *To see the immunohistochemical expression of p16 in colorectal carcinoma.* ***Materials and Methods:*** *This cross-sectional observational study was conducted in the Department of Pathology, BIRDEM General Hospital, Dhaka from March 2021 to February 2023. In this study 85 diagnosed cases of colorectal carcinoma were included. Tissue from tumorous area of colectomy sample and in some cases paraffin blocks of colorectal carcinoma were collected. Sections were taken from each paraffin block for routine haematoxylin and eosin (H&E) stain, and also for immunohistochemical stain (p16 antibody). Statistical analysis was carried out as required. Ethical practice was ensured in every step of the study.* ***Result:*** *In this study p16 expression was observed in 51% cases. Among these, 16 (18.82%) cases showed a scoring of 3+ and 27 (31.76%) cases showed a scoring of 4+. The mean age of colorectal carcinoma patient was 52.48±12.6 years with a male to female ratio of 1.4:1. The tumor was mostly (53%) located in the proximal colon (caecum, ascending colon, proximal 1/3 of transverse colon). In this study, a significant association of p16 expression was observed with location of tumor.* ***Conclusion:*** *Expression of p16 has been observed in 51% cases of the colorectal carcinoma patients with strongly positive in 31.76% cases. Its expression is significantly higher in distal colon. Further study is recommended for better understanding of p16 expression in colorectal cancer as a prognostic factor.*

Keywords: colorectal carcinoma, p16 expression, immunohistochemistry.

Introduction

Colorectal cancer is one of the most common neoplasms of the digestive system with high morbidity and mortality. Colorectal cancer has become the third most common cancer in the world, as reported by WHO International Agency for Research on Cancer (1,2). According to GLOBOCAN project, 1.9 million of new colorectal cancer cases were registered in 2020 which was 10% of all new cases and accounted for 9,35,000 deaths worldwide(3). It ranks third in terms of incidence, but second in terms of mortality (4). Treatment of colorectal cancer in advanced metastatic disease stage is challenging. Thus, early diagnosis in primary stages using sensitive molecular markers seems to be necessary.

Colorectal cancer's cause and pathogenesis involve both environmental and genetic factors (5). The disease follows diverse pathways, including chromosomal instability and microsatellite instability, with Lynch syndrome and familial adenomatous polyposis being specific genetic cause (6-10). Tumor suppressor gene p16 plays a significant role, being the second most common molecular defect in human cancer (11).

Prognosis depends on clinical and pathological parameters, such as tumor characteristics and patient factors. Poor prognostic factors include young or old age, male sex, elevated CEA level, obstruction, perforation, tumor burden, and various invasion factors. Mucinous and signet ring cell carcinomas exhibit worse prognosis than adenocarcinoma (12).

Molecular markers like p16, p53, Ki67, and kRAS are associated with prognosis (13). Downregulation of p16, often due to hypermethylation or gene mutations, promotes cell cycle progression, contributing to cancer development. Inactivation of p16 is observed in various malignancies, including cervix, oropharynx, lung, and pancreatic cancers (14). While survival rates have improved with early diagnosis and new treatment modalities, colorectal cancer mortality remains high (15). Chemotherapy is effective but not universally preventive (16). Ongoing research explores alternative adjuvant therapies, focusing on biological markers like p16 as prognostic factors and therapeutic targets (17).

Palbociclib, a targeted therapy drug, shows promise in cases with inactivated p16 gene through DNA methylation. Initial studies demonstrate modest antitumor activity, particularly in patients with alterations in CDKN2A (18). Further investigations are needed to confirm Palbociclib's efficacy and utility in this population.

The aim of this study is to see immunohistochemical expression of p16 in our population.

Materials and Methods

This cross-sectional type of study was conducted in the Department of Pathology, BIRDEM General Hospital, Dhaka from March 2021 to February 2023. The study had been approved by hospital ethical committee. It included 85 patients of colorectal carcinoma who underwent surgical resection. Patient who received chemotherapy/radiotherapy prior to surgery were excluded from the study. All surgical specimens were properly grossed and paraffin blocks and H&E stained glass slides were prepared as per standard guidelines.

Four micro meter thick sections were taken on slides from paraffin embedded block. Deparaffinization was done with xylene. Rehydration was done with graded concentration of alcohol. Endogenous peroxidase was blocked by 0.3% Hydrogen peroxide. Antigen retrieval was done by water bath or heat. The sections were stained with monoclonal mouse anti-human p16 antibody at a 1:50 dilution &

incubated for 30 minutes. Thereafter, peroxidase labeled polymer was applied & incubated for another 30 mins. After visualizing the reaction with 3, 3'- diaminobenzidine tetrahydrocholoride (DAB) using Anti-CDKN2A/p16INK4a antibody, the slides were counterstained with hematoxylin solution. Dehydration was done through increasing concentration of alcohol. Clearing was done by xylene & mounting with DPX. For control tissue sections from SCC of cervix was used. The slides are examined under microscope. p16 staining was observed in both nuclear and cytoplasm of the malignant cells.

The percentage of stained cells was assessed by using a 4- point scale [19] as follows:

Table 1: P16 Scoring System

Serial No	P16 score	Staining pattern
1	1	No staining or staining is observed in less than<10% of tumor cells
2	2	Staining is observed in 11-50% of the tumor cells.
3	3	Staining is observed in 51-75% of the tumor cells.
4	4	Staining is observed in >75% of the tumor cells.

Scores of 3 and 4 were considered to be positive for p16, and Scores of 1 and 2were considered to be Negative.

Results

The age of the present study population ranged from 23- 80 years with a mean age of 52.48±12.6 years. Maximum positivity of p16 was found in 50-59 years of age group which was 31%. Whereas minimum positivity was found in 20-29 years age group that is 2%. However, no significant correlation was found between expression of p16 and different age groups (Table 2).

Table 2: Expression of p16 in different age groups (n=85):

Age (years)	p16		p value*
	Positive	Negative	
20-29	01	01	
30-39	08	03	
40-49	08	12	
50-59	13	13	
60-69	09	09	0.624[ns]
70-80	04	04	
Mean ± SD	51.81 ± 12.8	53.17 ± 12.4	
Sex			
Male	27 (54%)	23 (46%)	0.532 [ns]
Female	16 (45.71%)	19 (54.29%)	

ns = not significant*Unpaired T-test, chi-square test was carried out to measure the level of significance.

In the present study, 54% of male patients and 45.71% of female patients were found p16 positive (Figure 1).

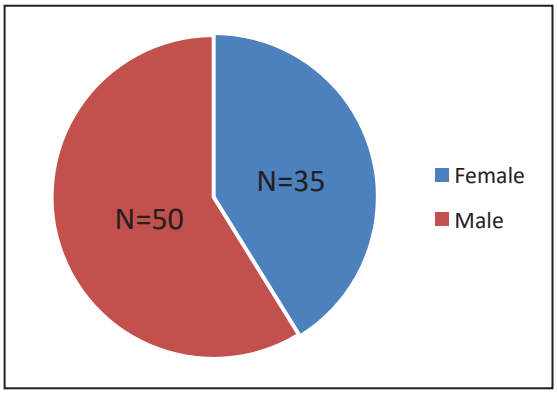


Figure 1: Pie chart showing sex distribution of patients (n=85)

However, no significant correlation was found between expression of p16 and sex of patients (Table 2).

Table 3: Immunohistochemical expression of p16 (n=85):

Expression of p16	No of Cases	Percentage
Negative	**42**	**49%**
1+	36	42.35%
2+	06	7.06%
Positive	**43**	**51%**
3+	16	18.82%
4+	27	31.76%

A total of 43 (51%) cases were found positive in term of expression of p16 (Score 3, 4). Remaining 42 cases were found negative (Score 1+,2+) which is 49% of the total number of cases (85). (Table 3)

Table 4: Correlation of p16 expression with size of tumor (n=85):

Size of tumor	p16		p value*
	Positive	Negative	
<5 cm	**20 (49%)**	**21 (51%)**	
>5 cm	**23 (52%)**	**21 (48%)**	
Total	**43 (50.59%)**	**42 (49.41%)**	**0.748 ns**

In this study, 49% of the cases having tumor size below 5 cm were found p16 positive. Whereas, 52% of the cases having tumor size equal and above 5 cm were found p16 positive. However, the data showed no significant correlation between expression of p16 and size of tumor (Table 4).

Table 5: Correlation of p16 expression with location of tumor (n=85):

Location of tumor	p16		p value*
	Positive	Negative	
Proximal Colon	18 (40%)	27 (60%)	
Distal Colon and Rectum	25 (62.5%)	15 (37.5%)	
Total	**43 (50.59%)**	**42 (49.41%)**	**0.038 s**

In this study, 18 (40%) cases in proximal colon and 25 (62.5%) cases in distal colon and rectum were found p16 positive. p16 stain is more positive in distal colon and rectum and it is statistically significant (p =.038) (Table 5)

Table 6: Expression of p16 in colorectal carcinoma in different studies:

Author	Year	Country	Study Population	p16 +ve cases (%)
Current Study	2023	Bangladesh	85	51%
Heidari	2017	Iran	137	25.4%
Lam	2008	Australia	194	84%
Qian	2015	China	30	23.33%
Al-Ahwal	2021	Saudi Arabia	193	73.6%
Balali	2022	Iran	38	65.8%
Lin	2009	China	60	60.0%
Malhotra	2010	India	36	72%
Tan	1998	China	127	85%
Karamitopoulou	2009	Switzerland	51	74.5 %
Kitamura	2018	Japan	101	50%
Tada	2006	Japan	84	72%
Carneiro	2006	Brazil	60	20%
Cui	2004	Japan	51	38%

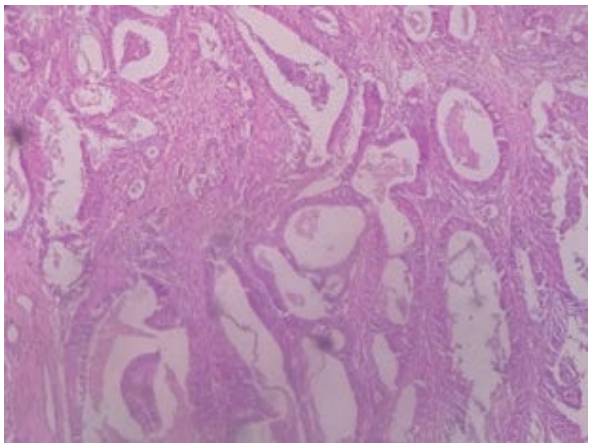


Figure 2: Photomicrograph of colonic adenocarcinoma, moderately differentiated (H&E 10x).

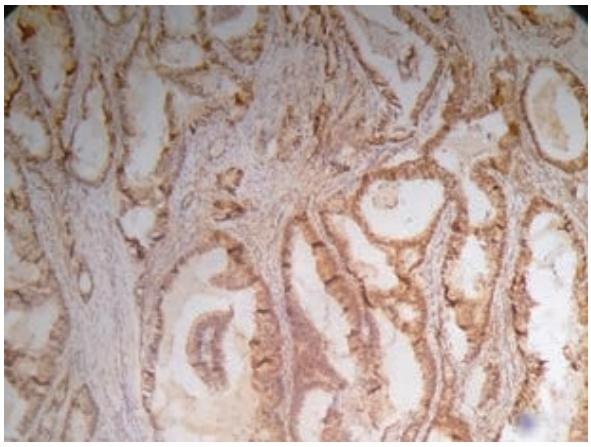
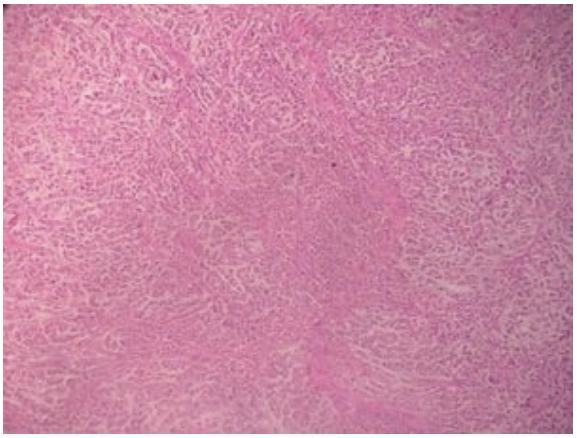
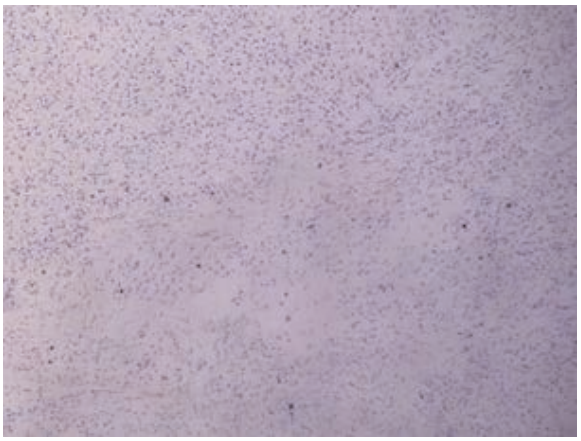


Figure 2: Photomicrograph of colonic adenocarcinoma, moderately differentiated showing positive p16 expression (score-4+) (IHC 10x).



Photomicrograph of colonic adenocarcinoma, poorly differentiated (H&E 10x).



Photomicrograph of colonic adenocarcinoma, poorly differentiated showing negative p16 expression (score-1+) (IHC 10x)

Discussion

Colorectal Cancer (CRC) is the third most common cancer in the world after lung cancer and breast cancer globally. According to recent statistics by International Agency for Research on Cancer, GLOBOCAN (2020) report, there were almost 1,931,590 new cases of colorectal cancer cases in 2020, of which around 9,35,173 people die of this disease (2). In the last two decades the cancer incidence of colorectal cancer has also increased in the Asia-Pacific region. Asia has the highest incidence of colon cancer with 49.9% and death from this cancer with 54.2% globally (20). As per the report, there were 2,753 new cases of colon cancer in Bangladesh in 2020, out of which 1,772 people died of the disease (3).

p16 is a tumor suppressor gene which is now recognized as the second most common point of mutation in human cancer. The p16 tumor suppressor gene binds to CD4/6 and prevents its interaction with cyclin

D. Finally, this reaction inhibits cell cycle progression from stage G1 to S. Thus, p16 is a key element in oncogenesis and cell aging processes. Decreased p16 expression by hypermethylation, point mutation, or gene deletion leads to cell cycle progression; while the

activation of this gene is associated with cellular aging. As a tumor suppressor gene, p16 is inactive in many tumors and is closely related to tumor formation and progression.

Inactivation of p16 has been reported in CRC, oropharyngeal cancer, pancreatic cancer, esophageal cancer, non-small cell lung cancer and mesothelioma. There are contradictory results in terms of the relationship between p16 expression with clinicopathological parameters in various studies in the world. In Bangladesh, as far as we are informed, there is no such study on p16 expression in CRC. So, the aim of this study was to investigate the expression pattern of the p16 marker in CRC. The study was done in the department of pathology, BIRDEM General Hospital Dhaka during the period of March 2021 to February 2023. A total of 85 diagnosed cases of CRC were included in this study and immunohistochemical examination was performed to see the expression of p16.

In the present study out of 85 cases 43 cases were p16 positive. These were scored 1+, 2+, 3+ and 4+ according to staining of <10%, 11-50%, 51-75%, >75% of the no of tumor cells respectively 19. Score of 1 and 2+ were considered negative and score of 3+ and 4+ were considered positive for p16 expression. Among our cases, 16 (18.82%) cases showed scoring of 3 + and 27 (31.76%) cases showed scoring of 4+. However, 42 cases were turned out to be negative with the scoring of 1+ in 36 (42.35%) cases and 2+ in 6 (7.06%) cases.

Variable expression of p16 has been observed in different studies conducted among different population of the world. Out of 85 samples 43 (51%) patients had positive staining which is similar to the study by Lin et al (2009) and Huang et al (2003) in China. But the positive p16 stain ranges from 20% to 90% in different studies in China, India, Iran, Saudi Arabia and Brazil (Zhou and Gu, 2018). In the study of Zhao et al. (2003), out of 74 CRC samples, 73 (98.6%) were positive for p16 immuno-stain. Positive expression of p16 in the study of Cui et al. (2004) in Japan was 38%. In the study of Tada et al. (2003) in Japan was 72% and in the study of Norrie et al. (2003) in Australia was 92% (Table 6). However, differences in the expression values reported in different studies may be related to various factors, including the number of patients tested for p16 staining, the p16 antibody used depending on manufacturer, the site of tumor, immunohistochemical testing method, and population heterogeneity and genetic differences (Heidari et al., 2017; Balali et al., 2022).

The age of the present study population ranges from 23 to 80 years with a mean age of 52.48±12.6 which is similar to the study by Heidari et al. (2017) from Iran (22).

In this study out of 85 cases of CRC, 50 cases were male and 35 cases were female with male to female ratio of 1.4:1 which is similar to the study by Al-Ahwal et al. from Saudi Arabia (24). The study results of the present study showed that p16 staining in tumor cells had no significant relationship with gender and age.

Specific sites of tumor in this study are categorized into two groups proximal colon and distal part of colon and rectum. In our study, more p16 expression was present in tumor of distal colon and rectum. It is statistically significant, similar to the study from Australia (7). Researchers have found that it is possible to diagnose left and right colorectal tumors using clinical and molecular methods (13). Pattern of expression of p16 varies in different parts of colon. It is because of the difference in bacterial flora and intestine passing time in right-sided and left-sided colon through exposure to normal colon mucosa with potential carcinogen factors (22).

Size was categorized as less than 5cm and more than 5 cm according to the study by Al-Ahwal et al. (2016). They found 42.9% and 57.1% of tumors to be <5cm and >5cm respectively,

which was not significant statistically. In our study p16 stain was positive in 49% of <5cm tumor and 51% of >5cm tumor. There was no significant relation was found between tumor size and p16 staining similar to the mentioned study.

Conclusion

This cross-sectional observational study was carried out in the department of pathology BIRDEM. The aim of the study was to determine the immunohistochemical expression of p16 in CRC. The mean age of colorectal carcinoma in this study was 52.48 years and the male to female ratio was 1.4:1. Among all 85 cases 45 located in the proximal whereas 40 in distal colon and rectum. Association between p16 expression with age, sex, and tumor size of the patient was evaluated and no statistically significant correlation was found. In this study p16 expression showed significant association with site of the tumor. Distal colon and rectum express more p16 positivity.

In conclusion, expression of p16 has been observed in more than half of the cases of colorectal carcinoma in this study. p16 is a tumor suppressor gene the expression of which may be lost due to methylation, deletion or other genetic factors. So, it can be stated that p16 immuno-marker may be used as a prognostic marker and can be used for potential targeted therapy.

Limitation and recommendations

Loss of p16 staining is mainly by DNA methylation or other genetic factors. It could not be determined in our study. So, further study with PCR or NGS facility might determine the cause of loss of p16 expression. And further multicenter studies can be carried out including large number of patients to see actual immuno-expression of p16 in our population.

Source(s) of Support: Self

Conflict of Interest: Nil

References

1. Minhajat R, Benyamin AF, Miskad UA. The Relationship Between Histopathological Grading and Metastasis in Colorectal Carcinoma Patients. Nusant Med Sci J. 2020;5(2):51-60. doi:10.20956/NMSJ.V5I2. 8786

2. Siegel RL, Miller KD, Sauer AG, et al. Colorectal cancer statistics, 2020. CA Cancer J Clin. 2020;70(3):145-164. doi:10.3322/-CAAC.21601

3. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-249. doi:10.3322/-CAAC.21660

4. Sung JJ, Lau JY, Goh KL, Leung W. Asia Pacific Working Group on Colorectal Cancer. Increasing incidence of colorectal cancer in Asia: implications for screening. Lancet Oncol. 2005;6:871-876.

5. Hamilton SR, Vogelstein B, Kudo S, Al. E. Carcinoma of the colon and rectum. Published online 2000:105-119.

6. McKay JA, Douglas JJ, Ross VG, al. et. Analysis of key cell-cycle checkpoint proteins in colorectal tumours. J Pathol. 2002;196:386-393.

7. Lam AK, Lo CY, Leung P, Lang BH, Chan WF, Luk JM. Clinicopathological roles of alterations of tumor suppressor gene p16 in papillary thyroid carcinoma. Ann Surg Oncol. 2007;14:1772-1779.

8. Carneiro FP, Ramalho LN, Britto-Garcia S, Ribeiro-Silva A, Zucoloto S. Immunohistochemical expression of p16, p53, and p63 in colorectal adenomas and adenocarcinomas. Dis Colon Rectum. 2006;49:588-594.

9. Kim WY, Sharpless NE. The regulation of INK4/ARF in cancer and aging. Cell. 2006;127:265-275.

10. Lam KY, Chan ACL, Chan KW, Leung ML, Srivastava G. Expression of p53 and its relationship with human papillomavirus in penile carcinomas. Eur J Surg Oncol. 1995;21:613-616.

11. Lam AKY, Ong K, Jafari Giv M, Ho YH. p16 expression in colorectal adenocarcinoma: Marker of aggressiveness and morphological types (Pathology (2008) 40, (580-585)). Pathology. doi:10.1080/00313020802524603

12. A T, MG D. New insights into the aetiology of colorectal cancer from genome-wide association studies. Nat Rev Genet. 2009;10(6):353-358. doi:10.1038/NRG2574

13. Li W, Qiu T, Zhi W, et al. Colorectal carcinomas with KRAS codon 12 mutation are associated with more advanced tumor stages. BMC Cancer. 2015;15(1). doi:10.1186/S12885-015-1345-3

14. Ogino S, Nosho K, Kirkner GJ, et al. CpG island methylator phenotype, microsatellite instability, BRAF mutation and clinical outcome in colon cancer. Gut. 2009;58(1):90-96. doi:10.1136/GUT.2008.155473

15. Iversen LH, Norgaard M, Jacobsen J, Laurberg S, Sorensen HT. The impact of comorbidity on survival of danish colorectal cancer patients from 1995 to 2006--a population-based cohort study. Dis Colon Rectum. 2009;52(1):71-78.

16. Goldstein J, Tran B, Ensor J, et al. Multicenter retrospective analysis of metastatic colorectal cancer (CRC) with high-level microsatellite instability (MSI-H). Ann Oncol. 2014;25(5):1032-1038. doi:10.1093/ANNONC/ MDU100

17. Mundade R, Imperiale TF, Prabhu L, Loehrer PJ, Lu T. Genetic pathways, prevention, and treatment of sporadic colorectal cancer. Oncoscience. 2014;1(6):400-406. doi:10.18632/ONCOSCIENCE.59

18. Li P, Zhang X, Gu L, Zhou J, Deng D. P16 methylation increases the sensitivity of cancer cells to the CDK4/6 inhibitor palbociclib. PLoS One. 2019;14(10):e0223084. doi:10.1371/JOURNAL.PONE.0223084

19. Qian-qian H. Expression of p16 in Human Colorectal Cancer and Its Clinical Significance. J Int Transl Med. 2015;3. doi:10.11910/2227-6394.2015.03.02.02

20. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. doi:10.3322/CAAC.21492

21. Zhou N, Gu Q. Prognostic and clinicopathological value of p16 protein aberrant expression in colorectal cancer: A PRISMA-compliant Meta-analysis. Med (United States). 2018;97(12). doi:10.1097/MD.0000000000010195

22. Heidari Z, Sagheb HM, Gorgich EAC. Immunohistochemical expression of P16ink4a in colorectal adenocarcinoma compared to adenomatous and normal tissue samples: A study on southeast iranian samples. Iran Red Crescent Med J. 2017;19(6). doi:10.5812/IRCMJ.15174

23. Balali B, Kheradmand P, Ranjbari N, Taheri-Moghadam M. Expression of p16 Marker in Colorectal Cancer and its Association with Clinicopathologic Parameters in Patients with Colectomy Surgery. J Appl Biotechnol Reports. 2022;9(3):719-725.

24. Al-Ahwal M, Gomaa W, Emam E, et al. p16 protein is upregulated in a stepwise fashion in colorectal adenoma and colorectal carcinoma. Saudi J Gastroenterol. 2016;22(6):435. doi:10.4103/1319-3767.195560

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