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Challenges of Burn Care in Bangladesh: A Continuing Public Health and Surgical Crisis

Burn injury remains one of the most devastating forms of trauma in Bangladesh, affecting thousands of individuals annually and imposing an enormous burden on healthcare systems, and society as a whole. Despite significant advancements in burn management and the establishment of specialized Burn Centers, the challenge of providing comprehensive burn care still remains substantial in Bangladesh.

Bangladesh is characterized by a high incidence of thermal, scald, flame, chemical, and electrical burns. Children and women remain particularly vulnerable due to domestic cooking practices, overcrowded living conditions, and inadequate safety measures. Unplanned industrialization, rapid urbanization, and unsafe electrical infrastructures have further contributed to the increasing prevalence of burn injuries. Recently it is seen that gas leakage, air conditioner and transformer blast are causing burn incidence frequently.¹

One of the greatest challenges in burn management is burn sepsis. Loss of skin integrity creates an ideal environment for microbial invasion. Bacterial infections caused by organisms such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and Methicillin-resistant *Staphylococcus aureus* (MRSA) are frequently encountered. In recent years, fungal infections have emerged as an additional threat, particularly among patients with extensive burns, prolonged hospitalization, and immunosuppression. The increasing prevalence of multidrug-resistant and extensively drug-resistant organisms has complicated treatment strategies and significantly increased healthcare costs.²

Public awareness regarding burn prevention and first aid remains inadequate. Harmful traditional practices, delayed presentation to specialized centers, and misconceptions regarding burn treatment continue to adversely affect outcomes. Community education programs focusing on prevention, safe cooking practices, electrical safety, regular maintenance of gas line, air conditioners and evidence-based first aid measures are urgently needed.³

The shortage of trained burn nurses represents another critical challenge. Burn nursing is a highly specialized discipline requiring expertise in wound care, infection control, rehabilitation, nutritional support, and psychological care. Similarly, there remains a shortage of physicians specifically

trained in burn surgery, critical care, rehabilitation, and reconstructive surgery. Expanding specialized training programs and retaining skilled professionals should be a national priority.

A unique social challenge in Bangladesh is the persistence of superstition and reliance on black magic, spiritual healers, and unscientific treatment methods. Some burn victims initially seek treatment from traditional practitioners, resulting in delayed medical intervention, wound contamination, infection, and preventable complications. Public health initiatives must address these cultural barriers through education and community engagement.

Electrical burns deserve special attention due to their increasing incidence and devastating consequences. Rapid urban development, unauthorized electrical connections, occupational hazards, and inadequate workplace safety contribute to a growing number of high-voltage electrical injuries. These injuries frequently result in deep tissue destruction, limb loss, severe disability, and prolonged rehabilitation. Strengthening occupational safety regulations and public awareness regarding electrical hazards is essential.⁴

Although Bangladesh has made remarkable progress in burn care infrastructure, significant challenges remain. Combating burn sepsis, addressing antimicrobial resistance, improving public awareness, strengthening specialized training for nurses and physicians, confronting harmful cultural practices, and preventing electrical injuries require coordinated efforts from healthcare professionals, policymakers, educators, and community leaders.

Burn injury is not merely a surgical problem; it is a public health challenge that demands a comprehensive national response. The future of burn care in Bangladesh depends on our collective commitment to prevention, timely treatment, infection control, rehabilitation, research, and sustained investment in specialized human resources.

[JNIBPS 2025 Jul; 1(1): 1-2]

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P53 Expression in Breast Cancer Considering a Potential Biomarker and its Correlation with Histomorphological Grade and ER, PR and Her2/Neu

Islam N¹, Talukdar MMI², Mehjabin M³, Sultana S⁴, Khatun S⁵, Asaduzzaman⁶, Begum F⁷

Abstract:

Background: P53, a tumor suppressor gene which is thought to play a crucial role in carcinogenesis. Mutant p53 can be detected by immunohistochemistry. It is already established that the hormones have an important role in breast carcinogenesis. p53 gene plays a role in genomic stability by controlling cell cycle and apoptosis in damaged cells beyond repair. Most of the studies have shown absence of p53 expression in breast cancers has a favorable outcome.

Methods: This study was carried out in the Department of Pathology of Bangladesh Medical University (Former BSMMU), Dhaka, Bangladesh from July 2016 to June 2017 with an aim to evaluate immunohistochemical expression of P53 in breast cancer. This study had 33 cases. These selected cases were diagnosed malignant in Fine needle aspiration cytology (FNAC). Core biopsy samples were obtained from the cases. All the biopsy samples of these cases were examined for histomorphological type and grading followed by immunohistochemical staining and scoring of p53, ER, PR and HER-2/neu.

Results: Tumor incidence was found highest among the age group of 45 to 50 years. Grade 2 was the most frequent type in the histomorphological evaluation. The study had significant correlation with tumor grade and nuclear expression of p53 protein and had no statistically significant correlation with the immunohistochemical expression of ER, PR and HER-2/neu.

Conclusion: Excluding the equivocal cases of HER-2/neu expression shows significant correlation with expression of p53 protein.

Key words: P53, Breast Cancer, Histomorphological grading.

[JNIBPS 2025 Jul; 1(1): 3-6]

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Introduction:

Breast cancers are complex, heterogeneous diseases with unclear etiologies; cell cycle dysregulation is often observed in such cancer. The cell cycle is monitored by checkpoints that ensure the integrity of the genome and the fidelity of chromosome separation via the ordered execution of cell cycle events. Cell cycle dysregulation can lead to uncontrolled cell growth and contribute to tumor formation. Dysregulated cell proliferation is characteristic of tumor cells, and gene mutation affecting controls of the cell cycle are extremely common in human cancers, including breast cancer.¹ Development and progression of breast cancer has proven to have alteration at the genomic level. TP53, a tumor suppressor gene, is thought to play a crucial role in the process of breast carcinogenesis. Most of the studies have shown an association between p53 proteins detected by immunohistochemical staining and reduced overall survival rate of breast cancer patients.²

The *TP53* gene is located on the short arm of chromosome 17 and encodes 375 amino acid nuclear phosphoprotein that prevent propagation of genetically altered cells.⁷ Wild type p53 a tumor suppressor protein that plays a vital role in regulating genomic stability by controlling the cell cycle and inducing apoptosis when cell damage is beyond repair.³ Several prognostic and predictive factors have been used for breast malignancies during these years. The most important factors include p53 protein, progesterone, estrogen receptors and human epidermal growth factor receptor-2.⁴ Mutations in the tumor suppressor gene *TP53* are present in 18-25% of primary breast carcinomas. Among the prognostic factors analyzed in studies focusing on breast cancer, an absence of *TP53* gene mutations appears to predict longer disease free state.³ Treatment for early breast cancer involves surgery with or without radiotherapy. Systemic therapy such as chemotherapy or hormone therapy is added if there are adverse prognostic factors such as lymph node involvement, indicating a high likelihood of metastatic relapse.⁵

Several factors, such as estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor-2 (HER-2/neu), age, stage, grade, and metastasis have all been well identified as predictive criteria for prognosis. P53 protein is a well-studied marker in breast cancer. But its significance in predicting clinical outcome remains controversial.³ Among the prognostic factors analyzed in studies focusing on breast cancer an absence of *TP53* gene mutations appear to predict longer disease free and overall survival following primary therapy. Knowledge about p53 protein is important because breast cancer is a clinically diverse and heterogeneous disease; the clinical course of the patients varies greatly with its expression.³ Therefore expression of p53 protein as a prognostic marker in relation to other commonly used prognostic marker should be carried out. This study was carried out with an objective of evaluation of the frequency of nuclear expression of p53 protein in invasive breast carcinoma by immunohistochemical method and its correlate with histomorphological grade of invasive breast carcinoma.

Materials and methods:

The study was conducted at the department of pathology BMU (Former BSMMU), Dhaka from July 2016 to June 2017. This was a cross-sectional study with a sample size of 33. Those cases were selected who had breast lump and diagnosed as malignant on FNAC. The cases which were benign, already received therapy, lesions with micro calcifications and cystic changes were excluded. Patients suffering from uncontrolled diabetes, severe hypertension, heart diseases and coagulopathy were also excluded. During

data collection, all relevant information was collected in a prescribed proforma. P53 immunostains and ER, PR and Her2/Neu were done in all cases by standard immunohistochemistry protocols. Statistical analysis was obtained by SPSS-20 and calculated by statistical formula spearman rank correlation coefficient test.

Result:

Out of 33 cases most of the cases belong to a range of 41 to 50 years. All the 33 cases were diagnosed as invasive ductal carcinoma(NST).10(30%) cases were grade 1, 16(48%) cases were grade 2 and 7(21%) were grade 3. Hormonal receptor status and Her-2 status are illustrated in the tables. These show the distribution of tumors according to grade p53 expression. . Grade I, grade II, grade III showed 2(20%), 10(62.5%), 4(57.1%) of high expression of p53 protein respectively. After the statistical analysis by SPSS 20 Spearman rank correlation coefficient was 0.175. t value was 3.50 with a 31 degree of freedom (df=n-2), the critical value is 1.68.

Table I
Age distribution of patients.

Age(in years)	Number of patient	Percentage
20-30	2	6%
31-40	10	30%
41-50	12	36%
51-60	6	18%
61-70	3	9%

Table II
Distribution of patients according to receptor status.

Receptor (n=33)	Number of Positive(%)	Number of Negative(%)
Estrogen receptor (ER)	25 (75%)	8 (24%)
Progesterone receptor (PR)	18 (54%)	15 (45%)

Table III
Correlation between ER and nuclear expression of p53 protein.

ER (number of cases)	p53	
	Low	High
Positive (25)	12 (48%)	13 (52%)
Negative (8)	6 (75%)	2 (33%)

Spearman rank correlation coefficient = 0.232
Result is not significant

Table IV

Correlation between PR and nuclear expression of p53 protein.

PR (number of cases)	p53	
	Low	High
Positive (18)	6 (33%)	12 (66%)
Negative (15)	4 (26%)	11 (73%)

Spearman rank correlation coefficient = 0.467

Result not significant

Table V

Correlation between HER-2/neu and nuclear expression of p53 protein.

HER-2/ neu (number of cases)	p53	
	Low	High
Negative (18)	4 (22%)	14 (77%)
Equivocal (9)	2 (22%)	7 (77%)
Positive (6)	2(33%)	4 (66%)

Spearman rank correlation coefficient = 0.468

Result is not significant

Seven cases were triple negative. Two of these cases showed high nuclear expression of p53 protein and rest of the five cases had low expression of p53 protein.

Table VI

Distribution of p53 protein in triple negative cases

Triple negative (number of cases)	p53	
	Low	High
7	5	2

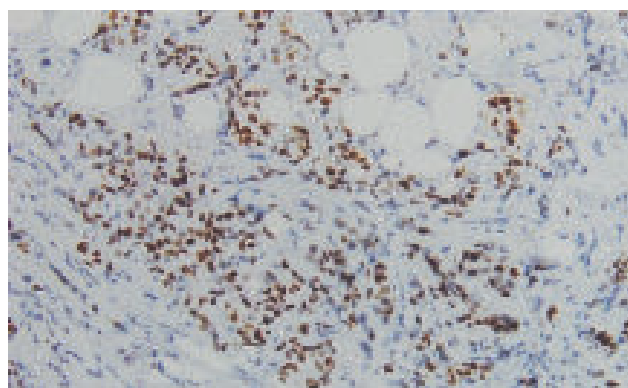


Fig.-1: (Case-10): Photomicrograph of high expression of p53 in IHC x 200

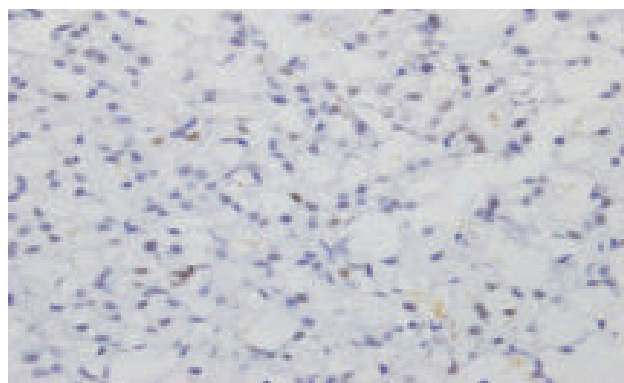


Fig.-2 (Case-16): Photomicrograph of low expression of p53 in IHC x 400

Discussion:

A total of 33 cases previously diagnosed as malignant on FNA and clinically indicated for core needle biopsy were selected. In each cases relevant history with attention to age, sex and clinical information were recorded. The obtained core biopsy specimen after proper fixation histopathological diagnosis and grading were done on the routine haematoxylin and eosin stain sections. P53 protein expression was assessed by immunohistochemistry. From paraffin-embedded blocks, 5-micrometer thick sections were cut, deparaffinized with xylene and rehydrated through a graded series of alcohol. Antigen retrieval was done by water bath. Then the sections were stained with Monoclonal Mouse Anti-Human p53, Code, used at a dilution 1:50 DAKO EnVision™ FLEX, High pH Detection system, peroxidase/ DAB+, Rabbit/Mouse(6). A total number of 33 cases were selected for the study out of these 33 cases most of the cases belong to a range of 41 to 50 years age group. Minimum age was 27 years, maximum age was 65 years. The mean age was 46.67 with a standard deviation (SD) 10.01. Table I shows the age distribution of the patients of the study. 15 (45%) cases among the total of 33 cases showed high nuclear expression of p53 protein and rest of the 18 (54%) cases showed low nuclear expression of p53 protein in immunohistochemical stain.

In this study, distribution of case according to the grade and the status of the nuclear expression of p53 protein. Grade I, grade II, grade III showed 2(20%), 10(62.5%), 4(57.1%) of high expression of p53 protein respectively. After the statistical analysis it appears that percentage of p53 protein expression increases with higher grade of tumor, which is statistically significant. Expression of p53 protein was variable in different studies in different subtypes of breast cancer. There was no significant relation in between the hormone receptor and p53 protein expression in breast cancers.^{9,10} Expression of p53 protein was variable in different studies in different subtypes of breast cancer. There was no significant relation in between the hormone receptor and p53 protein expression in breast cancers.^{3,9,10,12} Among

previous analysis of breast cancer with various ER, HER-2/neu status have shown that *TP53* gene abnormalities including mutation, LOH (loss of heterozygosity) or immunohistochemical over expression of p53 protein are significantly associated with resistance to anthracycline base chemotherapy where as others have not supported this conclusion.⁸ Although the relationship between p53 protein abnormality and sensitivity to neoadjuvant chemotherapy seems to be unproven among breast cancer, as a whole it is likely that immunohistochemical over expression of p53 protein is a reliable indicator of a good response to neoadjuvant chemotherapy in triple negative breast cancer (TNBC). TNBC cells that have lost their p53 protein function appear to accumulate DNA damage, resulting in cell death during or after neoadjuvant chemotherapy. In other words, a lack of normal p53 protein function TNBC cells appears to be one of the factors determining susceptibility to neoadjuvant chemotherapy.^{8,12} Studies have indicated that knock down of mutant p53 protein by siRNA was able to induce G₂ phase cell cycle arrest and apoptosis in human bladder cancer cells. This strategy corporate with cisplatin in the inhibition of cancer cells.³ Expression of p53 protein in breast may provide evidence that targeting mutant *TP53* gene in breast cancer may serve as a promising therapeutic strategy to treat, prevent visceral metastatic and relapse.^{11,13} In this study p53 expression was found to be low in grade-I diseases which are already proven to have better outcome after therapy. Where as a higher expression was found in tumors with increasing grade. Triple negative cases showed higher expression in two of the cases out of seven; however p53 expression was low to high in cases examined. Triple negative cases showed higher expression of mutant p53 in other studies also.^{11,12} Further studies with larger number of cases and duration may be carried out, which may lead to a new era of targeted therapy.

Conclusion:

P53 protein expression showed statistically significant correlation with increasing grade in invasive ductal carcinoma. But it had no significant correlation with the immunohistochemical expression of ER, PR and HER-2/neu status. Further studies can be carried out to find correlation with expression of p53 and HER-2/neu in breast cancer with the help of ancillary techniques as because both the genes are located on chromosome 17. The study was done over a short period of time and on limited number of cases and had more or less similar results to those in other studies.

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Reduction Mammoplasty Using Superomedial Technique - Versatile Technique for All Size of Breast Volume

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Abstract:

Background: Reduction mammoplasty is a surgical option which cannot be solved by only one technique for all cases. Rather various methods are required to meet the expectations of the patients, desired volume resection as well as surgeon's preference. Inferior pedicle technique is the most popular technique in Bangladesh and known as the most effective technique for huge breast. Our experience with superomedial technique is also precious in this respect.

Objective : To evaluate the operative outcome of superomedial technique in reduction mammoplasty of different voluminous breasts in terms of symptomatic relieve and aesthetic improvement.

Method : It is a retrospective study which included 11 cases. Purposive sampling was done. Study period was January 2018 to January 2021. Among them three patients had huge breast and eight patients had moderate sized breast. Pre-operative counselling was done about the possible cup size, volume to be resected, scar placement, possible complication and aftercare. All the cases were done in wise pattern technique. Post-operative outcome assessment was done both subjectively and objectively.

Results : Age range was 15 to 37 years. Massive resection of 1000 gm and above (in each breast) was done in 03 cases. Minor complications were found in 03 patients including wound dehiscence at T junction with mild asymmetry (n=2) and areolar widening (n=1). The majority of the patients (90.99%) were very satisfied with their results. Objectively 72.72% patients had satisfactory results. No revision surgery or procedure was done.

Conclusion : The superomedial pedicle reduction mammoplasty is a safe and reliable technique for a wide range of symptomatic macromastia. Its versatility allows for reproducible results in a broad range of patients providing consistent results with respect to breast contour, nipple viability and lasting superomedial fullness in a less operating time.

Keywords: Gigantomastia, Breast hypertrophy, Reduction mammoplasty, Superomedial technique

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Introduction:

Breast is one of the most dynamic structure of the body which changes with ages, hormones and parity. Traditionally, female breast is the icon of beauty for a female body shape as well as confidence. There is difference of cup size of average breast in Asian subcontinent than rest of the world. Usually breasts are well developed since teenage period and cup size ranges from B to C in her young life. However, with dietary habit, lack of exercise, early marriage, lack of selfcare and early pregnancy results in macromastia very common in our country. Women suffers symptomatically with backache, heaviness, intertrigo and lack of self-esteem. Idiopathic hypertrophic gigantomastia is another entity which also demands intervention.

Reduction mammoplasty was not very commonly done plastic surgical procedure in our country. The trend is now uprising. Various procedures have been described for reduction mammoplasty with specific skin incisions, pattern of breast parenchymal resection keeping blood supply to the remaining breast tissue and NAC. Although related but they are independent of each other. There is no single technique which can be used for all types of macromastia. Irrespective of all techniques it has been shown to alleviate the symptoms and restores the quality of life.¹

Up to date, there are few published case series available in Bangladesh on reduction mammoplasty done by inferior medial pedicle technique.² This procedure was a commonly done technique in early days. Now a days, so many variable techniques have been described. Each technique has two main components- Skin re-draping and NAC transposition which can be performed on different pedicles. Here we followed superomedial pedicle technique in wise pattern skin incision for different types macromastia. The superomedial pedicle technique was first described by Orlando and Guthrie in 1975 for reduction mammoplasty.³ Since then over the years it has been modified by several authors and now a days it is established as a popular one. The main cause of which is the combination of superomedial pedicle technique and wise pattern skin incision can provide variable amount of parenchymal tissue as well as skin envelope resection which results in good contour of breast and durable results.⁴ The Aim of the study was to evaluate the outcome in term of safety, reliability and durability of this combination in different types of breast volume.

Material and method:

It is a retrospective study which includes 11 cases of macromastia who underwent bilateral reduction mammoplasty by superomedial technique. All the procedures were done in private hospital between July 2017– July 2021. Preoperative counselling was done about possible cup size, volume to be resected, scar placement, possible complications and aftercare. Patient's demographic data, preoperative BMI, complaints, photography and weight of the resected tissue were recorded. There is variation in definition of gigantomastia. It is defined as a condition requiring a reduction of more than 800 -2000 gm per breast.^{3,6,7,8} Here we referred to those breasts which weighted more than 1000gm termed as gigantomastia. Rests are defined as macromastia.

Surgical Technique:

Breast shape and contour are influenced by volume of breast parenchyma, amount and location of subcutaneous and intra-parenchymal fat, skin's thickness, tightness and elasticity.

Entire procedure is designed before surgery with the patient standing and arm placed to the sides. Upper border of manubrium, midline, the breast meridian along the midportion of the gland, inframammary fold is determined. New nipple position is planned by the point on breast

meridian that sits on IMF. The point is usually corresponding to half way of middle point of arm. The distance from manubrium sterni to the new nipple position is found usually between 19 cm to 23 cm depending on body stature of the patient. The keyhole template is then traced 2 cm above the new nipple position. Then vertical limbs are planned as a wise pattern ending above the IMF.

The superomedial pedicle is designed on the keyhole pattern to the bottom end of medial vertical limb. It leaves usually 1-3 cm border around the areola. The width of the pedicle varies between 10 and 15cm. The marking on both breasts are rechecked for the symmetrical outcome. Then photography was done in 5 views in standing position and per operatively in different steps.

Under general anesthesia, patient is placed in supine position. Local anesthesia is infiltrated in subcutaneous plane in the designed area of de-epithelization and incision line. Skin incisions are performed and the pedicle is deepithelialized. Skin and glandular tissue is excised down to chest wall. The majority of reduction comes from the inferolateral portion of the breast avoiding parenchymal tissue beneath the pedicle. A wedge of tissue is excised above the areola to provide place for proposed NAC. Then excised tissue was measured with weighing scale and additional resection was done if needed. NAC is then laterally rotated and sutured into its new position. All the incisions were closed in layers keeping negative suction drains in situ.

First check dressing was done on 5th POD and sports bra were applied. Drains were removed usually on 5th to 8th POD when the collection is less than 20ml/breast/day. Patients were followed up at 14th POD, one month, 3month, 6 month and then yearly.

All the patients were evaluated objectively and subjectively regarding their response to the treatment on each visit. Average follow up period was 15 months. Subjective assessment included patient's satisfaction rate which was graded from 1 to 5 as follows:

1 – poor, 2 – acceptable, 3 – satisfactory, 4 – good, 5 – excellent.

Objective evaluation was done by the physician which included following parameters as follows:

Symmetry	: Satisfactory – 1	Not satisfactory – 0
Volume	: Satisfactory – 1	Not satisfactory – 0
Contour	: Satisfactory – 1	Not satisfactory – 0
Projection	: Satisfactory – 1	Not satisfactory – 0
Scar	: Satisfactory – 1	Not satisfactory – 0

Any incidence of immediate or delayed complications was assessed and recorded at each visit including wound infection or dehiscence, seroma or hematoma formation, fat necrosis, asymmetry, scar widening, areolar widening, skin flap necrosis and NAC loss.

Results:

This retrospective observational study included 11 patients who underwent bilateral reduction mammoplasty using superomedial pedicle. The patient characteristics are summarized in table 1.

Table-1
Distribution of variables and outcomes in all the samples (n=11)

Sl. No.	Age (yrs)	Occupation	Pre-operative breast volume	Volume deducted (gram)		Post-operative cup size	Complication	Outcome		Follow up period
				Right	Left			Subjective	Objective	
1.	23	Housewife	Macromastia	350	340	C	Areolar widening	3	4	2 years
2.	33	Housewife	Gigantomastia	1500	1800	D	Wound dehiscence	4	3	1 year
3.	37	Banker	Macromastia	190	170	B	No	4	5	8 months
4.	17	Student	Gigantomastia	1000	1200	C	No	4	4	1.5 years
5.	29	Businessman	Macromastia	350	330	B	No	4	4	1.8 years
6.	26	Housewife	Macromastia	300	320	C	No	4	4	1.5 years
7.	15	Student	Gigantomastia	3400	4800	D+	Wound dehiscence	4	2	6 months
8.	25	Housewife	Macromastia	200	220	B	No	4	4	8 months
9.	24	Student	Macromastia	130	140	B	No	4	4	1 year
10.	23	Student	Macromastia	200	200	B	No	4	4	1 year
11.	21	Teacher	Macromastia	350	400	C	No	4	4	6 months

Youngest patient was 15 years old and age range was 15-37. The mean age of the patients at the time of surgery was 24.82 years. Distributions are given in Table II.

Table-II
Age distribution of the sample (n=11)

Age range	No of case	Percentage
Below 20	2	18.18%
20-30	7	63.64%
>30	2	18.18%

All the patients came from urban area except one was from remote village. Among them 5 patients were students. All patients belong to middle class to lower middle class. Among the patient 3 patients had gigantomastia. Other patients had breast volume of D-G cup size with grade 3 ptosis. Regarding the reduced volume, we assessed per-operatively by weighing of the resected tissue shown in chart 1.

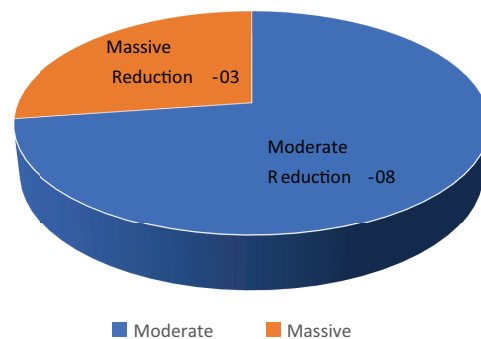


Chart:1 Distribution of the sample according to volume resected (n=11)

Patient 3:

37 years old lady who works in a bank presented with symptomatic Macromastia. She wanted moderate reduction with correction of ptosis. Finally, 190 gm on rt side and 170 gm on left side Reduction was done. She got relieved symptomatically and was satisfied subjectively and objectively.

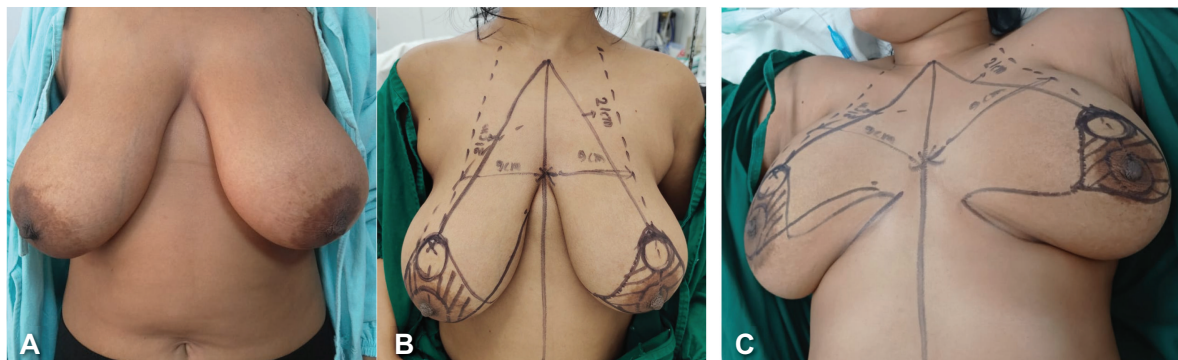


Fig: 1. a)Preoperative image on frontal view ;b) Planning and marking in standing position; c)In lying position



Fig.-1. d) Per operative image on frontal view ;b) On 5th Post operative day ;c) On 20th POD

Patient no 4:

17 years old girl presented with Idiopathic Juvenile Hypertrophy of both breast. She was suffering for last 6 years with this miserable gigantomastia. She couldn't go to school for last two years. Finally, 1000 gm on rt side and 1200 gm on left side reduction was done. She got relieved symptomatically and was highly satisfied subjectively.

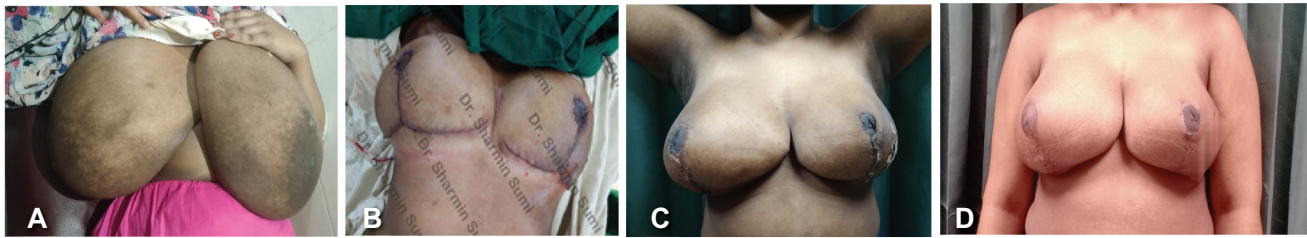


Fig.-2: a) Pre operative frontal view ;b) Immediate postoperative picture c) Follow up picture on one month ;d) Follow up picture on 8 month.

Patient no 9: 24 year old, unmarried student was suffering from neckache and loss of self-esteem with this ptotic and big size breast volume. Per operatively 130 gm in right side and 140 gram of tissue was excised on left side shown in Figure 3 (a – g).

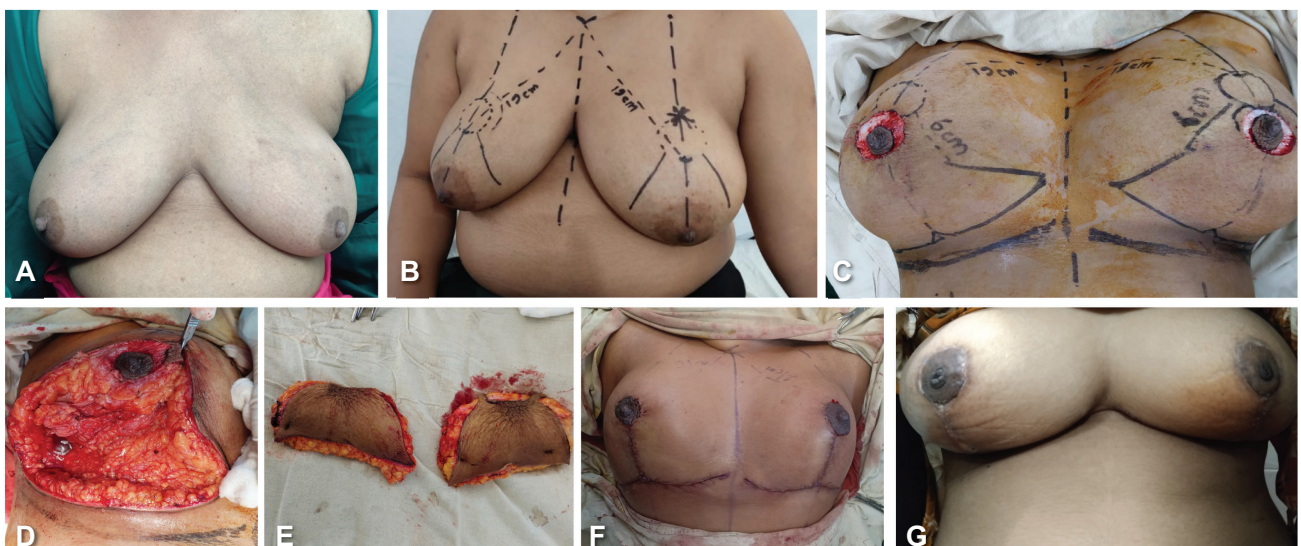


Fig.-3. a) Preoperative image on frontal view; b) Planning and marking c) Peroperative position ;d) Excision of tissue ;e) Resected tissue; f) Immediate postoperative picture g) Follow up picture on one month

Patient no 7: A 15 years old student was suffering from idiopathic juvenile hypertrophy of both breasts demonstrated in Figure 2(a – d). She underwent Massive reduction on both side.

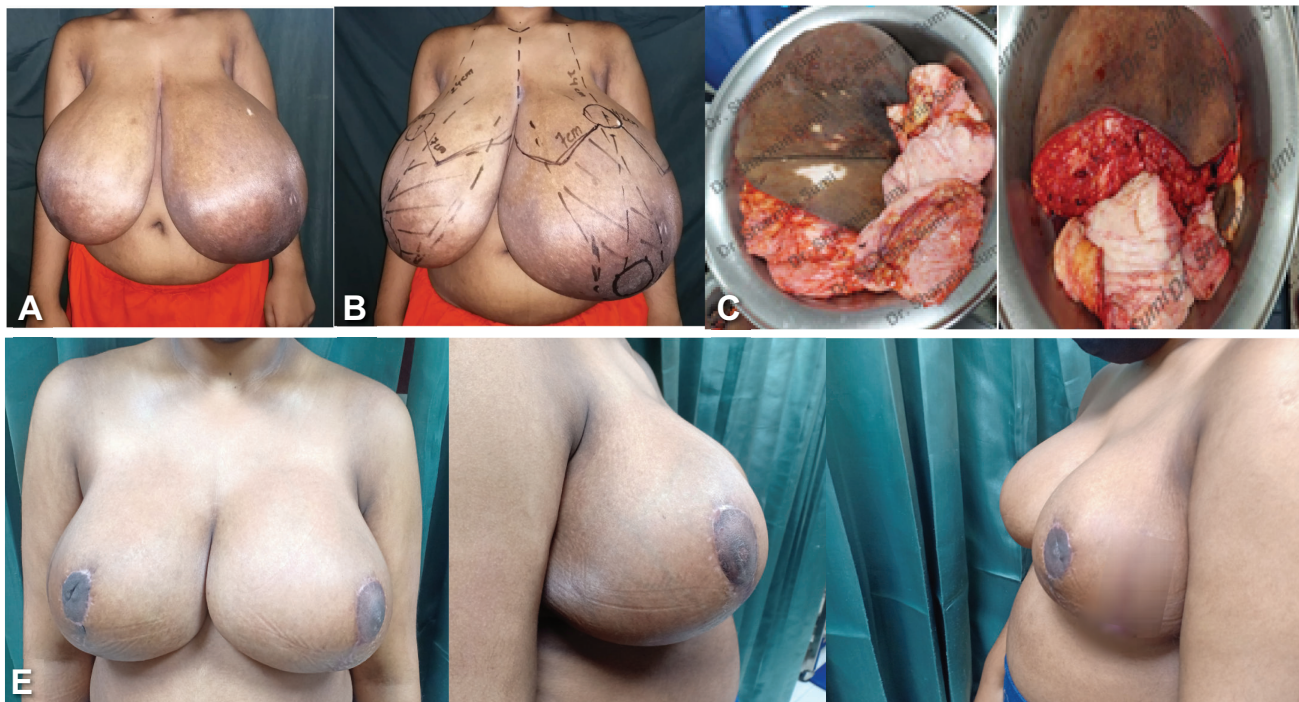


Fig.-4: a) Pre-operative in standing position b) Planning and Marking; c) Resected 4.8kg on left side and d) 3.4 kg on rt side. e) Follow up pictures on 3rd months postoperatively.

Clinically, every procedure was performed safely. There were no major complications. The common problem was healing difficulties in T junction. There was minor skin loss or scar widening in T junction over the new IMF. Only in two cases it was around one cm and it took additional dressing for recovery.

Table-III
Distribution of Clinical outcome (n=11)

Clinical Outcome	Problems	No of patient	Percentage
Eventful	1. T junction dehiscence-2	3	27.27%
	2. Areolar widening-1		
Unneventful		8	72.72%

The majority of the patients (90.99%) were very satisfied with their results. Objectively 72.72% patients had satisfactory results. No revision surgery or procedure was done.

Discussion:

Reduction mammoplasty techniques have evolved significantly with different pedicle and various skin excision patterns. In the hand of experienced surgeons, all the techniques provide satisfactory results. Still superomedial pedicle with wise pattern reduction is most frequently preferred among the plastic surgeons worldwide because of most probably the comfort level that surgeons have in applying this technique in all varieties and sizes of breast reduction and it's achieving predictable results.^{5,8}

In this study, the mean age of our patient was 24.82 years ranging from 15 to 37 years. It varies in different articles. The average age of 42 years (range: 16-76 years) was found in a study published in aesthetic surgery journal.⁹ Whereas Brownlee P, et al. reveals the mean age of 38 years (range: 18-74 years).¹⁰ In our study, the age variation is less as the procedure is less common among the lady beyond middle age because of socio-economical and religious factors. Small sample size may be another important contributing factor.

The mean resection weight per breast was 883.64 gm (range 130-4800gm) in this study. In the study of Brownlee p, et al. shows the mean resection volume per breast was 1016.7 gm (range: 74- 2469gm).¹⁰ Finger RE, et al. suggested the

applicability of the technique in reduction of 4100gm.¹¹ According to Bauermeister AJ, et al. the mean reduction weight was 730 gm per breast (range:100-4700gm) in a retrospective review study of 938 reduction mammoplasties with superomedial pedicle technique.¹² The result is very much consistent with available studies.

3 of the 11 patients reported complications in the form of wound dehiscence (n=2) and areolar widening (n=1), all of which were minor and didn't require secondary procedure. The result was almost similar in the study of Kemaloglu CA, et al. which were wound breakdown(1) and decreased nipple sensation (1) and there was also no major complication.⁵ In a retrospective review study of 938 superomedial pedicle based reduction mammoplasties conducted by Adam J. Bauermeister et al ,the overall complication rate was 16% .Of which 10% were minor complications related to delayed wound healing. Total complications included hematoma2%,infection 1%, partial nipple necrosis 3%.There was no cases of full nipple areolar complex or skin flap necrosis.¹³ Another retrospective study of 290 patients conducted by Keith C. Neaman et all , the total complication rate was 22.7%, with superficial dehiscence (8.8%) and hypertrophic scarring (8.8%) comprising the majority, with no episodes of nipple necrosis.⁹

According to the subjective assessment majority of the patients (90.99%) in the present study were very satisfied with their results, whereas 72.72% patients had satisfactory results in objective assessment. In a retrospective study conducted by Peymaneh Amini et al of cases of gigantomastia undergoing superomedial pedicled vertical reduction mammaplasty 91% patients were very satisfied with their results.³

Conclusion:

Superomedial flap technique resist the gravity over time, gives an elegant curve to lower border of the breast with better projection. The medial pedicle rotates easily into the position without any kinking or compression, less surgical time with less blood loss and can be done in all types of breast volume. Further studies need to be conducted with larger sample size and assess its superiority over other available techniques.

Limitations:

Retrospective study with a small sample size.

Financial disclosure:

None

Conflict of interest:

None

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No Skin Graft Required Over the Pedicle: A Modified Technique of Reverse Sural Island Flap

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Abstract

Background: The principles of reverse sural artery flaps, first described by Masquelet in 1992, represented a new concept in skin vascularization. The distally based superficial sural artery flap is an example of this kind of flap, which is supplied by the vascular axis that accompanies the sural nerve. The coverage of defects of the lower leg, achilles tendon, malleoli, ankle and heel remains a challenge to reconstructive surgeons. Modified reverse sural island flap is what we found handy in solving the problem for those defects.

Introduction: Modified reverse flow sural island flap is presented as an alternative to flaps used for coverage of defect over distal third of the leg, ankle, heel and tendo-achillis. This flap is based on the reverse flow of the superficial sural artery, which mainly depends on the anatomy of the perforators of the peroneal artery system. The anatomic structures that constitute the pedicle are the superficial and deep fascia, the sural nerve, the short saphenous vein, and the superficial sural artery.

Materials and method: We used the modified reverse sural artery island flaps in 97 patients between 2011 and 2020 in the department of Burn and Plastic surgery of Dhaka Medical College Hospital and National Institute of Trauma and Orthopedic Rehabilitation, Dhaka. Patients with soft tissue defect over distal leg, ankle, heel and tendo-achillis were included. We made a modification of reverse sural island flap. We left a skin extension over the fasciovascular pedicle and used it as a roof of the tunnel. We took the sural nerve and the deep fascia in all cases.

Results: The largest flap we have used was 10 cm in width and 12 cm in length. All flaps have survived. We observed cutaneous hypoaesthesia in all cases, venous congestion and edema in four flaps and marginal necrosis in three flaps. The functional result was good in all the patients, while the aesthetic appearance was acceptable even in female patients.

Conclusions: The main advantage of modified reverse sural island flap is a constant and reliable blood supply without sacrifice of a major artery and needs no skin graft over the pedicle of the flap as it is used as roof of the tunnel. This flap is useful in coverage of soft tissue defects over the achillis tendon, lower leg, ankle and heel, whenever reasons not to use a microsurgical free transfer.

Keywords: Reverse sural island flap, Ankle, Heel, Lower leg, Tendo-achillis.

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Introduction:

The reverse sural artery flap is a distally based fasciocutaneous or adipofascial flap used for wound coverage of the distal third of the lower extremity,

ankle and posterior heel [16]. Distally based or reverse sural artery flap, first described as a distally based neuro-cutaneous flap by Masquelet et al, in 1992, is a skin island flap supplied by the vascular axis of sural nerve. The superficial sural artery island flap is based on the superficial sural artery, which accompanies the sural nerve. The Modified reverse sural artery island flap is a “island flap” based on vascular axis of the sural nerve which gets reverse blood flow through communication with the perforating branch of the peroneal artery situated in the region of lateral malleolar gutter. The flap is vascularized by the median superficial sural artery, posterolateral septal perforators originating from the peroneal artery, neurovascular arteries of the sural nerve and combinations of these systems as suprafascial plexus. Coverage of the defects on lower leg ankle and heel areas asks for thorough knowledge of all the reconstructive options, starting with the use of local tissues. The scarce availability of such, makes this task difficult and demanding. Unique nature of blood supply around the lower leg and ankle, complicates this issue even more. The sural flaps provide good coverage of the defects, both from a functional and an aesthetic point of view. The major advantage of this flap is its easy and quick dissection. Because the major arterial axis is not sacrificed, this flap can be used in a traumatic leg with damaged major arteries. This axial pattern flap depends on the vascular axis of the superficial sural artery which is usually constant. Doppler study helps in detection of perforators preoperatively. Duplex scan could be of added advantage in the planning but is not mandatory.

Materials and methods:

Patients with soft tissue defect at the lower leg, ankle, heel or over tendo-achillis due to various causes represented by trauma, deep burn, unstable scars, chronic osteomyelitis, cancer excision, in which a microsurgical free transfer had no indication, were included for reconstruction in the Department of Burn and Plastic Surgery, Dhaka Medical College Hospital and National Institute of Trauma & Orthopedic Rehabilitation, Dhaka. There were 73 male patients and 24 female patients. The average age of patient was 35.5 year with age ranges from 21 to 55 years. The age of the defect on average was 14 days with the range of 6 to 24 days. Patient with Diabetes Mellitus, IHD and cigarette smokers were excluded.

Surgical Procedure:

After giving spinal anaesthesia, patient was placed in prone position. Tourniquet was used and removed after 90 minutes. We used hand held Doppler to locate the perforators around 6

cm from the lateral malleolus. After preparing the defect for flap coverage, the flap is outlined and raised according to the requirement of the defect from the posterior aspect of lower two-thirds of the leg centred around the midline of the leg. The flap was raised according to the anatomical landmark.

The upper limit of the flap was in the line between upper third and the lower two-third of the leg. The centre of the flap placed in the midline of the posterior surface of the leg with the pivot point of the pedicle located at least 6 cm proximal to the lateral malleolus. Direction distal to this point risks damaging the anastomotic connection with the peroneal artery and consequently of the flap itself. The pivot point was the site of anastomosis of the peroneal artery with the suprafascial sural artery that accompanies the sural nerve. To preserve the anastomosis within the suprafascial plane, the deep fascia was always included in the flap and pedicle. The pedicle was at least 3 cm wide containing subdermal layer with the sural nerve, accompanying superficial sural vessels and short saphenous vein. The lower limit of the flap is the line drawn above the desired length of the pedicle. The size of the flap varied depending on the size of the defect.

We made a modification of reverse sural island flap. The flap was raised keeping a skin extension over the fasciovascular pedicle and used it as a roof of the tunnel. The flap was rotated and transferred to cover the defect through a incision towards the defect. The donor site of the flap was covered by split skin graft from the ipsilateral thigh.

The limb was immobilized by POP anterior slab. Daily monitoring of the flap was done up to 7th POD. Dressing changes were done on 1st, 5th and 7th POD. Stitches were removed on 14th POD. All the patients were kept in POP cast for 3 weeks

with ankle in neutral position and further 6 weeks without plaster slab but non-weight bearing crutch walking. Patients were followed up to average of 6 months (4 months to 8 months). Patients were evaluated for flap acceptability, healing of the flap, durability of the flap, ambulation and sensation on the lateral side of the foot and also on the flap. Flap donor site was also examined for scar and keloid formation, pain and neuroma formation.

Results:

All flaps survived without any major complication. Four flaps showed slight venous congestion which cleared within a few days. Two patients developed infection, which was controlled with antibiotics and daily dressing later required a small area skin graft. Marginal necrosis was seen among three cases. It is probably because of tight suture and venous stasis and these cases were managed by secondary suture. Cutaneous hypoaesthesia was seen along the distribution of sural nerve in all cases, but this was improved within 6 months. The average healing time was 20 days and hospital stay time was 28 days.



Fig.-1: *Defect over tendo achillis.*



Fig.-2: *Modified reverse sural island flaps elevated.*



Fig.-3: *Modified reverse sural island flap rotated and placing on defect over posterior heel.*



Fig.-4: *Modified reverse island flap placed over the the defect of posterior heel*



Fig.-5: Modified sural island flap is placed over tendo achillis.



Fig.-6: Modified reversed sural island flap is placed over heel.

No debulking was needed in any of the flaps. None of the patients had any problem of wearing shoes. Any of the flap did not show any sort of ulceration during the follow up period. Donor area healed without problems like neuroma or ulceration, pain or ugly scar. There was no loss of split skin graft.

Discussion:

Soft-tissue defects of the distal third of the leg, ankle, foot and exposed achillis tendon are difficult to reconstruct. There are many options for coverage, including distally based fascio-cutaneous flap, muscle flaps, septo-cutaneous flaps, axial flaps, local transposition flaps and free flaps. Each one has its own specific indications and limitations 21. Fasciocutaneous flaps first introduced by Ponten B in 1981, are in use for the reconstruction of soft tissue defects of lower 1/3 leg and foot. Distally based fasciocutaneous flap based on perforators of either peroneal or post tibial arteries, needs to maintain length- breadth ratio, and is a two staged surgery. A huge amount of tissue is required to cover small to moderate-size defects 14. Lateral calcaneal flap can cover defect of 3 cm in diameter, so it is not suitable for larger defects. Cross leg flap is cumbersome and not suitable for elderly patients due to prolonged immobilization. It is also a difficult prohibition for younger patient. Free flaps may be an alternative but it needs expertise, well-trained surgical team and is a lengthy procedure requiring general anaesthesia and it is costly. It also becomes a big procedure when small to moderate-size defects require to be covered.

Reversed island flap e.g., peroneal artery flap, anterior tibial artery flap and posterior tibial artery flap can be transferred to the ankle or foot. However, it needs sacrifice of a major artery which constitutes a potentially serious disadvantage 21. Considering these limitations pedicle flaps can be considered a first-line therapeutic option 4.

The superficial sural artery based island flap has many advantages 17. The important advantage of the distal sural flap is that the blood supply is reliable, making this flap safe, even in patients with distal arterial insufficiency and there is no sacrifice of major arteries or nerves. In fact, this flap can be used in traumatic legs with damaged major arteries. It is necessary that the pedicle is at least 3 cm wide containing subdermal layer with the sural nerve, accompanying superficial sural vessels, and short saphenous vein. It should not extend beyond the line drawn 6 cm proximal to lateral malleolus. The superficial sural island flap is a good choice to the management of exposed achillis tendon. It has wide range of arc of rotation 180° for Achillis tendon coverage and is easy to perform by someone with less expertise. The operative procedure is easy and can be

accomplished in a short period of time with regional anaesthesia, which is very advantageous for patients with a generally poor medical condition. The success rate is high and minimal flap loss and other complications. Because this flap is fasciocutaneous, its durability is excellent, even in weight-bearing areas at the back of the heel on tendo-Achillis. The under surface of the flap provides a good surface for gliding of the tendon. For reconstructions in the Achillis' tendon area, all the flaps used were fasciocutaneous, and no debulking procedure was necessary. This flap has some limitations like maximum safe length-breadth ratio yet to be defined. There are no studies regarding maximum flap dimension (specifically, width) and safety, but usually a relatively large flap can be harvested with little donor site deformity or morbidity.

Kalam MA, et al, in 2005, described a largest flap measured 14x12 cm could be harvested without risk of flap loss. That large flap healed without any complications. The largest flap that we have used was 12 cm in length and 10 cm in breadth.

The main disadvantages of this flap are the sacrifice of the sural nerve and the final scar, mainly when there is a need for skin grafts to close the donor area. This is important particularly in women.

When the donor area is closed directly, the final result is aesthetically more acceptable. Direct closure of the donor area is possible for flaps less than 4 cm in width [17]. In all our cases the donor site was closed by split skin graft. In our series, all of the cases developed hyposthesia in the distribution of sural nerve area and recovered within 6 months of the harvest of this flap. All cases have recovered despite the fact that the nerve was always cut and raised with flap. There was no neuroma at the donor site as well.

Pirwani et al, in 2007, showed in their study that all flaps survived except one. Paraesthesia developed on the lateral border of the foot but recovered within two months and most flaps showed venous congestion and disappeared within few days.

Kalam MA, et al, in 2005, described the reverse sural island flap technique for coverage of the exposed tendo-achillis and showed that out of 30, 26 flaps taken off without any complication, 4 patients developed flap oedema and marginal necrosis were seen in 3 cases. One patient developed infection which was controlled by antibiotics.

Heisinga RL, et al, in 1988, used distally based sural flap on 15 patients for soft tissue coverage in the lower leg, malleolar, and heel regions. Twelve flaps survived, two partially survived, and one flap failed due to persistent infection.

Jeng SF, et al, in 1997, used the reverse sural artery flap to cover exposed achilles tendon and soft tissue defects of the

ankle and the heel. Of the 22 patients described, 20 had complete success with two minor complications that were treated uneventfully.

The modified reverse sural island flap is a one-stage, safe and easy procedure that can be used for defects over lower leg, ankle, heel and tendo-achillis. Advantages of this flap are that no skin graft is needed over the pedicle over the flap, the blood supply is reliable, execution is easy and fast, the operation can be performed under regional anesthesia, the flap has a large arc of rotation, direct closure of the donor area is possible for small flaps, major arteries or nerves are not sacrificed, and excellent durability is achieved, even on weight-bearing areas.

Conclusion:

The modified reverse sural island flap as a good choice for treating exposed achilles tendon, lower leg, ankle and heel because the flap has good number of advantages. It is a one stage operation, which does not require microsurgical techniques. Elevation of the flap is easy and quick. The donor site has minimal morbidity as it can be closed primarily when small flap is raised and skin graft when large flap is raised. The vascular supply to the arterial network of the sural area is constant and reliable, and there is no need to sacrifice any major artery and or sensory nerve. The pedicle is long, and the island flap can be transferred around the ankle. The deep fascia under the flap provides a good gliding surface for excursion of the tendon. It does not need skin graft over the pedicle of the flap. This flap should no longer be regarded as a flap of secondary choice to free tissue transfer, but as an equally valuable alternative for defects around the lower leg, ankle, heel and exposed tendo-achillis.

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A Comparative Study of Renal Biochemical Parameter between Preeclampsia and Normal Pregnant Women

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Abstract:

Introduction: Preeclampsia is a multisystem disorder, unique to pregnancy that is usually associated with high blood pressure and proteinuria after 20 weeks of gestation. Renal functions are also impaired in preeclampsia, resulting in alteration of renal biochemical parameters. These are associated with a higher risk of adverse maternal and fetal outcome. The aim of this study to observe the alteration of renal biochemical markers in preeclampsia.

Material and Methods: The present cross-sectional study was carried out in the Department of Biochemistry, Dhaka Medical College, and Dhaka from July 2015 to June 2016. A total number of 100 pregnant women in third trimester of pregnancy with or without preeclampsia, attending in the outpatient Department of Obstetrics and Gynecology in DMCH, were selected as study subjects. Of them fifty pregnant women in third trimester were with preeclampsia and fifty were normal healthy pregnant women. Both groups were age matched. Data was collected using a preformed data collection sheet, enquiring about demographic data and details of risk factors. Estimation of renal biochemical parameters like blood urea, serum creatinine, serum uric acid and eGFR were done in both preeclampsia and normal pregnant patient and mean values of the variables were compared between them.

Result: Blood urea increased in preeclampsia than normal pregnancy (42.4 ± 16.0 mg/dl vs 16.8 mg/dl ± 2.6 mg/dl, $p .007$), serum creatinine also increased in preeclampsia than normal pregnancy (2.0 ± 1.0 mg /dl vs 1.0 ± 0.3 mg/dl $p .002$). In preeclampsia uric acid level were also increased than normal pregnancy (5.7 ± 1.5 mg/dl vs 3.8 ± 1.0 mg/dl, $p < .001$). The level of eGFR were 41.0 ± 25.3 ml/min vs 75.0 ± 10.5 ml/min ($p < .001$), which was significantly lower in preeclampsia than normal pregnancy.

Conclusion: Renal functions are impaired in preeclampsia. So routine assessment of these parameters may helpful to prevent worse outcome of preeclampsia patients.

Keywords: Preeclampsia, Renal biochemical parameter, Pregnant women.

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Introduction:

Preeclampsia is a syndrome defined by hypertension and proteinuria that also may be associated with other signs and symptoms, such as edema, visual disturbances, headache, and epigastric pain. Laboratory

abnormalities may include hemolysis, elevated liver enzymes, and low platelet counts (HELLP syndrome). Women with chronic hypertension also may have superimposed preeclampsia, who develop headache, scotomata or epigastric pain in there gestationaol period.¹ The risk of preeclampsia is 4.1% in women in first pregnancy and 1.7% in later pregnancies. However, this risk rises to 14.7% in the second pregnancy in woman who had preeclampsia in their first pregnancy.

The risk is 31.9% in woman who had preeclampsia in their previous two pregnancies². Incidence of preeclampsia varies with geographic location. It is the leading global cause of maternal and perinatal mortality and approximately 50,000 to 60,000 women die each year. Maternal deaths in Asia are about 9%³. In approximately 15% of pregnancies there is mild preeclampsia, In around 8% case there is moderate

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to severe preeclampsia and severe preeclampsia in about 1% to 2 %. Preeclampsia is responsible for 16% maternal morbidity and 28% of perinatal mortality⁴. Preeclampsia is the 3rd leading cause for maternal mortality and the 7th leading cause for the perinatal mortality all over the world⁵.

Dhaka Medical College Hospital is one of the well-known tertiary referral hospitals in Bangladesh and has a separate well equipped eclampsia unit functioning since 1992. Among the total obstetric admission each year around 600-700 patients are admitted in the eclampsia unit, which is recorded as 7.0 -8.5%⁶.

During pregnancy, certain changes occur in kidney such as increase in size and length of the kidneys. There is increased renal blood flow and the renal vascular volume that causes slight hypertrophy of the kidney⁷. Renal plasma flow increase in pregnancy due to increased cardiac output and afferent and efferent arteriolar vasodilatation, secondary to action of some humoral factors or the resistance to aldosterone action. In preeclampsia there is increase in the afferent arteriolar resistance that causes increased Renal vascular resistance⁸.

In preeclampsia endothelial cells appear primarily to be injured in contrast to other nephrotic diseases⁹. Pathologic finding reveals "Glomerular endotheliosis" which is responsible for renal dysfunction in Preeclampsia.¹⁰The common renal biochemical parameters which determined the renal functions are: a) blood urea, b) serum creatinine, c) serum uric acid and d) e-GFR. Patients are more likely prone to develop preeclampsia who have both hyperurecemia and hypertension in second half of pregnancy even in absence of proteinuria¹¹

In preeclampsia there is vasospasm and glomerular capillary endothelial swelling that causes decreased renal blood flow and GFR with the development of toxemia. The decrease in GFR is about 25% below the rate of the normal pregnancy. Due to decreased GFR, urea and creatinine excretion are decreased, so that serum urea and creatinine concentration rise¹².The eGFR is a test that is used to assess how well kidneys are working. The test estimates the volume of blood that is filtered by kidneys over a given period of time. The kidneys are consisting of glomeruli that are the tiny filters. The kidney is said to have reduced or impaired kidney function when these filters do not do their job properly.¹³They also stated that eGFR test involves a blood test which measures a chemical called creatinine. The level of creatinine in the blood goes up If kidneys do not work properly. In this study renal biochemical parameters were assessed to predict adverse maternal outcomes in women with preeclampsia.

Material and Methods:

This cross sectional study was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka, from July 2015 to June 2016. A total one hundred patients with preeclampsia and healthy pregnant women attending in the department of obstetrics and gynecology were taken as study population, fifty with preeclampsia and fifty with normal pregnancy without preeclampsia. Sample was taken purposively. Data were collected by using a preformed data collection sheet. Blood urea, serum creatinine, serum uric acid, urinary protein and estimated GFR of both groups were measured. Estimation of seum urea was carried out using a modified urease Berthelot color/end point method. Estimation of serum creatinine was done by alkaline picrate methods using reagents. Estimation of serum uric acid was done by Uricase POD. Urinary protein was estimated by heat coagulation test. Statistical analysis was performed by using the SPSS version 20.0.All data were processed to compute mean and standard deviation. Difference of mean among two groups was compared by unpaired t test. Determinations of correlation between variables were done by Pearson's correlation test. Statistical analysis was performed by using the SPSS version 20.0. Data was presented by table and graphs.

Results:

Systolic and diastolic blood pressures as well as BMI were significantly higher in preeclampsia than normal pregnancy but there was no statistical significant difference in age between these two groups (table I).

Table I shows age, blood pressure and BMI in preeclampsia and normal pregnancy.

Table I
General and physical characteristics of study subjects (n=100)

Variables	Group		p value
	Preeclampsia Mean $\pm$ SD	Normal pregnancy Mean $\pm$ SD	
Age (years)	28.06 $\pm$ 5.93	26.20 $\pm$ 5.32	0.102 ^{ns}
Systolic (mmHg)	153.4 $\pm$ 16.7	113.4 $\pm$ 4.5	0.001 ^s
Diastolic (mmHg)	91.7 $\pm$ 5.2	74.1 $\pm$ 6.6	0.001 ^s
BMI (kg/m ²)	29.9 $\pm$ 5.1	26.5 $\pm$ 4.0	0.001 ^s

Renal biochemical parameters like blood urea, serum creatinine, serum uric acid, urinary protein were increased and eGFR was decreased in preeclampsia than normal pregnancy (Table II).

Table II
Renal biochemical parameters level of study subjects
(n=100)

Renal biochemical parameters	Group		p value
	Preeclampsia Mean $\pm$ SD	Normal pregnancy Mean $\pm$ SD	
Blood urea	42.4 $\pm$ 16.0	16.8 $\pm$ 2.6	0.001 ^s
Serum creatinine	2.0 $\pm$ 1.0	1.0 $\pm$ 0.3	0.002 ^s
Serum uric acid	5.7 $\pm$ 1.5	3.8 $\pm$ 1.0	0.001 ^s
eGFR	41.0 $\pm$ 25.3	75.0 $\pm$ 10.5	0.001 ^s

All the renal parameters were positively correlated with systolic blood pressure in both groups but only blood urea was significantly correlated in preeclampsia group.(Table III).

Table III
Correlation of systolic blood pressure with renal biochemical parameters

Renal biochemical Parameters	Group			
	Preeclampsia		Normal pregnancy	
	r value	p value	r value	p value
Blood urea	0.337	0.017 ^s	0.280	0.049 ^s
Serum creatinine	0.256	0.073 ^{ns}	0.058	0.689 ^{ns}
Serum uric acid	0.201	0.162 ^{ns}	0.109	0.451 ^{ns}
eGFR	0.232	0.104 ^{ns}	0.004	0.980 ^{ns}

All the renal parameters were positively correlated with diastolic blood pressure in preeclampsia but not significantly. In normal pregnancy, blood urea, serum uric acid and eGFR were negatively and serum creatinine was positively correlated with diastolic BP but not significantly.

Table IV
Correlation of diastolic blood pressure with renal biochemical parameters

Renal biochemical Parameters	Group			
	Preeclampsia		Normal pregnancy	
	r value	p value	r value	p value
Blood urea	0.167	0.246 ^{ns}	-0.137	0.341 ^{ns}
Serum creatinine	0.251	0.078 ^{ns}	0.026	0.858 ^{ns}
Serum uric acid	0.110	0.446 ^{ns}	-0.024	0.871 ^{ns}
eGFR	0.198	0.169 ^{ns}	-0.057	0.696 ^{ns}

Discussion:

This cross-sectional study was carried out with the aim to compare the renal biochemical parameters between preeclampsia and normal pregnancy. Of the 100 patients 50 were with preeclampsia and 50 were normal healthy pregnant women. In the present study in preeclampsia, mean value of blood urea was 42.4 $\pm$ 16.0 mg/dl, serum creatinine was 2.0 $\pm$ 1.0 mg/dl and serum uric acid level was 5.7 $\pm$ 1.5 mg/dl. Where as in normal pregnancy the values were 16.8 $\pm$ 2.6 mg/dl, 1.0 $\pm$ 0.3 mg/dl, 3.8 $\pm$ 1.0 mg/dl respectively. These parameters were higher in preeclampsia in comparison to normal pregnancy (Table-II). The renal biochemical parameters correlate positively with systolic and diastolic blood pressure.

In the study conducted by Babu et al.¹⁴ in 2013 it was observed that blood urea, serum creatinine and serum uric acid was also higher in preeclampsia than the normal pregnancy. Blood urea, serum creatinine level correlated positively, but the raised uric acid level did not correlate with the systolic or diastolic blood pressure. It may be due to their study design and large sample size. Study conducted by Jamiel et al.¹⁵ in 2014, revealed that, uric acid levels differ significantly ($p < 0.001$) between control and preeclampsia group. Serum creatinine levels were observed to be significantly higher in preeclampsia group compared to control group. There was significant increase in creatinine levels between control and PET group ($p < 0.001$). In their study uric acid and creatinine positively correlated with systolic and diastolic blood pressure. In the Study conducted by Kamath.¹⁶ in 2006 the mean uric acid levels in the control group was found to be 3.07 mg/dl, in moderate to severe preeclampsia the value was 5.57 mg/dl.

Mean value of eGFR in our study was 41.0 $\pm$ 25.3 ml/min in preeclampsia and 75.0 $\pm$ 10.5 ml/min in normal pregnancy (Table-II). The result was statistically significant between two groups ($P < 0.001$). eGFR correlate positively with systolic and diastolic blood pressure in preeclampsia. Study conducted by Sonagra et al.¹⁷ in 2015, eGFR was significantly lower in preeclamptic women when compared with normal pregnant women. Such decline in GFR can be attributed to renal damage caused by preeclampsia. There was positive correlation of this finding with systolic and diastolic blood pressure. Alper et al.¹⁸ conducted a study in 2007, in normal pregnancy significant increase of GFR is noted, this change was absent in preeclampsia.

Conclusion:

The finding of this study shows that there is an association between preeclampsia and renal biochemical parameters like blood urea, serum creatinine, serum uric acid, eGFR.

Estimation of these parameters have predictive role as an alert of preeclampsia. These findings may be very useful to prevent the adverse outcome of preeclampsia.

Conflict of interest:

No conflict of interest was reported.

Consent:

Informed written consent was taken from the patients regarding the study.

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Comparison of Conventional Methods and Polymerase Chain Reaction for Detection of *Neisseria gonorrhoeae* in Male Urethritis Patients

Mustary JF¹, Chowdhury AHMSK², Sultana A³, Ahmed KI⁴, Akter N⁵

Abstract

Background: Urethritis is an important sexually transmitted infection. *Neisseria gonorrhoeae* is one of the most common bacterial causes of urethritis. The aim of this study to detect *Neisseria gonorrhoeae* infection in men by Gram stain, culture and PCR and comparison among them.

Methods: It was a cross sectional study and conducted in Microbiology department of Chittagong medical college, Chattogram from July 2017 to June 2018. Urethral discharge was collected from 142 clinically suspected patients attending at skin and venereal disease department of CMCH. *Neisseria gonorrhoeae* was detected by gram stain, culture in Chocolate agar media and Thayer martin media and PCR.

Results: Out of 142 samples, 27.46% were positive in Gram stain, 24.65% yielded growth in culture media and 31.69% cases were positive by PCR. Considering culture as gold standard, the sensitivity of PCR was 100%, specificity was 90.65%, positive predictive value was 77.78%, negative predictive value was 100% and accuracy was 92.98%. Six smear negative and ten culture negative samples were positive by PCR.

Conclusion: Early detection of gonococcal urethritis is important to prevent of its complications and spread of this disease. PCR was the most sensitive and rapid method for detection of gonococcal urethritis.

Key words: PCR, *Neisseria gonorrhoeae*, Urethritis, STD.

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Introduction:

Inflammation of the urethra is called urethritis, characterized by discharge, dysuria and or urethral itching. Sexually transmitted pathogens are responsible for urethritis¹. Primary pathogens are *Neisseria gonorrhoeae* and *Chlamydia trachomatis*.² The most common bacterial sexually transmitted infections (STIs) worldwide is *Neisseria*

gonorrhoeae. Each year 106.1 million cases of gonorrhoea occur among adults³. Prevalence of gonorrhea in adult male in different regions are 1.72% in Africa, 0.68% in the region of America, 0.21% in European region, 1.1% in South- East Asia and 0.52% in Western Pacific region⁴. In Bangladesh, the prevalence of *N. Gonorrhoeae* infection among hotel-based and street-based sex-workers are 35.8% and 35.5% respectively^{5,6} and 30.27% cases reported as bacterial causes of urethritis in men in Dhaka medical college hospital⁷. *N. gonorrhoeae* infection occurs most commonly as an acute urethritis in men. However, a small percentage of men will develop asymptomatic gonococcal urethritis⁸. Severe sequelae includes epididymitis, prostatitis and urethral stricture may develop if urethritis left untreated⁹. Human immunodeficiency virus (HIV) may transmit in gonococcal infection. Men who are infected with both gonorrhea and HIV have 10 times higher HIV concentration in their semen¹⁰. There are a number of laboratory methods which detect organisms causing urethritis ranges from cell culture

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to nucleic acid amplification tests¹¹. Microscopy, culture and various other non-culture methods are used for diagnosis of gonorrhoeae. However, serology is not useful for diagnosis of this infection¹². Microscopy is cheap, provides rapid results, and has a high sensitivity and specificity for the diagnosis of symptomatic men with urethral discharge. However, cervical, pharyngeal, or rectal gonorrhoea or for asymptomatic patients, microscopy is not recommended as the only method to diagnose these infections¹³. A positive result of Gram stain of urethral smear is helpful to diagnose gonorrhoea but the infection cannot be ruled out by negative smear result due to its comparatively lower sensitivity (90%)¹⁴. Culture has been considered as the gold standard for the diagnosis of both genital and extra-genital gonorrhoea. It is sensitive and highly specific and importantly allows antimicrobial susceptibility testing¹⁵. However, it requires well-trained staff and false-negative results can occur due to poor specimen storage, transport problems or growth inhibition by components of selective media¹⁶. Multiple infections are difficult to treat. For the detection of multiple pathogens in a single specimen, multiplex PCR is very sensitive and more rapid method now a day's¹⁷. Polymerase chain reaction (PCR) can detect both viable and nonviable bacteria and it is useful for identification of microorganisms that are difficult to cultivate and those grows slowly¹⁸. The higher sensitivity and better specificity of PCR is its main advantages over other tests¹⁹.

Methods:

This cross sectional study was carried out in the department of Microbiology, Chittagong Medical College, Chattagram from July, 2017 to June, 2018 after approval from Ethical Review Committee. A total 142 patients having urethral discharge were enrolled as the study group. Informed written consent was taken from the participants after proper briefing about the purpose of the study. At least one hour after urination, three urethral swabs were collected directly from each patient. First swab was used for making a smear of the discharge on two separate clean glass slides, the second swab was used for culture. Third swab for PCR and store at -20°. After fixing with methanol, the prepared smear stains by Gram's stain and methylene blue stain and examine with the 100X objective to detect pus cells, intracellular or extracellular gram negative diplococci. The specimen of urethral discharge was inoculated at collection site on Chocolate agar media and Thayer Martin (TM) media with proper labeling. Culture plates were examined after 24 hours of incubation for growth of *Neisseria gonorrhoeae*.

Presumptive identification was done by standard procedure. DNA was extracted from clinical samples by DNA extraction kit (Thermo Scientific Gene JET Genomic DNA Purification Kit, Lithuania). Oligonucleotide primers were used for PCR amplification of *Neisseria gonorrhoeae*. *Neisseria gonorrhoeae* DNA was detected by PCR targeting a sequence of *cppB* gene using primer 5'GCTACGCATACCCGCGTTGC3' and 5'CGAAGACCTTCGAGCAGAC3'. Size of amplified product of *Neisseria gonorrhoeae* was 390 bp²⁰. For each sample, a total 25µl of mixture was prepared by mixing of 12.5µl of mastermix (mixture of dNTP, taq polymerase *Mgcl2* and PCR buffer), 2µl of forward primer, 2µl of reverse primer, 2µl of DNA template and 6.5µl of nuclease free water in a PCR tube for *N.gonorrhoeae*. All the reagents were taken in a 0.2 ml PCR tube, then centrifuge briefly to remove any bubble. Thirty six cycles of amplification were performed in a DNA thermal cycler (Eppendorf AG, Mastercycler gradient, Hamburg, Germany). Each cycle consisted of a one minute denaturation step at 94°C, 45 second annealing step at 62°C and one minute thirty second amplification step at 72°C for *N.gonorrhoeae*. Each reaction was preceded by 10 minute initial denaturation and followed by 10 minutes final extension steps. The amplified DNA were loaded into a 1.2% agarose gel, electrophoresed at 120 volt and 90 mA for 30 minutes and visualized under UV light.

Results:

Among 142 cases, ages of the patients were recorded from 20-60 years and highest cases were in the age group 21-30 years (51.40%). The mean age of the patients was 30 ± 7 years.

Table - I
Age distribution of study subjects (n = 142)

Age Group	Frequency	Percent (%)
<20 years	13	09.15
21-30	73	51.40
31-40	46	32.40
41-50	06	4.23
51-60	04	2.82
>60 years	00	0.00
Total	142	100

Mean age±SD= 30.71± 7.48

Out of the 142 cases having urethral discharge, 27.46% cases were detected by Gram stain, 24.65% cases were positive for culture and DNA of *N.gonorrhoeae* was detected by PCR in 31.69% cases.

Table - II

Different methods for detection of N. gonorrhoeae among the suspected cases (n=142)

Method	Positive cases n (%)
Gram stain	27.46%
Culture	24.65%
PCR for <i>N. gonorrhoeae</i>	31.69%

Of the 142 samples, 39 were positive by both Gram stain and PCR, whereas 97 were negative by both methods. Remaining 6 samples were positive by PCR but negative by Gram stain.

Table-III

Comparison of results of Gram stain with PCR for detection of Neisseria gonorrhoeae (n=142)

PCR	Gram stain		No of cases
	Positive	Negative	
Positive	39	06	45
Negative	00	97	97
Total	39	103	142

In case of PCR

Sensitivity	:	100%
Specificity	:	94.17%
Positive predictive value	:	86.66%
Negative predictive value	:	100%
Accuracy	:	95.77%

Out of the 142 samples, 35 were positive by both PCR and culture and 97 cases were negative by both methods. Remaining 10 samples were positive by PCR but negative by culture. Considering culture as gold standard, the sensitivity of PCR was 100%, specificity was 90.65%, positive predictive value was 77.78%, negative predictive value was 100% and accuracy was 92.98%.

Table-IV

Comparison of results of culture with PCR for detection of Neisseria gonorrhoeae (n=142)

PCR	Culture		No of cases
	Positive	Negative	
Positive	35	10	45
Negative	00	97	97
Total	35	107	142

In case of PCR

Sensitivity	:	100%
Specificity	:	90.65%
Positive predictive value	:	77.78%
Negative predictive value	:	100%
Accuracy	:	92.98%

Discussion:

Urethritis, an inflammation of urethra is a multifactorial condition which is primarily sexually acquired²¹. Despite a sharp decline in the incidence of gonococcal infection in developed countries during the last decade, gonorrhoea still remains one of the most common STIs in developing countries and a global health problem²². In the present study, 142 male patients having urethral discharge were enrolled. It was observed that 51.40% of the cases were in 21-30 years of age. Similar study from Bangladesh found the highest age group was belonged to 21-30 years²³. The mean age was 30±7 years in this study. Amin *et al.* 2007²⁴ reported that mean age of the male patients having acute urethritis was 29±9 year which is comparable with the current study. Among 142 male patients, *N. gonorrhoeae* was detected by Gram stain in 27.46% cases and yield growth in culture in 24.65% cases. This is correlate with Jahanet *al.* 2014⁷. The rate of *N.gonorrhoeae* isolation by culture was low in this study for the reason that prior antimicrobial therapy, loss of viability of the organisms during transport, low concentrations of the organisms²⁵. In this study, 31.69% gonococcal infections were detected by PCR among 142 sexually active male patients. Similarly, Jahan *et al.* 2014⁷ and Nessa *et al.* 2004⁵ found 30.27% & 35.8% gonococcal infections respectively. In another study, among 669 patient specimens 11% were gonococci positive²⁶. The difference in gonococcal infection rates reflect that the infection varies in different population, different regions and different in social and sexual behavior of patients. In the study population, 45 were identified by PCR and 39 were identified by Gram stain. Among them six were positive by PCR but negative

by Gram stain. The sensitivity of PCR was 100% and specificity was 94.17%. Amin *et al.* 2007²⁴ reported that the sensitivity of PCR was 100% and specificity was 85.71% which is consistent with this study. In this study, 142 urethral discharge samples were compared for diagnosis of gonorrhoea infection using culture and PCR. Among them, 35 were positive by both culture and PCR, 10 of the 107 culture negative cases were positive by PCR. Considering culture as gold standard, the sensitivity of PCR was 100% and specificity was 90.65%, positive predictive value 77.78%, negative predictive value 100%, accuracy 92.98%. Jahan *et al.* 2014⁷ reported the sensitivity of PCR was 100% and specificity was 94.85% which is correlate with this study. Considering the findings of the study, it is suggests that PCR is a useful tool for diagnosis of gonococcal urethritis.

Conclusion:

PCR is a rapid and sensitive method especially in clinically suspected urethritis patients who remain negative by conventional methods. It is recommended that PCR may be included as a highly sensitive technique along with conventional methods in routine diagnostic procedures.

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Juvenile Carcinoma of Breast - A Case Study

Hossain MD¹, Awwal R², Razzak M³, Talukder M⁴

Abstract:

Secretory breast carcinoma (SBC) is a rare, invasive type of breast tumor which accounts for < 0.1% of all cases of invasive breast cancers. It was originally described as a juvenile breast carcinoma, occurring in young children and adolescent women. SBC is associated with a characteristic balanced translocation, t(12;15), that creates a ETV6-NTRK3 gene fusion. It is difficult to differentiate malignant from benign lesions with MRI. Hence, core needle biopsy of a solid portion is essential for early detection of secretory carcinoma, in order to prevent delayed diagnosis of malignancy. This tumour occurs in individuals of various ages. The symptoms and clinical characteristics also differ in each patient. Therefore, therapeutic strategy should be selected based on the overall status of the patient and the characteristics of this rare disease.

Keywords: Breast cancer, Breast surgery, ETV6-NTRK3, Fluorescence in situ hybridization, Immunohistochemistry, Secretory breast carcinoma.

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Introduction:

Secretory breast carcinoma (SBC) was first described by Mc Divitt and Stewart in 1966¹, who reported seven cases of this tumoural strain in children and therefore named it “juvenile carcinoma”. However, a couple of decades later, Tavassoli and Norris reported a series of 19 cases and found that most occurred in adults, and therefore they proposed changing its name to “secretory carcinoma.” Since then, approximately 100 cases have been reported in the world literature². Juvenile carcinoma is the most common mammary carcinoma in children³. The age of presentation documented ranges from 3 to 83 years^{2,3} with a mean of 33 and a median of 40.¹

We like to attract the attention of the clinicians on this case report and literature review to raise awareness about SBC by demonstrating how uniquely this pathology can present

itself and to present our specific approach to this rare cancer. To our knowledge, only a few cases have been reported in Bangladeshi patients.

Presentation of the Case:

A 29-year- female Hindu woman was admitted on May 25, 2021 with the complaints of development of a lump in her right breast at upper outer quadrant with enlargement of right sided axillary lymph node which the patient noticed since Jan, 2021. She had no significant previous medical history. She was referred to the Breast Unit of NIPBS (Former SHNIBPS), Dhaka with no relevant family history. She had no history of diabetes or hypertension and after physical examination she is found having a small lump in her right breast which is mobile, non tender and not fixed with right sided axillary lymph node enlargement. Then mammography and ultrasound reports show a 50x42 mm tumor in the right breast, classified as BIRADS 3 suggestive of malignancy. Her Hb: 9.6 gm/dl, ESR: 34 mm at the end of one hour, ANA: Negative, contralateral breast is normal on USG, CA 15.3: Normal, APTT: Normal, Prothrombin Time: also within normal limit.

Intra-operative cytology from two sentinel lymph nodes is carried out in NIPBS (Former SHNIBPS) at the department of Pathology on 25.05.2021 and found positive for malignant cells and operation was proceeded accordingly. The specimen is then processed for histopathology and confirmation is ensured as metastatic adenocarcinoma.

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Simple mastectomy and axillary dissected specimen of this patient are received at laboratory in 10% Formalin and processed accordingly.

It is diagnosed as a case of infiltrating carcinoma with PAS stain: positive and axillary metastasis.

Nottingham Histologic SCORE: found a total score: 6 and **Tumour Grade: II.** Pathological stage IIA by pT2aN2M1.

Immunohistochemical examination revealed 50% of tumour cells show positive nuclear staining for Oestrogen receptor, 40% of tumour cells show positive nuclear staining for Progesterone receptor, no membrane staining in any tumour cells for Her-2/Neu and for Ki-67 shows <5% positive staining.

Molecular testing is advised for ETV6 and NTRK3 on Fluorescence *In-Situ* Hybridization (FISH). These morphologic, immunohistochemical and molecular findings favor diagnostic of secretory carcinoma of the breast.

Adjuvant chemotherapy is recommended by the radiation oncologist Inj. Doxorubicin 70 mg D1 for 6-8 cycle and Endocrine therapy. Patient is planned for follow up with clinical examinations every 3-4 months, tumor markers, PET/CT every six months for two years, followed by once annually for three additional years. At present, the patient remains disease free.

Pathogenesis:

SBC is associated with a characteristic balanced translocation, t(12;15) (p13;q25). This translocation is

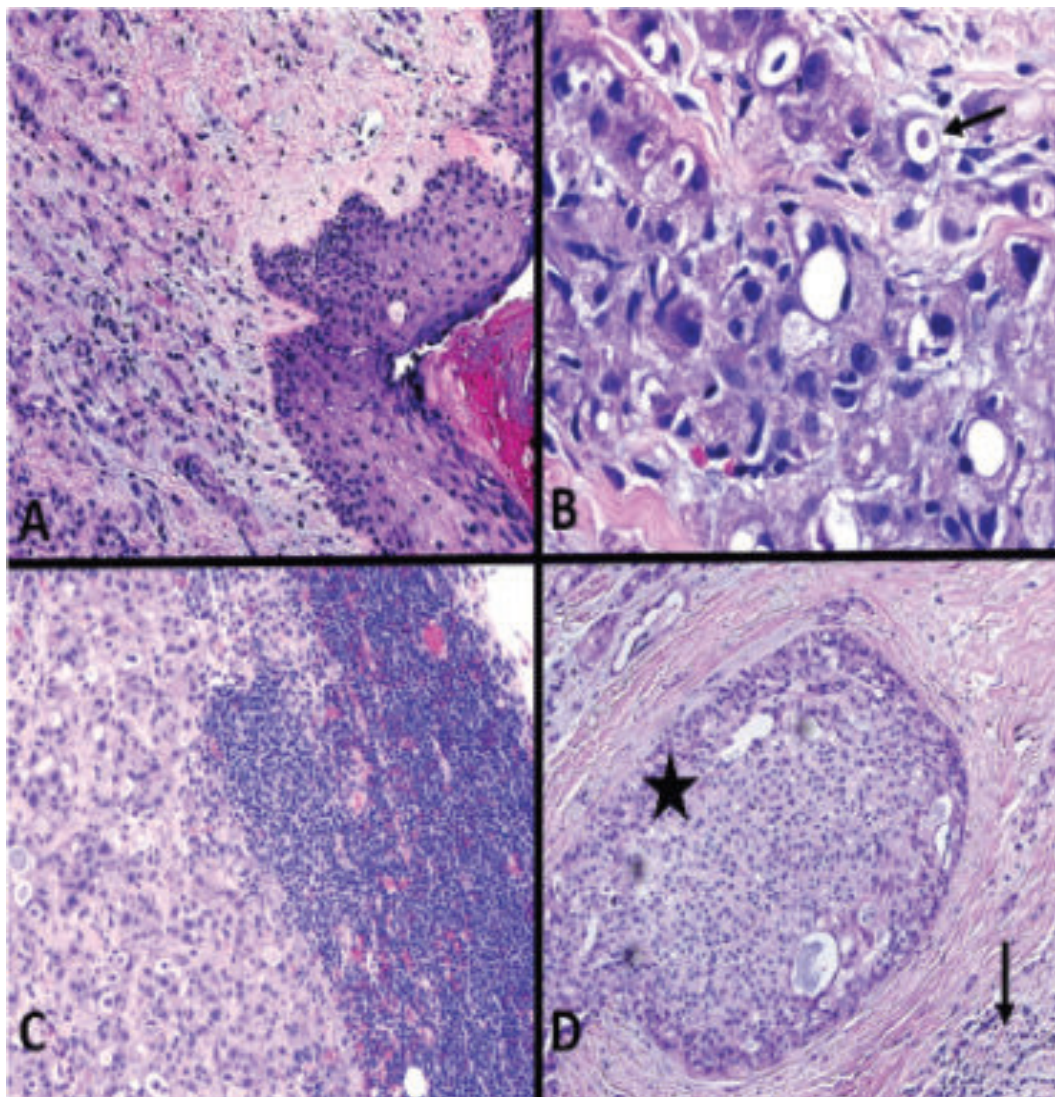


Fig.- 1: A: Normal skin surface with tumor in the dermis, 100x; B: Dermis with tumor cells, with frothy granular, relatively abundant cytoplasm and intracytoplasmic vacuoles containing secretory material (arrow), nuclei have conspicuous nucleoli, 400x; C: Lymph node metastasis, 100x; D: Intraductal cancer (star) surrounded by invasive tumor (arrow), 100x.

known to be oncogenic also in another types of neoplasia^{4, 5, 6}. It affects genes *ETV6 (TEL)* on the chromosome 12 and *NTRK3 (TRKC)* on the chromosome 15. The most often it comes to the breakage in the intron 5 of the gene *ETV6* and the intron 15 of the gene *NTRK3*. This creates a fusion gene; or more precisely a protein, where there is N-terminal helix-loop-helix (HLH) domain of the highly expressed transcription factor *ETV6* linked to tyrosine kinase domain of the gene *NTRK3*. The chimeric protein is subject to the ligand dependent HLH mediated dimerization with a subsequent activation of *NTRK3* tyrosine kinase domain. The activated tyrosine kinase, then, through a number of signaling pathways, acts in the cell transformation^{11, 19}. The differential diagnosis with acinic carcinoma is based on the absence of the *ETV6-NTRK3* translocation in acinic carcinomas.

Discussion:

Overall, secretory breast carcinoma is a rarely encountered clinical entity accounting for less than 0.015% of all breast cancers.³ The reported female to male ratio is 6:1^{1, 9} and SBC has been reported in almost every age group. The reported case after failing treatment for presumed mastitis, a more thorough physical exam revealed a mass of 50x42 mm. This is consistent with existing data that shows that SBC most often presents as a palpable mass,¹ and although it can affect any quadrant and even the axilla, it often involves the nipple areolar complex, especially in males.⁴ At the time of presentation, 15-35% of patients have been noted to have nodal metastasis.^{2, 3, 7} Although distant metastasis is very rare, local recurrence is described, recurring as far as 16 years after treatment⁸. At present the primary treatment remains surgical. Despite this, distant metastasis remains exceedingly rare, and our literature review was able to uncover five reported cases.⁷

SBC is slow-growing and can mimic benign lesions, such as fibroadenoma; and the differential diagnosis includes a wide range of benign or malignant lesions. Based on the imaging characteristics including MRI findings, differential diagnoses include papillary carcinoma, matrix-producing carcinoma, high grade invasive ductal carcinoma with necrosis.

Radiologically, secretory carcinoma usually presents as a well-circumscribed, rounded or oval mass with microlobulated borders³ and may even mimic benign pathology such as fibroadenoma or other malignant disease such as medullary, papillary or mucinous carcinoma.⁶ The ultrasound findings also mimic benign lesions, demonstrating a well-circumscribed, hypoechoic to isoechoic mass, sometimes with microlobulations.⁶ The lesion is usually homogeneous, but it can be heterogeneous.⁵ In SBC three morphologic patterns are seen in various combinations: microcystic, solid and tubular.

Pathologically, SBC is typically triple negative but low-grade, and the copious amount of intra/extracellular secretions make the tumors strongly S-100 reactive.⁵ Secretory breast carcinoma has also recently been noted to belong to the basal-like spectrum of breast carcinomas. Even so, and as in our reported case, there may be expression of hormone receptors. This was noted by Lae, et al. who found that in addition to being triple negative, SBC was expressed CK5/6 and/or CK14 and/or KIT.¹⁰ In our case, pathologic analysis was not able to make a definitive diagnosis until the specimen was sent for expert consultation and genetic testing. FISH revealed the presence of an *ETV6-NTRK3* fusion gene, which in the setting of breast cancer is pathognomonic for SBC. This gene is a result of a balanced translocation t(12; 15)⁶, and is known to be associated with congenital fibrosarcoma and mesoblastic nephroma. However, it was not studied in relation to breast cancer until 2002. Although not present in every case of SBC, it is present in the vast majority of cases and is not seen in any other forms of breast cancer.⁶ Expression of this *ETV6-NTRK3* gene leads to formation of a chimeric tyrosine kinase that activates the Ras-MAPK and inositol-3'-kinase Akt pathways, which are noted to be the first event in the oncogenesis of SBC.^{11, 12} Furthermore, it was shown that a retroviral transfer of the same fusion gene induced SBC in mice.⁶

The tumor is positive for cytokeratins 5, 14 and c-Kit protein (CD117), diffuse IHC positivity for S100, MUC4, EMA, and scattered positivity for gross cystic disease fluid protein 15. Pan-TRK staining is provided to detect possible neurotrophic tyrosine receptor kinase (NTRK) fusions. Axillary metastasis is rare, particularly if the tumor is <2 cm.¹⁹ However, axillary lymph node metastasis has been reported from a 1.5-cm secretory tumor.²¹ Involvement of more than three lymph nodes may indicate a risk for distant metastasis and a poor outcome.²⁰ Therefore, examination of lymph node status using a sentinel lymph node biopsy or axillary lymph node dissection should be performed.^{9, 15} In general, adjuvant radiation therapy following breast conserving surgery improves loco regional control and disease-specific survival.

The existing data supports surgery as the primary treatment. Partial mastectomy is a reasonable approach to most tumors, with total mastectomy reserved for cancers not amenable to breast conserving surgery (cosmetic result, multi-centric disease, patient desire, etc.). Regarding nodal sampling, there is no consensus guideline at present, but a recent review of data from Survival, Epidemiology, and End Results (SEER) database showed that as many as 34.9% of patients can have

positive nodes at the time of presentation. As a result Horowitz, et al. have recommended nodal sampling with a minimum of a sentinel lymph node biopsy be performed.³ The same study also examined the role of radiation therapy in regards to SBC. Recently, a novel tyrosine kinase inhibitor that targets NTRK3, Entrectinib, was developed and is currently in phase II clinical trials (STARTRK-2) with promising preliminary results.¹³

Patient is strongly recommended enrollment in the STARTRK-2 trial as initial data shows that Entrectinib has reasonable efficacy and is well tolerated.¹³ This tumour is considered to be an indolent disease with an estimated disease specific survival of >90%.³

However, in the secretory carcinoma, even with this immunophenotype, the prognosis is usually highly favorable.^{3,4} The average tumor size is 3cm and up to 15% of the cases there is lymph node involvement at the time of diagnosis.¹ When this happens, more than 3 nodes affection is rare.³ But four lymph nodes out of nine were involved in our case.

Condition of the patient after three months of chemotherapy:

Her whole body F-18 FDG (Radionuclide Fluorodeoxyglucose) PET-CT for evaluation showed no focal lesion or abnormal FDG uptake in the whole body but only thickening of Pectoralis Major muscle with mild FDG uptake might be due to postoperative changes. FDG avid hypodense lesion in left ovary and advised to follow up. It also reveals hepatomegaly without any focal lesion. No other suspicious mass or abnormal FDG uptake elsewhere in the body surveyed.

Conclusion:

Overall, secretory breast carcinoma should be treated in a similar fashion to all breast cancers. Understanding patient goals of care and utilizing a multi-disciplinary approach to patient care ultimately yields the best results while minimizing morbidity. Local resection with partial mastectomy or total mastectomy remains the corner stone of treatment. Nodal sampling with either sentinel lymph node biopsy or formal axillary dissection should be obtained due to the reported frequency of nodal metastasis. Beyond that, the decision to pursue chemotherapy, radiation, hormonal therapy, or other novel treatments is highly individualized. Written informed consent was obtained from the patient's family.

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- The title page should include the article title and the corresponding author's full name, highest academic degrees (about maximum 3), designation, department, institute, mailing address and cell number. It should also list the full name, degrees, designation, department, institute, cell number, and e-mail address of every author(s).
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Main Body Page

Abstract

Please write the article title without any author's name on the top of this page to facilitate in the process of double-blinded peer-review policy.

Structured format (Introduction, Methods, Results, and Conclusions) is necessary for original articles. Word count should be within 300 words. The abstract should briefly outline the content of the article and any conclusion it may reach.

Keywords: The keywords should be words a reader would be likely to use in searching for the content of the article. About 3-10 MeSH words.

Introduction

The introduction will acquaint the readers with the problem and it should include:

- Nature and purpose of the study
- Rationale of the study/observation

- Strictly pertinent references
- Brief review of the subject excepting data and conclusion.

Materials and Methods

This section of the study should be very clear and describe:

- The selection criteria of the study population including Controls (if any).
- The methods and the apparatus used in the research.
- The procedure of the study in such a detail so that other workers can reproduce the results.
- Previously published methods (if applicable) with Appropriate citations.

Results

The findings of the research should be described here and it should be:

- Presented in logical sequence in the text, tables, and illustrations.
- Described without comment.
- Supplemented by concise textual description of the data presented in tables and figures where it is necessary.

Tables

- Data given in tables should be commented on but not repeated in the text. Be sure that lists or columns of related data are composed in a word-processing programme like the rest of the text.
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Discussion

The discussion section should reflect:

- The authors' comment on the results and to relate them to those of other authors.
- The relevance to experimental research or clinical practice.
- Well founded arguments.

Conclusion

- The conclusion serves as the final "take-home message," summarizing findings and their clinical relevance. Conclusion must meet the following criteria:
- Evidence-Based: Every claim must be directly supported by your reported data. Avoid "unqualified statements" not proven by your study.
- No New Information: You are strictly forbidden from introducing new data, evidence, or external references that were not already presented in the earlier sections.
- Conciseness: It should be brief or 1-2 paragraphs for original research.
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- Transparency: Do not hide "negative" or inconsistent results; these must be interpreted honestly as they prevent unwarranted replication of effort.

Acknowledgments

Individuals, organizations or bodies may be acknowledged in the article and may include:

- Name (or a list) of funding bodies.
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