

The **ORION** Medical Journal

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The Orion Medical Journal is rejoicing nineteen years of trust and service to the medical community. The Orion Medical Journal achieves the choice of thousand readers nationally and in the international arena. This medical journal contains information from reputable sources and although reasonable efforts have been made to publish accurate information. Any information or guidance contained in this book is intended for use solely by medical professionals strictly as a supplement to the medical professional's own judgement, knowledge of the patient's medical history, relevant manufacture's instructions and the appropriate best guidelines.

Editorial article (P-02) of this issue "Efficacy of bone transport with external fixator plus antibiotic-impregnated calcium sulfate implantation in the treatment of lower limb chronic osteomyelitis". The finding of this study indicate the bone transport with external fixator plus antibiotic impregnated calcium sulfate implantation for treating lower limb chronic osteomyelitis is a successful method, it significantly decreased infection recurrence & docking failure, leakage after surgery didn't worsen patients outcome.

Original article (P-08) "Study of the relative frequency of different diseases in fever with thrombocytopenia". This study says fever with thrombocytopenia is an important clinical condition commonly caused infection, particularly dengue and malaria. In majority of patients thrombocytopenia was transient & symptomatic, but in significant number of case there were bleeding manifestation.

The first review article (P-13) "Role of Gynaecologist in Hysterosalpingography: An Easy Test For Evaluation of Tubal Factor in Infertile Woman." Hysterosalpingography remain the front line imaging modalities in the investigation of infertility. In addition the gynecologist is very much familiar with the vaginal operation.

Second review article (P-16) "Slow breathing exercise can improves lung function status in depressive illness." From this study it may concluded that SBE is very effective & potent method for improvement of poor lung function associated with all types of pulmonary disorder in MDD.

Third review article (P-21) "Bronchorrhea- A distressing respiratory symptom".

Case report (P-23) "A Case Report of Rickettsial meningitis" This study gives us a thought about Rickettsial infection which may present as meningitis & should be included in the differential diagnosis.

A observational study (P-27) "Sociodemographic and Clinicopathological Features in Patients with Vulvar Squamous Cell Carcinoma in Bangladesh". This study is on 50 Bangladeshi cases of squamous cell carcinoma of vulvar.

Thanks all of readers, contributors & reviewers for their continued support.

Let us be a better human being, a better person and a better citizen. New Year is a time to better ourselves for a better world. Have a grand New Year!



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Efficacy of bone transport with external fixator plus antibiotic-impregnated calcium sulfate implantation in the treatment of lower limb chronic osteomyelitis

Dr. Cheng-He Qin¹

ABSTRACT

Aims: We aimed to evaluate the efficacy of bone transport with external fixator plus antibiotic-impregnated calcium sulfate implantation in the treatment of lower limb chronic osteomyelitis.

Patients and Methods: Adult patients with lower limb chronic osteomyelitis treated at our hospital by means of segmental bone resection, antibiotic-impregnated calcium sulfate implantation, followed by bone transport with external fixator from January 2011 to July 2016 were retrospectively evaluated. The laboratory results, docking failure, infection recurrence were summarized.

Results: There were totally 250 patients met the inclusion criteria. Docking failure rate is less than 8%, and infection recurrence is less than 2%. Leakage of the incision after surgery was common, as high as 34%, but it seemed not to be a risk factor for docking failure and infection recurrence.

Conclusions: The findings of our study indicate that bone transport with external fixator plus antibiotic-impregnated calcium sulfate implantation for treating lower limb chronic osteomyelitis is a successful method, it significantly decreased infection recurrence and docking failure. Leakage after surgery didn't worsen patient's outcome.

Key words: chronic osteomyelitis, calcium sulfate, docking failure, infection recurrence

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INTRODUCTION

Chronic osteomyelitis of the lower limb remains a big clinical challenge for both orthopaedic surgeons and patients. Microorganisms cause inflammation to the cortical, trabecular bone, bone marrow or periosteum¹. Staphylococcus aureus the most common pathogen that forms biofilm, which is the culprit for most chronic osteomyelitis cases². It may follow haematogenous, traumatic, or post-operative bacterial colonization and superficial wound³. Treatment involves antimicrobial administration, debridement and bone transport in selected case where segmental bone removal is performed⁴. However, despite radical and aggressive bone excision, re-infection may still occur from dormant organisms which form biofilms and internalize in osteoblasts thus preventing antibiotics and the immune system to completely eradicate the infection⁵. In addition, successful management of osteomyelitis involves several factors, such as host immune status; severity and site of infection; and the extent of bony necrosis⁶.

Questions have arisen on how to fully eradicate infection in osteomyelitis of lower limb. A widely used method to reduce

infection recurrence is to implant local antibiotic carriers such as calcium-sulfate and polymethylmethacrylate (PMMA) in combination with antibiotics to counter biofilm formation in the wound sites⁷⁻¹¹.

In our study, we aim to find out the efficacy of bone transport with external fixator plus antibiotic-impregnated calcium sulfate implantation in the treatment of lower limb chronic osteomyelitis.

PATIENTS AND METHODS

Inclusion/Exclusion Criteria

Our study focused on patients with lower limb chronic osteomyelitis that were treated in our hospital. Chronic osteomyelitis is defined as the presence of radiographic osteolytic changes in the long bones of patients with a background history of local onset of infection¹. Data were collected retrospectively between January 2011 and June 2016. Inclusion criteria were adult patients (age ≥ 18 years), chronic osteomyelitis of femur or tibia treated with segmental bone resection followed by antibiotic-impregnated calcium sulfate plus bone transport with circular or unilateral external fixator without acute bone

shortening during surgery. Exclusion criteria were cases accompanied with deformity correction, associated severe dysfunction of liver or kidney, diabetes with uncontrolled blood glucose.

Surgical Procedure

During the surgery, after debridement, antibiotic-impregnated calcium sulfate was used to fill in the defect, including part of

upper and lower medullary cavity. Then, external fixator is fixed for bone transport (Fig 1).

Postoperative Treatment

Patients were given intravenous antibiotics and regular wound care. Bone transport to repair the bony defect were started one week after the osteotomy with a speed of 1mm/day.

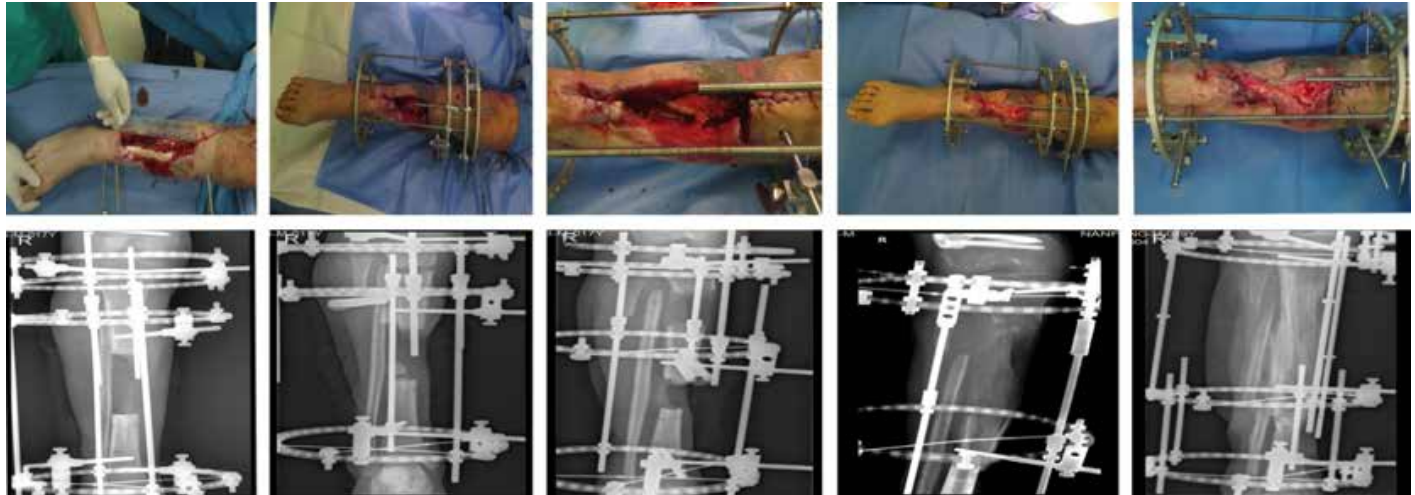


TABLE 1. Patient Demographic Characteristics

No. of patients	250
Mean age(yrs)*	38.25(35.30 to 52.30)
Site(Femur/Tibia) †	
Femur	93
Tibia	157
Side†	
Right	113
Left	137
Sinus‡	184 (73.6%)
Fever‡	14 (5.56%)
Mean Symptom duration(months)*	13.2 (6.35 to 14.71)
Ciorny-Mader classification†	
Stage 1-medullary osteomyelitis	31
Stage 2-superficial osteomyelitis	23
Stage 3-localized osteomyelitis	57
Stage 4-diffuse osteomyelitis	139
Number of previous surgeries§	3(2)

Remarks:*The values were given as the mean,with the 95% CI inparentheses.†The values were given as the number of patients.‡The values were given as the number of patients, with the percentage in parentheses.§The values were given as the median, with the interquartile range in parentheses.

TABLE 2. Etiology of Osteomyelitis

Hematogenous spread†	13 (5.2%)
Superficial wound†	10 (4%)
Trauma†	227 (90.8%)
Falling height	20
Traffic accident	57
Heavy pound injury	150

Remarks: †The values were given as the number of patients, with the percentage in parentheses.

TABLE 3. Systemic Risk Factors

Without systemic risk factors†	208(83.33%)
With systemic risk factors†	42(16.67%)
Smoking	15
Drinking	4
Hypertension	3
Chronic hepatitis	5
Diabetes	7
Tuberculosis	8

Remarks: †The values were given as the number of patients, with the percentage in parentheses.

TABLE 4. Laboratory Results

Pre-operative†	
White blood-cell count(x10 ⁹ /L)	6.71 (6.09 to 8.32)
Erythrocyte Sedimentation Rate(mm/h)	25.04 (20.38 to 33.18)
C-reactive protein(mg/L)	16.22 (11.20 to 17.24)
Post-operative†	
White blood-cell count(x10 ⁹ /L)	6.86 (6.12 to 8.59)
Erythrocyte Sedimentation Rate(mm/h)	31.37 (23.54 to 37.19)
C-reactive protein(mg/L)	12.63 (7.88 to 13.39)

Remarks: †The values were given as the mean with the 95% CI in parentheses.

TABLE 5. Operation and Post-operative Data Comparison

Surgery time(mins)†	130.65 (127.66 to 153.63)
Bleeding volume(ml) †	148.22 (143.69 to 190.75)
Length of bone defect(mm) †	83.15(76.72 to 95.51)
Febrile‡	17(6.8%)
Leakage‡	85(34%)
Hospital stay(days) †	20.61(18.01 to 23.21)
Follow-up(months) †	27.50 (7.25)
External Fixator Index(days/cm) †	38.85(36.57 to 47.13)
Docking obstruction‡	19(7.2%)
Infection Recurrence‡	(1.6%)

Remarks: † The values were given as the mean, with the 95% CI in parentheses. ‡ The values were given as the number of patients with the percentage in parentheses.

RESULTS

Profile, Etiology and Risk Factors

Comparison of the patients' profile are demonstrated in Table 1. Their etiology and risk factors are summarized in Table 2 and Table 3. More than 80% did not have systemic risk factors, but some patients have several of them.

Preoperative and postoperative laboratory results

Laboratory results of preoperative and postoperative laboratory are summarized in Table 4. Preoperative WBC, ESR and CRP were collected from the first time as an in-patient before antibiotic treatment. Postoperative WBC, ESR and CRP were collected from the final time within two weeks following surgery.

DISCUSSION

At present, many methods are available to manage lower limb chronic osteomyelitis however it continues to be challenging and often the recurrence rates remain high. Infection eradication and bone defect reconstruction remain to be the main challenge in treating chronic osteomyelitis¹¹. The Masquelet technique is recognized as two-stage surgery¹² to reduce the initial hospital stay and allows patient for an easier rehabilitation period¹³. Interestingly, our study showed that antibiotic-impregnated calcium sulfate implantation plus bone transport with external fixator was a effective method for treating lower limb osteomyelitis. It repaired bone defect and decrease infection re-currence due to a high local concentration of antibiotics above the minimum inhibitory concentration, which suggestively able to penetrate biofilm formation¹⁴⁻¹⁸.

Surgery remain the cornerstone of the management of osteo-

myelitis⁶. When local carrier of antibiotic is used, the outcomes are better than systemic therapy or surgical treatment alone¹⁹. Especially local high concentration of antibiotic is crucial to destroy the residual organism in biofilm thus help to reduce infection recurrence as is proven in our study. Bransetter et al showed that antibiotic-impregnated calcium sulfate eradicated infection better than calcium sulfate alone in their animal studies²⁰.

Docking failure is a condition where the transported bone is unable to perch nicely onto the final destined site. This complication commonly presents in bone transport procedures therefore result in additional surgery and delay of the healing time by several months. Options to prevent docking failure are available. Hatzokos I et al shared their experience in using autologous bone marrow combined with demineralized bone matrix to improve docking site consolidation. However, autologous bone graft contributes to donor site morbidity²¹.

Postoperative leakage is common when calcium-based bone substitute are im-planted however it did not increase the recurrence of infection²². Our study shows a high occurrence up to 35.2% in the calcium sulfate group which similar to other studies²³. We concluded several explanation for leakage as follows: there were not enough soft tissue to cover and contain the calcium sulfate; the lesion was too superficial, especially for tibia; and calcium sulfate was squeezed out of the cavity during bone transport. Though outcome were not affected, it increase patients' distress during the treatment process as they do mimic the presence of recurrence of infection with the substance leaking out of their wounds.

There are several limitations of this study which are small samples size, non-randomized trial, and absence of the general photograph of the membrane around calcium sulfate. A larger sample size and a well conducted randomized controlled

clinical trial will greatly assist in the verification of such a study. Basic science study is encouraged to discover type of membrane and its properties induced by calcium sulphate.

CONCLUSION

Our study demonstrated good outcomes of antibiotic-impregnated calcium sulfate implantation plus bone transport with external fixator in the treatment of lower limb chronic osteomyelitis. This technique can improve prognosis of such condition and offer a patient-friendly treatment.

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Study of the relative frequency of different diseases in fever with thrombocytopenia

Kabir MA¹, Shamim MMA,² Ahmed N³, Dutta BR⁴, Yasmin D⁵

ABSTRACT

Background: Febrile thrombocytopenia is a condition commonly caused by infections. It is common condition that is associated with an increased risk of morbidity and mortality. Different studies on thrombocytopenia are done in the past have connected to specific etiologies.

Objective:

- To find out the relative frequency of different diseases in fever with thrombocytopenia
- To detect the different bleeding manifestations in fever with thrombocytopenia and relation with platelet count.

Methodology: This observational, descriptive, cross-sectional, prospective hospital based study was carried out in the Department of Medicine, Khulna Medical College Hospital (KMCH), Khulna from February 2016 to June 2018. All cases attending the Department of Medicine age more than 14years, fever less than 15 days duration, Fever more than 1000F at least once a day, platelet count less than 1,50,000/ μ l were included in this study. Known patients of Primary Thrombocytopenia, drug induced thrombocytopenia and diagnosed cases of Thrombocytopenic purpura on treatment were excluded in this study.

Results: Majority 51(46.4%) patients had dengue fever, 21(19.1%) had malaria, 18(16.4%) had unexplained fever, 12(10.9%) had septicemia, 5(4.5%) had dengue+malaria, 2(1.8%) had enteric fever and 1(0.9%) had leptospirosis. Majority 42(38.2%) patients had petechiae, 14(12.7%) had SC haemorrhage, 10(9.1%) had melena, 8(7.3%) had bleeding gum, 7(6.4%) had epistaxis, 5(4.5%) had hematemesis and 20(17.3%) patients had no bleeding. Forty two patients had petechiae among them 15 patients had platelet counts 50000-150000 per μ l. Nineteen patients had no bleeding among them 16 patients had platelet counts 50000-150000 per μ l. Fourteen (14) patients had SC haemorrhage among them 6 patients had platelet counts 20000-<50000 per μ l.

Conclusion: Fever with thrombocytopenia is an important clinical condition commonly caused by infections, particularly dengue and malaria. In majority of patients thrombocytopenia was transient and asymptomatic, but in significant number of cases there were bleeding manifestations.

Key words: Fever, Thrombocytopenia, Malaria, Dengue

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INTRODUCTION

Infection is a common cause of thrombocytopenia. Fever with thrombocytopenia is a common condition that is associated with an increased risk of morbidity and mortality. Infections like Malaria, Dengue, Typhoid and septicaemia are some of the common causes of fever with thrombocytopenia.¹ Fever is a response to cytokines and acute phase proteins and occurs in infections and in non infectious conditions.² The normal platelet count is 150000-450000/mm³. Thrombocytopenia is

defined as platelet count less than 150000/mm³. It results from one of three mechanisms i.e. reduced production, excessive peripheral destruction and increased platelet sequestration in spleen.³ At times, the fever course is prolonged and fever with thrombocytopenia narrows the differential diagnosis of the clinical entity. Septicemia, infections like malaria, dengue, leptospirosis, typhoid, human immunodeficiency virus (HIV) and miliary tuberculosis are some of the common causes of fever with thrombocytopenia.⁴

MATERIALS AND METHODS

This observational, descriptive, cross-sectional, prospective hospital based study was carried out in the Department of Medicine, Khulna Medical College Hospital (KMCH), Khulna from February 2016 to June 2018. Detailed history was taken. Presenting complaints and haemorrhagic manifestation were noted. The bleeding manifestations that the patients presented with or developed during their course in hospital were recorded. All the patients were subjected to routine haematological investigation like haemoglobin, total leukocyte count, platelet count, peripheral smear study, peripheral smear for malarial parasites, MCV (mean corpuscular volume), Dengue IgM and IgG, Prothrombin time with INR, Activated partial thromboplastin time, renal function test and liver function test. Baseline platelet counts were done on the day of presentation. Repeat platelet counts were done in subjects with marked thrombocytopenia until normal or near-normal values were reached. Other investigations as necessary were done to achieve diagnosis such as bone marrow trephine biopsy, serological study for HIV infection, TSH, S. Widal, D-Dimer, Serum vitamin B12 level, Anti Nuclear Antibody (ANA).

Inclusion Criteria

- Age more than 14 years.
- Fever less than 15 days duration.
- Fever more than 1000F at least once a day.
- Platelet count less than 1, 50,000/ μ l.

Exclusion Criteria

- Known patients of Primary Thrombocytopenia.
- Drug induced thrombocytopenia.
- Diagnosed cases of Thrombocytopenic purpura on treatment.

Patients with thrombocytopenia already diagnosed to have hematological disorder /malignancy, on treatment with chemotherapy and other immunosuppressant. The patients fulfilling the selection criterion after excluding patients were selected for the study and consent was obtained.

RESULTS

Out of 110 cases majority 29(26.4%) patients belonged to age 21-30 years. The mean age was found 34.7 ± 11.3 years. Male was found 63(57.3%) and female was 47(42.7%). Male: female ratio was 1.3:1. Majority 43(39.1%) patients had fever during the period of 1-5 days. The mean duration of fever was found 6.3 ± 3.6 days (Table I). Majority 45(40.9%) patients had platelet counts 50000-150000 per μ l followed by 36(32.7%) had 20000-<50000 per μ l, 22(20.0%) had 10000-<20000 per μ l and 7(6.4%) had <10000 per μ l (Table II). Majority 51(46.4%) patients had dengue fever, 21(19.1%) had malaria, 18(16.4%) had unexplained fever, 12(10.9%) had septicemia, 5(4.5%) had

dengue+malaria, 2(1.8%) had enteric fever and 1(0.9%) had leptospirosis (Table III). Majority 42(38.2%) patients had petechiae, 14(12.7%) had SC haemorrhage, 10(9.1%) had melena, 8(7.3%) had bleeding gum, 7(6.4%) had epistaxis, 5(4.5%) had hematemesis and 20(17.3%) patients had no bleeding (Table IV). 51 patients had dengue among them 23 patients had platelet counts 50000-150000 per μ l. Twenty one (21) patients had malaria among them 9 patients had platelet counts 50000-150000 per μ l. Eighteen (18) patients had unexplained fever among them 7 patients had platelet counts 50000-150000 per μ l (Table V). Forty two patients had petechiae among them 15 patients had platelet counts 50000-150000 per μ l. Nineteen patients had no bleeding among them 16 patients had platelet counts 50000-150000 per μ l. Fourteen (14) patients had SC haemorrhage among them 6 patients had platelet counts 20000-<50000 per μ l (Table VI).

Table I: Sociodemographic characteristics of the patients (n=110)

Sociodemographic characteristics	Frequency	Percentage
Age (years)		
≤ 20	17	15.5
21-30	29	26.4
31-40	22	20.0
41-50	19	17.3
>50	23	20.9
Mean $\pm$ SD	34.7 ± 11.3	
Sex		
Male	63	57.3
Female	47	42.7
Duration Fever (days)		
1-5	43	39.1
6-10	37	33.6
>10	30	27.3
Mean $\pm$ SD		

Table II: Distribution of the patients by platelet counts (n=110)

Platelet counts (μ l)	Frequency	Percentage
<10000	7	6.4
10000-<20000	22	20.0
20000-<50000	36	32.7
50000-150000	45	40.9

Table III: Distribution of the patients by etiology of fever with thrombocytopenia (n=110)

Etiology of fever with thrombocytopenia	Frequency	Percentage
Dengue	51	46.4
Malaria	21	19.1
Unexplained	18	16.4
Septicemia	12	10.9
Dengue+Malaria	5	4.5
Enteric fever	2	1.8
Leptospirosis	1	0.9

Table IV: Distribution of the patients by thrombocytopenia and bleeding symptoms (n=110)

Thrombocytopenia and bleeding symptoms	Frequency	Percentage
Bleeding PR	1	0.9
Hematuria	2	1.8
Menorrhagia	2	1.8
Hematemesis	5	4.5
Epistaxis	7	6.4
Bleeding gum	8	7.3
Melena	10	9.1
SC Haemorrhage	14	12.7
Petechiae	42	38.2
No bleeding	20	17.3

Table V: Fever-associated thrombocytopenia in different platelet count ranges (n=110)

Disease	Platelet count (/μl)				Total
	<10000	10000- <20000	20000- <50000	50000- 150000	
Dengue	3	10	15	23	51
Malaria	2	3	7	9	21
Unexplained	0	5	6	7	18
Septicemia	1	3	5	3	12
Dengue+Malaria	1	1	2	1	5
Enteric fever	0	0	1	1	2
Leptospirosis	0	0	0	1	1
Total	7	22	36	45	110

Table VI: Site of bleeding in different platelet count ranges (n=110)

Disease	Platelet count (/μl)				Total
	<10000	10000- <20000	20000- <50000	50000- 150000	
Bleeding PR	0	0	0	1	1
Hematuria	0	0	1	1	2
Menorrhagia	1	1	0	0	2
Hematemesis	0	0	3	2	5
Epistaxis	0	0	2	5	7
Bleeding gum	0	2	2	4	8
Melena	3	4	3	0	10
SC Haemorrhage	2	5	6	1	14
Petechiae	1	10	16	15	42
No bleeding	0	0	3	16	19
Total	7	22	36	45	110

DISCUSSION

In present study majority 29(26.4%) patients belonged to age 21-30 years. The mean age was found 34.7 ± 11.3 years. Male was found 63(57.3%) and female was 47(42.7%). Male: female ratio was 1.3:1. Majority 43(39.1%) patients had fever during the period of 1-5 days. The mean duration of fever was found 6.3 ± 3.6 days. Saini et al.4 study observed that similar observation out of 1217 cases of fever with thrombocytopenia, 858 were males and 359 were females in a study by Nair et al.5 at St. Stephen's hospital, New Delhi, for period of one and half years, a total of 109 cases (76 male, 33 female patients) were studied with the same criteria as in our study. Gandhi and Akholkar¹ study observed that 112 patients aged >18 years with fever and thrombocytopenias were observed for bleeding manifestations. Bhalara et al.6 study observed that there were 236 men and 176 women in the study population.

In this study majority 45(40.9%) patients had platelet counts 50000-150000 per μl followed by 36(32.7%) had 20000-<50000 per μl , 22(20.0%) had 10000-<20000 per μl and 7(6.4%) had <10000 per μl . In Saini et al.4 study 24% of the patients were in the range of 50,000 <platelet count $\leq$ 1,50,000, followed by 38%, 25% and 13% of the patients in the range of 20,000 < platelet count $\leq$ 50,000; 10000 < platelet count $\leq$ 20,000 and up to 10000 respectively. Bhalara et al.6 study showed out of 109 patients, 62 (56.8%) had platelet count between 50,000 and 1,00,000, followed by 28(25.7%) patients

who had count between 20,000 and 50,000. In Gandhi and Akholkar¹ study observed that 112 patients platelet count range of $>50000/\text{mm}^3$ was found in 64(57.14%) patients, while 33 (29.47%) had platelet count in range of 20000- 50000/ mm^3 . Fifteen (13.33%) patients had count $<20000/\text{mm}^3$. These findings correlate with Nair and Bhalara study were they found 56.8% and 59.8% incidence of platelet count $>50000/\text{mm}^3$ respectively.⁵⁻⁶

In current study revealed majority 51(46.4%) patients had dengue fever, 21(19.1%) had malaria, 18(16.4%) had unexplained fever, 12(10.9%) had septicemia, 5(4.5%) had dengue+malaria, 2(1.8%) had enteric fever and 1(0.9%) had leptospirosis. Similar observation was found Saini et al.⁴ study they showed dengue was the major cause accounting for 572 (47%) of the total cases. Second major cause was malaria in 243 (20%) cases followed by unexplained causes in 200(16.43%) cases, septicemia in 128(10.5%), enteric fever in 12(1%) and leptospirosis in 6 (.5%). In a study by Lohitashwa et al.⁷ infections were also the most common cause but here malaria (41%) was the most common cause of fever with thrombocytopenia followed by enteric fever (24%), septicemia (19%), dengue (14%). In another study by Patil et al.⁸ malaria (54%) remained the most common cause followed by dengue (15%), other causes (21%), enteric fever (6%), septicemia (4%). Bhalara et al.⁶ from the 412 patients studied, dengue was diagnosed in 28.6% of patients followed by malaria in 22.8%, chronic liver disease in 15.2%, hypersplenism in 12.3%, septicemia in 6.3%, Gandhi and Akholkar¹ study showed the commonest causes of thrombocytopenia in our study were Malaria 46(41.07%) followed by Dengue 30(26.78%), viral fever 18(16.07%), megaloblastic anaemia 6(5.36%), enteric fever 4.46% (5) and septicaemia 4.46% (5).

In this study majority 42(38.2%) patients had petechiae, 14(12.7%) had SC haemorrhage, 10(9.1%) had melena, 8(7.3%) had bleeding gum, 7(6.4%) had epistaxis, 5(4.5%) had hematemesis and 20(17.3%) patients had no bleeding. In the study by Nair et al.⁵, the most common bleeding manifestation was purpura, followed by gum bleed and epistaxis. However in this study, gum bleed was the most common bleeding manifestation followed by purpura. Saini et al.⁴ reported similar observation they showed out of 512 patients, 468 (91.40%) patients had petechiae/purpura. Spontaneous bleeding was seen in 292 (57%) patients. Out of the 292 cases having spontaneous bleeding, 152 (52%) cases had Sub-conjunctival hemorrhages, 116 (39.8%) cases had malena, 91(31.16%) cases had bleeding gums, 67(23%) cases had epistaxis, 55 (18.8%) cases had hematemesis, 24(8.2%) cases had menorrhagia, 18(6%) cases had hematuria and 6 (2%) case had bleeding per rectum. Gandhi and Akholkar¹ study showed that bleeding manifesta-

tions were seen in 38.40% of patients. 76.74% of patients had patechie/purpura as the commonest bleeding manifestation followed by gum bleeding in 16.28 %.

In this series 51 patients had dengue among them 23 patients had platelet counts 50000-150000 per μL . Twenty one (21) patients had malaria among them 9 patients had platelet counts 50000-150000 per μL . Eighteen (18) patients had unexplained fever among them 7 patients had platelet counts 50000-150000 per μL . In Gandhi and Akholkar¹ study, among 30 patients with dengue fever 15 (50%) had moderate thrombocytopenia. Out of 23 patients with *P. Falciparum* malaria 13 (56%) had mild thrombocytopenia and 9 (39%) had severe thrombocytopenia. In study done by Bhalra et al.⁶ moderate thrombocytopenia was more common among all types of malaria. Gandhi and Akholkar¹ also reported distribution of platelet count in the range of $> 50000\text{-}150000/\text{mm}^3$ was seen in 57.14 %. Platelet count in the range of 20000-50000/ mm^3 was seen in 29.47% and Platelet count in the range of 0-20000/ mm^3 was seen in 13.39%. Severe thrombocytopenia was seen more with *P.falci-parum* malaria compare to *P. Vivax* malaria.

In current study observed 42 patients had petechiae among them 15 patients had platelet counts 50000-150000 per μL . Nineteen patients had no bleeding among them 16 patients had platelet counts 50000-150000 per μL . Fourteen (14) patients had SC haemorrhage among them 6 patients had platelet counts 20000- <50000 per μL . Saini et al.⁴ Petechiae/purpura are more commonly seen in patients with platelet count less than 20,000 and usually seen up to platelet counts of 50,000. Generally, spontaneous bleeding was noted in platelet count $< 20,000$ but in some may be due to qualitative defects, it was seen in platelet count in the range of $> 50,000/\mu\text{L}$ also. Some patients with platelet count of 10,000 did not have spontaneous bleeding. Bhalara et al.⁶ majority of bleeding manifestations occurred in patients with platelet count less than 10,000/ μL .

CONCLUSION

Fever with thrombocytopenia reveals among infections dengue and malaria are common causes because of seasonal and regional variations. Thrombocytopenia is a commonly observed hematological entity. Fever with thrombocytopenia is an important clinical condition commonly caused by infections, particularly dengue and malaria. In majority of patients thrombocytopenia was transient and asymptomatic, but in significant number of cases there were bleeding manifestations.

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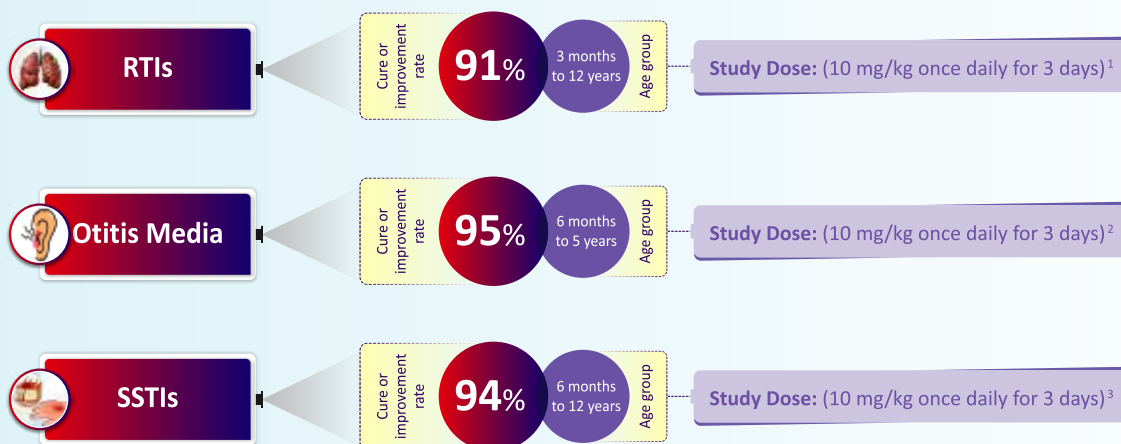
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Role of Gynaecologist in Hysterosalpingography: An Easy Test For Evaluation of Tubal Factor in Infertile Woman

Dr. Mala Banik¹

Tubal factor is responsible for 25-40% of infertile woman. There are three main modalities to detect tubal patency are Hysterosalpingography(HSG), SIS (saline infusion sonography) and Laparoscopic chromopertubation (Diagnostic Laparoscopy dye Test). Hysterosalpingography is a relatively noninvasive, easy procedure with rare complication. Short procedure, usually completed within 30 minutes. SIS is the procedure where saline is introduced through the cervical catheter. Passage of fluid through the tube and fimbria end into the peritoneal cavity is assessed sonographically by using transvaginal sonography. A ultrasound machine and sonologist is needed. But during HSG Gynaecologist is alone can do it in the radiology department.

On the contrary Diagnostic Laparoscopy dye test is a invasive, time consuming costly procedure. Anaesthesia is required and postoperative complications are more. Hysterosalpingography also gives valuable informations about the abnormalities of uterine cavity that causes infertility. HSG is now considered as a screening test for evaluation of tubal factor.

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INTRODUCTION

Hysterosalpingography

Hysterosalpingography is an x-ray examination of a woman's uterus and fallopian tubes that uses a special form of x-ray called fluoroscopy and a contrast material. During a hysterosalpingogram, the uterus and fallopian tubes are filled with a water-soluble contrast material which is passed through cervical catheter by the physician and the radiologist is able to use fluoroscopy to view and assess their anatomy and function.

Uses of Hysterosalpingography

Hysterosalpingography is primarily used to examine infertile women by evaluating the shape and structure of the uterus, the patency of the fallopian tubes. The procedure can be used to investigate recurrent mid trimester pregnancy loss to see congenital or acquired abnormalities of uterus such as bicornuate or unicornuate uterus, cervical incompetence, submucous fibroids and uterine synechiae.

Steps of the procedure

This examination is usually done in the Radiology Department on an outpatient basis. The procedure is like a gynecological exam. The patient is positioned on her back on the exam table, with her knees bent or her feet held up with stirrups and a

speculum is inserted into the vagina. The cervix is then cleaned, and a catheter is inserted into the cervix. The speculum is removed and the patient is carefully positioned underneath the fluoroscopy camera. The contrast material then begins to fill the uterine cavity, fallopian tubes and peritoneal cavity through the catheter and fluoroscopic images are taken. In some cases, if certain abnormalities are encountered, the patient will be asked to rest and wait up to 30 minutes so that a delayed image can be obtained. This delayed image may provide clues to a patient's condition that the original images with contrast material do not. When the procedure is complete, the catheter will be removed and the patient will be allowed to sit up. The hysterosalpingogram is usually completed within 30 minutes.

Complications

The two most common complications of HSG are pain and infection. Uterine contractions and discomfort due to the introduction of contrast medium into the uterine cavity the most common type of pain referenced is sub abdominal colic caused by dilation of the uterine cavity. A more diffuse pain, caused by irritation of the peritoneum due to the contrast low-osmolar nonionic contrast agents currently available.

Normal finding:



FIG1: Normal hysterosalpingography. Uterus in right inclination. Full-length drawing of the vagina, the uterus cavity, and the fallopian tubes.

On face radiographs, the uterine cavity has a normal trigonal shape and the apex of the triangle corresponds to the isthmus, which is nearly 3.7 cm wide. The apex is pointed downwards and connected to the internal ostium of the cervix uteri, which is 2.5 cm in total length. The base of triangular uterine cavity is the fundus, which can be concave, flattened or slightly convex. On both sides of its base, in the area of the lateral horns, the two fallopian tubes are drowned. The fallopian tubes are separated into three segments: isthmus (attached to the uterus, not imaged in several cases), ampullary (in the middle, the longest and widest segment), and bell-shaped (to the distal end). There are two ostiums: the internal or uterine and the external or abdominal (Fig 2). From the abdominal ostium, the contrast medium disperses and diffuses into the peritoneal cavity. Remaining contrast medium in the furrows of the peritoneum can be observed up to 3 hours after administration.

Abnormal findings:



FIG2: Unicornous uterus. Hysterosalpingography shows opacification of a single right uterine horn. A single fallopian tube is also visualized.



FIG3: Didelphys uterus. Hysterosalpingography shows two uterine Cavities, two cervixes, and one single vagina.

CONCLUSION

Hysterosalpingography remains the front-line imaging modality in the investigation of infertility. It is an accurate means of assessing the uterine cavity and tubal patency. It is an easy test and patient compliance is very good when the Gynaecologist introduce dye through the cervical catheter. In addition the Gynaecologist is very much familiar with the vaginal operations and has immense knowledge of female anatomy so the pitfalls and misinterpretation can be avoided.

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Slow breathing exercise can improves lung function status in depressive illness.

Daniul Alam ¹, Md. Hasibuzzaman ², Khandaker Nadia Afreen ³, Syeda Rubayat Hilmi ⁴

ABSTRACT

Background: Major Depressive Disorder (MDD) is associated with depressed lung function. This depressed lung function may be improved by slow breathing exercise.

Objectives: To observe the change in lung function measures (FVC, FEV1) in patients newly diagnosed with MDD before initiation of antidepressive medication and after three months of regular practice of slow breathing exercise along with antidepressive medication.

Methods: This prospective study was carried out in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from January to December, 2014. Thirty female patients newly diagnosed with MDD age 20 to 50 years were enrolled. FVC, FEV1 were assessed by a portable digital spirometer before initiation of antidepressive medication and after three months of regular practice of slow breathing exercise. Changes in the three measures were done using the paired sample-‘t’-test was done with $p \leq 0.05$ considered significant. Results: There was significant ($p \leq 0.001$) improvement of all three lung function status after three months of regular practicing of slow breathing exercise.

Conclusion: From this study it may be concluded that SBE is very effective and potent method for improvement of poor lung function associated with all types of pulmonary functional disorder in MDD.

Key words: Major Depressive Disorder (MDD), Slow Breathing Exercise (SBE).

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INTRODUCTION

Depression is the most common chronic condition next to hypertension experienced in general medical practice throughout the world. Out of ten patients visiting our psychiatric outpatient department, typically one patient is suffering from Major Depressive Disorder (MDD)¹.

MDD is defined by depressed mood or loss of interest in nearly all activities or both for at least two weeks, accompanied by a minimum of three or four of the following symptoms (for a total of at least five symptoms altogether) such as insomnia or hypersomnia, feeling of worthlessness or excessive guilt, fatigue or loss of energy, diminished ability to think or concentrate, substantial change in appetite or weight, psychomotor agitation or retardation and recurrent thoughts of death or suicide¹.

MDD is a major cause of morbidity worldwide. The WHO ranks MDD as the fourth leading cause of disability worldwide and by 2020, it will be the second leading. Population studies have consistently shown MDD is about twice as common in women, although the underlying cause for the risk factor is unclear.

Older aged persons are also more affected. People are most likely to suffer their first MDD at 25.7 years in high income countries and at 24 years in low to middle income countries².

Researchers have found depressed lung function in patients with MDD³.

Slow breathing exercise, such as practiced in yoga, offers a possible safe intervention to improves lung function among patients with MDD as evidenced by a line of recent research. Chanavirut and his colleagues investigated the effect of breathing and chest wall expansion exercise on lung function parameters in young, healthy. They found significant increase in FVC, FEV1 after practicing breathing exercise for 6 weeks⁴.

Sayyad and his colleagues studied lung function parameters on asthma patients after practicing eight weeks of yoga. They found significant increase in FVC and FEV15.

Ahmed and his coworkers studied lung functions in healthy volunteers who were exposed to yoga practice by employing posture and controlled breathing exercise (pranayam) for 30 days and 60 days in two age groups. They found significant

increase in all spirometric parameters in all age groups after 60 days but these values were found increased in old age groups after 30 days⁶.

Though there is an accumulation of evidence in favor of improvement of lung functions in healthy adults the effect of slow breathing exercise as a part of yoga on lung function status in patients with MDD so far has not been studied.

The ultimate aim of this study is to find out whether there is any improvement of poor lung function of major depressive disorder after three months practicing of slow breathing exercise.

METHODS

This interventional study was carried out in the Department of Physiology, BSMMU, Dhaka, between January to December 2014. Thirty female newly diagnosed Major Depressive Disorder patients aged 20 to 50 years constituted study group. Study protocol was approved by Institutional Review Board (IRB) of BSMMU. Patients were randomly selected from out patients of Psychiatry Department. Women with pregnancy, lactation and history of lung diseases, coronary heart disease, diabetes mellitus, neurological disorders and current smokers were excluded from the study. After selection and agreeing to participate, written informed consent was obtained. A detailed personal, medical, family, socioeconomic, occupational and drug history were recorded in a preformed questionnaire and through physical examinations were done. After history and physical exam,

Table I

Baseline characteristics of 30 female newly diagnosed Major Depressive Disorder patients (MDD), Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, 2014.

Characteristics	N	%
Age		
<25	10	34
25-35	5	16
>35	15	50
Level of education		
Primary school	13	44
Junior high school	10	33
High school	3	10
Degree and above	4	13
Occupation		
Employed	7	23
Unemployed	23	77
Religion		
Muslim	30	100

the benefit of slow breathing exercise and its potential useful effect on lung function, as well as depression itself were explained to the patient and their accompanying relatives. In addition, the steps of Slow breathing exercise were taught in detail, including the time period and environment of practice required was taught. Special emphasis was given to ensure the regular practice of this exercise by the patients everyday at morning and evening for half an hour. For this, relatives were trained to monitor and help the patients ensure its regular adherence. The subjects were regularly contacted and monitored through telephone everyday and occasionally by visiting the home. They were also asked questions to make sure the exercise was practiced correctly.

For assessment of lung function, FVC, FEV1 of all patients were recorded by a digital spirometer before initiation of antidepressive medication and after three months of antidepressive- medication. Data were expressed as mean $\pm$ SE (Standard Error). Paired sample-‘t’- test was done to compare lung function measure changes for individuals before and after using SPSS (Windows version 16). In the interpretation of results, P value < 0.05 was accepted as significant.

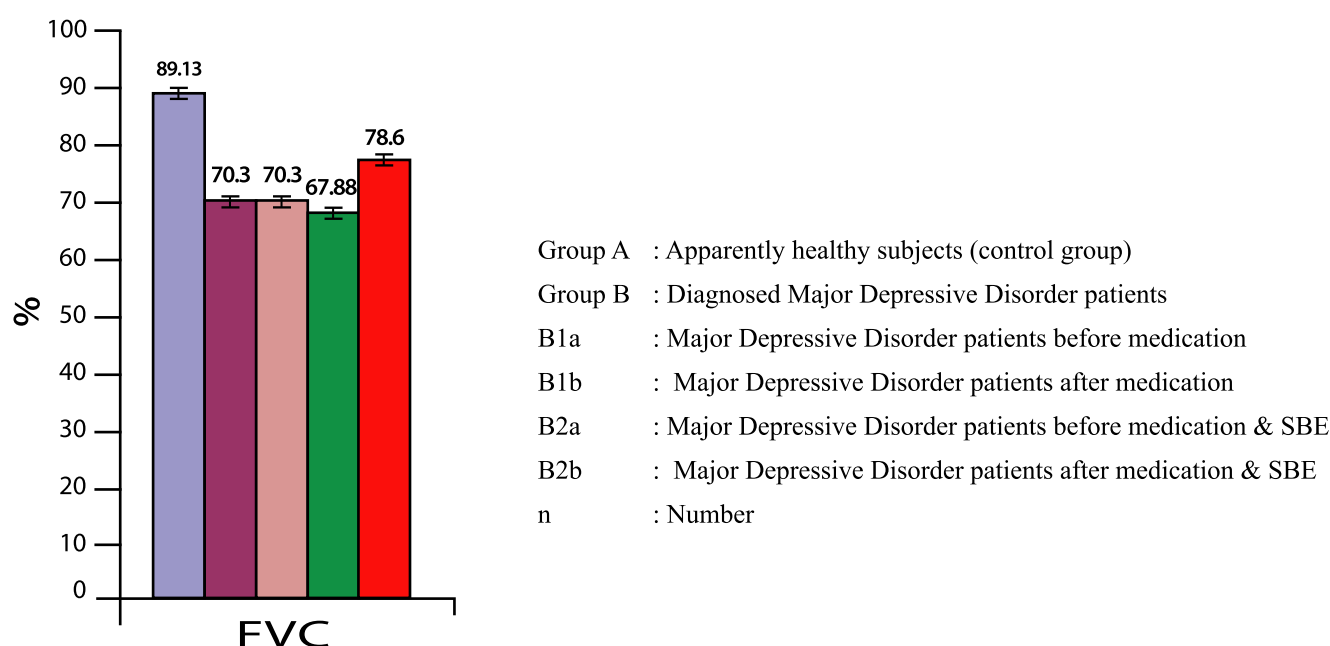
RESULTS

The characteristics of the 30 female patients newly diagnosed with MDD enrolled in the study are described in table (1).

Table II

Percentage of predicted values of FVC, FEV1 of 30 female Major Depressive Disorder patients (MDD), Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, 2014.

Parameters	MDD newly diagnosed	MDD after three months of SBE	P value
FVC	67.86±1.99 (38-86)	78.60±1.87 (57-108)	0.001***
FEV1	52.26±3.88 (15-92)	74.00±2.34 (53-100)	0.001***



DISCUSSION

Our study finds encouraging evidence that slow breathing exercise can improves lung function among patients with MDD. The present study has been undertaken to observe pulmonary functions in 30 female MDD patients before and after three months of practicing yoga based relaxation technique, the slow breathing exercise⁷. Pulmonary functions were assessed by measuring FCV, FEV1 with a portable micro spirometer. All measures shows significant and substantial improvement over baseline.

Our findings are consistent with the weight of literature and in the likely mechanism for the effect. Different researchers found that pulmonary functions are significantly reduced in patients with depressive illness especially in major depressive disorder patients. Islam and his colleagues investigated lung function by

spirometry in depressive disorder patients and found lung function parameters were significantly lower in depressive disorder patients in comparison to healthy subjects³. On the other hand, one another study on US soldiers with Vietnam experience did not find any association between MDD with lung function⁸. Calikoglu and his colleagues investigated lung function test by spirometry in 30 female patients with MDD. After comparing with control group, they found that dyspnea was higher in patients with MDD. In this study, PEFR in patients newly diagnosed with MDD were significantly lower than those of apparently healthy subjects. The apparent effect of depression on poor lung function may be explained by the reduced psychomotor activity along with poor respiratory muscle strength in depressive illness⁹. It is surprisingly noted that in MDD patients after 3 months of slow breathing exercise

(Anuloma Viloma) beside antidepressive medicine, overall lung function was significantly improved, evidenced by the significantly higher values of all spirometric indices.

The benefit of Slow breathing exercise for improvement of respiratory efficiency is derived from multiple factors. One suggested causal mechanism for improvement of respiratory efficiency by Slow breathing exercise is, its deep inhalation and prolonged expiration develop efficient use of diaphragm, abdominal muscles and intercostals muscles which ultimately improves strength of this respiratory muscles. In addition, the stress on more prolonged expiration deep inspiration trains the respiratory apparatus for more efficient and complete emptying and filling of airways.

The poor strength for spirometric performance due to poor muscular strength due to depression is thus overcome by the increased strength of respiratory muscle achieved by SBE.

In the slow breathing exercise procedure, deep breathing at slow phase also reduces dead space and increased alveolar ventilation. Consequently, this increases vital capacity. The significant improvement of FVC and FEV1 after practicing SBE for 3 months provides the evidence of improved ventilator function of lung.

During SBE, the thoracic and lung compliance increases, airway resistance decreases which is supporting the increased value of FEV1, FEV1/FVC ratio in MDD patients in the present study¹⁰⁻¹¹.

We recognize limitations of our study. First we did not randomize patients to receive the slow breathing exercise intervention versus control or no intervention. Second, it is possible that the change in lung function could be due to other causes. Third, our sample size is small and findings need to be replicated in a larger, externally controlled experiment.

CONCLUSION

Our results are encouraging that safe intervention of slow breathing exercise can the lung function of patients with MDD. The intervention is also nearly cost free and culturally appropriate to south Asia and other parts of the world. If confirmed Slow breathing exercise may be effective and potent for improvement of poor lung function associated with many types of pulmonary functional disorders other than that associated with MDD.

Thus Slow breathing exercise may form an alternative or adjunct to antidepressive medication in the MDD for improvement of their respiratory efficiency.

ACKNOWLEDGEMENT

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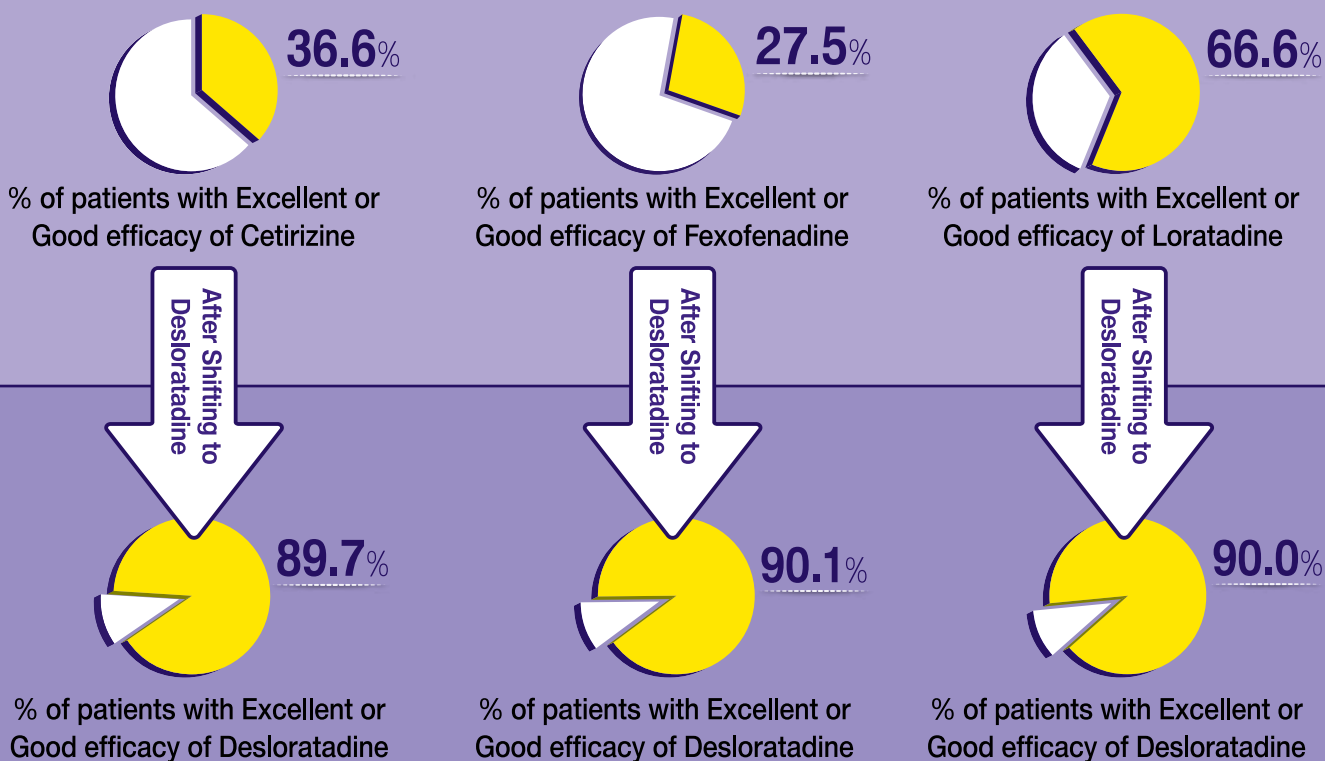
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Bronchorrhea- A distressing respiratory symptom

Bronchorrhea is arbitrarily defined as watery sputum production of over 100 ml per day.¹ Up to 9 Liters per day has been reported.² It can be caused by primary lung malignancy especially of bronchioloalveolar cell type and metastases to lung especially from cells of glandular origin (e.g. adenocarcinoma of cervix, colonic adeno- carcinoma, and pancreatic cancer).³⁻⁵ It can also be caused by non-malignant conditions like chronic bronchitis, asthma and endobronchial.

tuberculosis. There are three postulated pathophysiological mechanisms for bronchorrhea:

1. Hyper-secretion of mucus-glycoprotein and other glandular products from mucus- glycoprotein producing cells – neutrophils accumulating in airway mucosa may stimulate goblet cells secretion.
2. Increased transepithelial chloride secretion- this can be mediated by receptors for prostaglandins (PGE2 PEF2 α) or secretin in the bronchial epithelium.
3. Excessive transudation of plasma products into the airway.6Bronchorrhea has negative impact on both survival and quality of life. It can cause excessive cough, sleep disturbance and dyspnea. When severe, it may lead to respiratory failure, dehydration and electrolyte disturbance

The management of bronchorrhea includes general supportive measures to promote comfort, maintenance of fluid and electrolyte balance and measures to reduce bronchial secretion production. The following seven entities have been tried in reducing bronchial secretions:

1. Radiotherapy and traditional chemotherapy
2. Anticholinergic agents
3. Macrolides
4. Pulsed methylprednisolone
5. Inhaled indomethacin
6. Gefitinib (EGFR-TKI)
7. Octreotide

migration and activities in the lung and inhibiting the synthesis and secretion of a mucus secretagogue from pulmonary macrophages.⁷ There were case reports the responses of bronchorrhea to radio-therapy, traditional chemotherapy and anticholinergic drugs are variable. Macrolides act by affecting neutrophil using oral clarithromycin combined with inhaled beclomethasone in managing bronchorrhea in alveolar cell carcinoma,⁸ pulsed methylprednisolone in a patient with Bronchiolo-Alveolar

Carcinoma (BAC),⁹ and inhaled indomethacin in patients with chronic airway diseases like chronic bronchitis, diffuse panbronchiolitis and bronchiectasis, presumably by reducing the levels of prostaglandins and its metabolites in sputum.¹⁰ Nebulised indomethacin was successful in patients with BAC suffering from bronchorrhea in reducing the sputum volume, improving the quality of life, and possibly prolonging the survival.¹¹ Two more recent weapons in treating bronchorrhea are Gefitinib and Octreotide. Gefitinib, an Epidermal Growth Factor Tyrosine Kinase Inhibitor, is thought to reduce bronchorrhea by inhibiting the expression of a major mucin in BAC cells, the MUC5AC mucin, based on findings from animal study and laboratory setting.¹²⁻¹³ There were case reports of its successful reduction of sputum volume in BAC patients.¹⁴⁻¹⁵ As the onset of improvement occurred within 24 hours of use, it is likely that its inhibitory action on mucin production is independent of its anti-proliferative effect. Octreotide, a somatostatin analogue, has been reported to significantly reduce the volume of secretions with the acinar type of adenocarcinoma of lung at a dose 300-500 micrograms daily.

There is limited evidence for effective drug treatment of bronchorrhea, making any recommendations for its treatment almost impossible. Taking local availability, treatment costs, and tolerability into account, the following steps are suggested from a pragmatic point of view: treatment of first choice should be a corticosteroid or macrolide antibiotic. If a treatment course with either gefitinib or erlotinib is considered as antitumor treatment, accompanying bronchorrhea can support this treatment choice. If the sole purpose of drug therapy is symptom control, a first-line treatment should be taken into consideration initially. If inhaled indomethacin is available, it can be considered as a second-line treatment.

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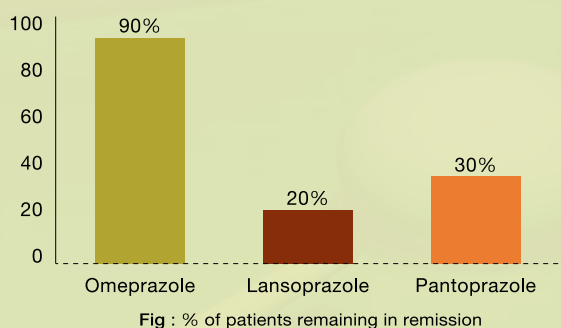
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Omeprazole, Lansoprazole & Pantoprazole were compared to each other in maintenance treatment of patients with complicated Esophagitis. Following result was observed-



Study type : Controlled
No. of patients : 36
Duration : 4 weeks
Drugs Used : Omeprazole 20 mg b.d.
Lansoprazole 30 mg b.d.
Pantoprazole 40 mg b.d.

Procap showed superiority over Lansoprazole & Pantoprazole in complicated GERD.

A Case Report of Rickettsial meningitis

Sadia Islam¹, S W Rahman², Tasrina SS³

ABSTRACT

Rickettsial diseases are a group of infections caused by the obligate intracellular bacteria Rickettsia. Rickettsial infections are common in southern Europe and the most frequent and lethal type is Mediterranean spotted fever, caused by Rickettsia conorii. The disease is usually characterized by the classical triad of fever, eschar and rash. Complications including neurological involvement are rarely described. We report an unusual case of meningitis in a 55 years – old man presenting with high grade fever for 8 days and associated with persistent headache. The patient was suspected of enteric fever and treated with injection ceftriaxone. Forty-eight hours after admission, the presence of continued high grade fever, conjunctival congestion, headache, cough, low platelet, increased WBC count, elevated transaminase raised the possibility of a different aetiology. Finally, Rickettsial meningitis was confirmed due to history of field visit, presence of eschar, neck rigidity, raised titre of WF OXK antigen and the cerebrospinal fluid analysis revealed increased cellularity, hypoglycorrhachia, hyperproteinorrhachia (106 mg/dL). Gram stain (No organism found) and Z.N. stain (AFB Not found), GeneXpert for detection MTB not detected. All other causes of fever were ruled out by history, clinical examination and relevant investigations. Patient was treated with capsule doxycycline and other supportive therapy and become afebrile within 48 hours. This uncommon clinical scenario should be taken into account in the management of patients with high grade fever on admission.

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INTRODUCTION

Rickettsia may be responsible for certain febrile illness of unknown origin. It is often misdiagnosed and treated as other febrile illness because of its similarity of symptoms and lack of confirmation by laboratory investigations. And when untreated Rickettsial diseases can be fatal sometime.

Co-infection of typhoid and Rickettsial fever can be overlooked if not suspected clinically. High grade continued fever with variable associated symptoms, such as malaise, headache, and myalgia, are usually present in both typhoid and Rickettsial fever. Therefore, clinical suspicion is of paramount importance in the diagnosis of both typhoid and Rickettsial fever. Confirmation of the diagnosis is important as the treatment is different but may not always be possible. In most cases of Rickettsial fever, treatment is given based on clinical suspicion due to presence of eschar or a positive Weil-Felix test. In clinically-suspected cases of typhus fever, a rising titre of OX-K antigens supports the diagnosis but confirmation of the diagnosis may be difficult. Isolation of Salmonella Typhi from blood confirms the diagnosis of typhoid fever. Here, a case of Rickettsial meningitis having an eschar and highly rising titre of OXK antigen in weil felix reaction is presented - recently admitted to the Delta Medical College United Hospital Limited.

CASE PRESENTATION

In March 2018, a previously-healthy 55-year old non-smoker, non-alcoholic, married, fisherman hailing from Comilla, admitted with complaints of high grade continued fever for 10 days associated with vomiting, abdominal discomfort, headache, body ache, and cough. No significant past illness was reported. He has no H/O visiting in malaria endemic zone.

On admission, the patient was conscious, oriented, dehydrated with high fever 105° F. His radial pulse was 120 bpm, regular and good in volume; respiration rate was 20 per minute; and BP was 120/80 mmHg. On examination, there were no signs of anemia, jaundice. Skin rash, lymphadenopathy, neck rigidity absent. Systemic examination revealed his breath sounds were vesicular, with no added sounds, abdomen was soft and non-tender, no hepato-splenomegaly and bowel sound present. First and second heart sounds were normal without any murmur. Neurological and musculoskeletal system examination revealed normal. Relevant investigations were sent and intravenous (IV) ceftriaxone 2 gm 12 hourly was started.

Laboratory investigation showed that total WBC was 16000/Cumm with polymorphs– 56%, lymphocyte–38%, and monocyte–6%, platelet: $95 \times 10^3/\mu\text{L}$. with raised transaminase. His renal function test, chest X-ray, urine routine examination, USG of whole abdomen were normal.

After 24 hours, the patient was found to be toxic, hyperthermic and developed conjunctival congestion. After two days, the patient was disoriented and neck rigidity was present. To further investigate, CSF study was done and found increased cellularity, hypoglycorrhachia, hyperproteinorrhachia (106 mg/dL). Gram stain (No organism found) and Z.N. stain (AFB Not found), GeneXpert for detection MTB not detected. PFB for MP: absent, ICT for Malaria and Kala-Azar were negative.

On the 5th day of admission, the patient suddenly develop hypotension not responding to IV fluid challenge and on re-examination of patient there was found to have eschar in back of the chest(left side) and regional lymphadenopathy along with 105° F and 70/ 50 mmhg- blood pressure. Blood culture revealed no growth. Widal titres were not rising. Reconsidering of other investigations Fevrile Antigen was done where Weil-Felix titres were: OX2=1:80, OX19=1:80, and OXK=1:640. Then the patient was treated with cap doxycycline 100 mg 12 hourly and other supportive therapy. After getting 4 dose of doxycycline patient became afebrile, clinically improved, neck rigidity absent and patient became conscious. Finally, the patient was diagnosed with Rickettsial meningitis.



Figure 1: Eschar in the right side of the chest of the patient

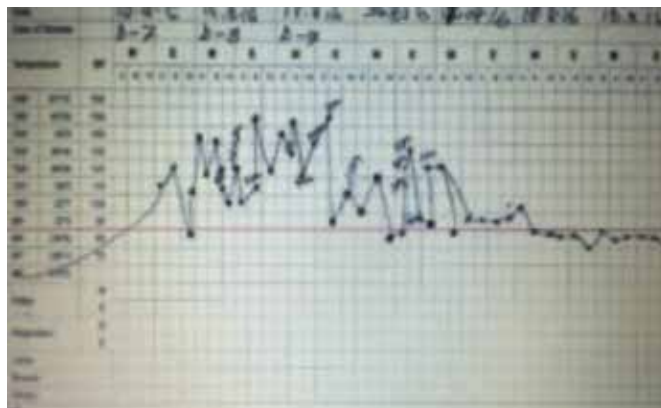


Figure 2: Temperature chart of patient showing high grade fever. After 48 hours of starting doxycycline, fever subsides

DIFFERENTIAL DIAGNOSIS

Our patient presented with meningitis and was empirically treated with ceftriaxone with no improvement. At this time, other less frequent aetiologies were considered.

M tuberculosis, is the commonest agent in Bangladesh, can cause meningitis with hypoglycorrhachia. However, the negative tuberculin intradermal reaction, CSF study (Gram stain, Z.N. stain, GeneXpert) and culture did not support this diagnosis.

Viruses can also cause meningitis, namely enteroviruses and arboviruses, especially during summer months, but these were also ruled out by initial presentation of fever for 10 days without any neck rigidity.

TREATMENT

Recommended treatment for rickettsial infections is doxycycline 100 mg twice a day for 5–10 days (or at least 3 days following defervescence).¹⁻⁹ Our patient completed 10 days of doxycycline. Cephalosporins and penicillins are ineffective as observed in this case.⁹

OUTCOME AND FOLLOW-UP

The patient evolved favourably with remission of symptoms 48 h after starting doxycycline and had no sequelae.

DISCUSSION

The atypical presentation of high fever and the paucity of additional symptoms (no rash or eschar), and as the Rickettsia meningitis is not common infectious disease for Bangladesh challenged the initial diagnosis in this case. After non responding to treatment (Ceftriaxone), CSF study, febrile antigen, and

re-examined the patient by seeing Eschar raised the suspicion of a zoonotic infection and led us to change the antibiotic therapy to doxycycline, with improvement.

Owing to the presence of shared protein and lipopolysaccharide antigens, it is extremely difficult to distinguish closely related agents within the rickettsial spotted fever group by serological methods.¹⁰ Only successful isolation of the agent or molecular detection in blood or tissue can determine the *Rickettsia* species.⁷ However, this was not achievable in this case, which might be related to treatment with clarithromycin prior to admission.

Central nervous system involvement, namely rickettsial encephalitis, is characterised by confusion and obtundation due to increased intracranial pressure and has been associated with a worse prognosis.⁷ Our patient did not show signs of cerebral parenchymal disease.

In general, rickettsial meningitis behaves like a viral meningitis but responds only to doxycycline or chloramphenicol instead of symptomatic therapy.¹¹⁻¹² Our patient was improved by doxycycline. We hypothesise that rickettsial spp response in doxycycline the lack of response was due to the short duration of therapy and the erratic central nervous system penetration.

CONCLUSION

We conclude that, although *Rickettsia* meningitis is not common for Bangladesh, *Rickettsia* infection may present as meningitis and should be included in the differential diagnosis. Definitive diagnosis of rickettsial infections relies mainly on serological methods that can be limited in an initial phase (due to latency in antibody response), emphasising the need for a high clinical suspicion. Early treatment should be instituted empirically, since it improves prognosis, diminishes mortality and sequelae associated with rickettsioses. There are an increasing number of reports regarding emerging *Rickettsia* spp responsible for incomplete and atypical presentations that should be considered.

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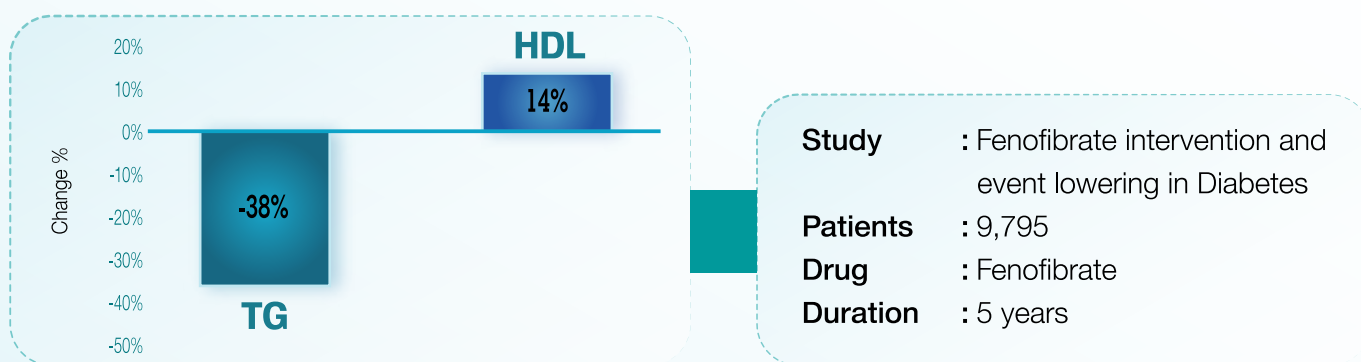


Fig.: Improvement of TG & HDL level with Fenofibrate

Significantly improves CV events

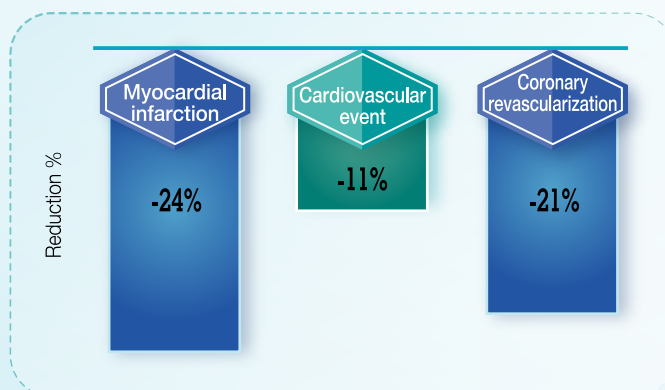


Fig.: Reduction % of CV events with Fenofibrate

TG= Triglyceride
HDL= High Density Lipoprotein cholesterol

Sociodemographic and Clinicopathological Features in Patients with Vulvar Squamous Cell Carcinoma in Bangladesh

Farhana Ahmed, Syed Md. Ali Romel, Tahmina Ahmed, Salma Parvin

ABSTRACT

Objectives: To observe sociodemographic and clinical-epidemiological profiles of patients with vulvar carcinoma in Bangladesh.

Methods: A retrospective study was performed using 50 medical records from patients diagnosed with squamous cell carcinoma of the vulva and surgically treated at NICRH Dhaka.

Results: The median age of onset was 70 years, ranging from 15 to 98 years. Most patients (83.54%) had little or no schooling and had the lowest survival curve. Many patients were diagnosed in the early stages of the disease (57.09% FIGO IB), 59% had complications due to surgery and 43.71% had disease recurrence, of which about 70% died.

Conclusions: Our study is on 50 Bangladeshi cases of squamous cell carcinoma of vulva. Given the high rate of disease recurrence and mortality in Bangladesh, we conclude that regular gynecologic evaluation and educational policies should be reinforced in order to raise awareness for vulvar cancer.

Key words: Vulvar cancer –Treatment- Surgery- Demographics- Clinical pathology

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INTRODUCTION

Vulvar carcinoma is a disease that accounts for approximately 3–5% of all malignant tumors in the female genital tract¹⁻³ and has traditionally been considered a disease of elderly women (aged between 65 and 75 years)^{4,5}. However, in recent decades, its incidence has risen in younger women^{6,7}, possibly due to the higher frequency of precursor lesions – vulvar intraepithelial lesions (VINs) – and their association with HPV infection^{7,8}.

The number of new cases of vulvar carcinoma was 2.5 per 100,000 women per year. The number of death was 5 per 100,000 women per year. These rates are based on 2011-15 cases and deaths. Approximately 3% women will be diagnosed with vulvar cancer at some point during their lifetime, based on 2013-2015 data. The National Cancer Institute (NCI) of the United States estimates that 6,190 new cases of vulvar cancer diagnosed in the USA in the year 2018 with 0.4% of all new cancer cases. Estimated deaths 1200 and 0.2% of all cancer deaths. There is no statistical data available in Bangladesh.

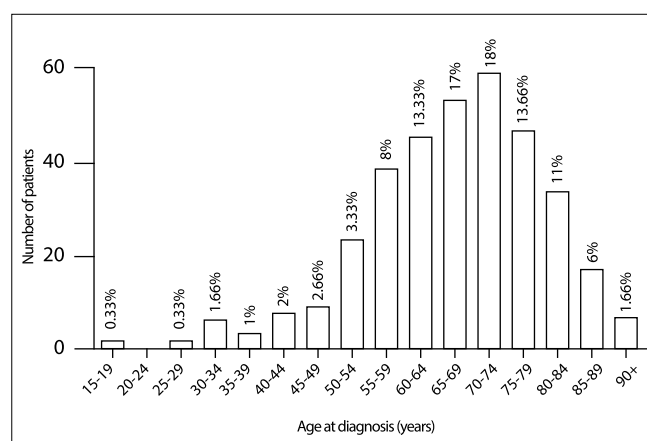


Fig:1 Vulvar carcinoma: age-specific incidence at NICRH, Bangladesh (2015-2018), Please notice that the age group between 65 and 74 years has the highest number of women.

In spite of the rising incidence of this disease, literature data regarding epidemiologic aspects of vulvar carcinoma are still scarce. Due to HPV infection, this incidence is likely to grow further in the next years, but data regarding the sociodemographic and clinicopathological features are few.

Table 1. Sociodemographic features related to marital status and education of patients with vulvar SCC (2015-2018, NICRH, Bangladesh)

Sociodemographic variables	n	%
Marital status		
Single	7	13.40
Married	26	54.29
Divorced	2	2.74
Widow	15	29.55
Education		
Illiterate	18	39.76
Elementary school	20	43.78
High school	6	13.65
College or over	6	2.81

MATERIALS AND METHODS

These patients were from various regions of Bangladesh, and treated surgically and/or with radio therapy treated at NICRH, Bangladesh from 2015 to 2018. The study was approved by the Ethics Committee for Medical Research in this institution.

The survey was based on information from patient's medical files. All data were stored in a Windows Excel database. For quantitative variables, main summary measures such as mean, standard deviation, minimum and maximum values were presented, and the qualitative variables were presented to the respective distributions of absolute and relative frequencies. Kaplan-Meier survival curves were plotted and the log-rank test compared the results. Survival was calculated from the date of diagnosis to the date of death or last follow-up, and p was set at a <0.05 significance level. Software Prism 5 was used for statistical analyzes.

RESULTS

Sample Description

The sample consisted of 50 patients. The median age of onset was 70 years, mean age 68 years ($SD = 12.69$), with a range of 15–98 years. Most patients were aged between 65 and 74 years,

as shown in figure 1. When divided into two groups – younger (under 50 years) and older women (50 years or above) –, lower survival rates were shown for the group of older women ($p = 0.0576$, fig. 2a).

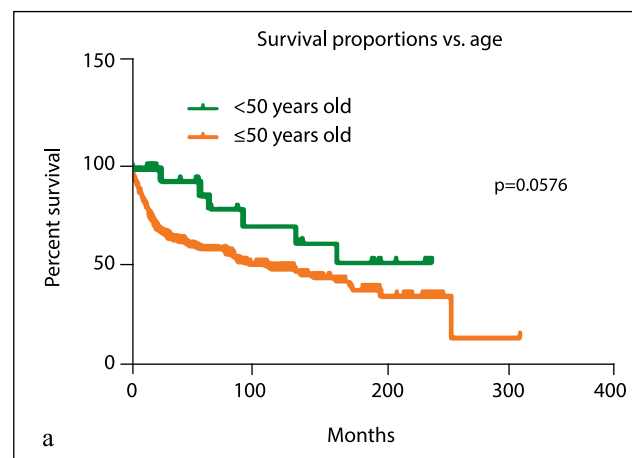
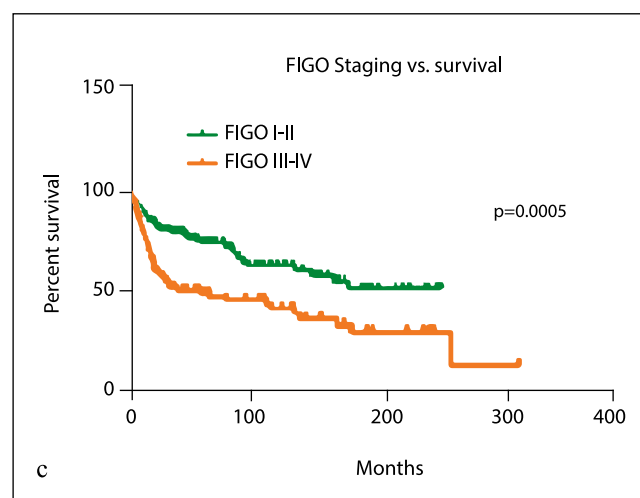
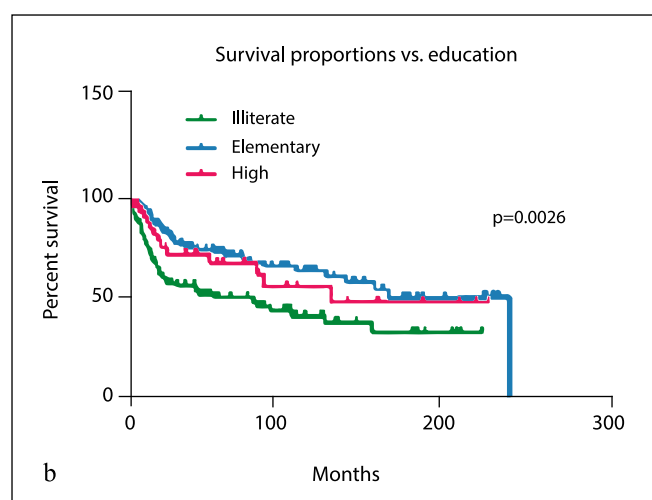


Fig. 2. Kaplan-Meier curves for survival proportions versus patient's age (a), education level (b), and FIGO stages (early vs. late stages) (c). a Survival proportions for women aged <50 years (green line) and ≥ 50 years (orange line). b Survival curves for illiterate women (green), women with elementary education (blue) and higher levels of education (pink). c Survival proportions versus FIGO staging are shown in green as early stages (FIGO I–II) and orange as late stages (FIGO III–IV).

Most patients were married (54.29%) or widowed (29.55%). Additionally, most women had little or no formal education: 39.76% were classified as illiterate, while 43.78% had only reached elementary school level education (table 1). Patients with no schooling had the lowest survival rates compared to those who had any level of formal education ($p = 0.0026$), as shown in figure 2b. Other Kaplan-Meier survival analyses such as age at menarche and menopause, race, smoking, number of sexual partners and age at first intercourse had no statistical significance on survival.

The average age for menarche was 14 years ($SD = 3.66$) ranging from 10 to 20 years, and average age at menopause was 49 years ($SD = 5.64$) ranging from 31 (early menopause) to 64 years. Twenty patients (6.6%) were premenopausal women. The average age at first intercourse was 13 years ($SD = 8.57$). In relation to the number of pregnancies, births and abortions, our results showed averages of 6 ($SD = 4.84$), 5 ($SD = 4.38$) and 1 ($SD = 1.53$), respectively. Most of the patients (90%) acknowledged only one sexual partner during their lives. 93.99% of the group had never used oral contraceptives,



5.15% had used them in the past, and 0.85% ($n = 2$) were current users. 100% and 82.28% of the patients related no alcohol or smoking use, respectively (table 2).

Clinicopathological Aspects

The most common symptoms related by patients and duration of these symptoms are shown in figure 3. Pruritus was the most common symptom (33.22%), followed by ulceration (26.57%) and presence of a vulvar mass (20.43%). Bleeding (8.97%), pain (4.81%), secretion

Table 2. Clinicoepidemiological features related to menarche, menopause, age at first intercourse, pregnancies, births, abortion, sexual partner, oral contraceptive use, consumption of alcohol, and smoking of patients with vulvar SCC (2015-2018, NICRH, Bangladesh)

Clinicoepidemiological features	
Menarche	
Average, years	14
Median $\pm$ SD, years	13 $\pm$ 3.66
Minimum age–maximum age, years	10-20
Menopause	
Average, years	49
Median $\pm$ SD, years	50 $\pm$ 5.64
Minimum age–maximum age, years	31-64
Age at first intercourse	
Average, years	19
Median $\pm$ SD, years	18 $\pm$ 8.57
Minimum age–maximum age, years	11-51
Pregnancies	
Average	6
Median $\pm$ SD	5 $\pm$ 4.84
Minimum–maximum	0-22
Births	
Average	5
Median $\pm$ SD	5 $\pm$ 4.38
Minimum–maximum	0-20
Abortions	
Average	1
Median $\pm$ SD	0 $\pm$ 1.53
Minimum–maximum	0-11

	n	%
Sexual partners		
0	0	0
1	45	90
2	5	10
≥ 3	0	0
Countless	0	0
Oral contraceptive use		
No	46	92
Yes, currently	0	0
Yes, in the past	4	8
Alcohol		
No	50	100
Yes, currently	0	0
Yes, in the past	0	0
Smoking		
No	41	82
Yes, currently	7	14
Yes, in the past	2	4

Table 3. Invasion of tumor adjacencies of the patients with vulvar SCC from 2015 to 2018 (NICRH, Bangladesh)

Tumor invasion	N	%
Sites		
Vagina	45	15
Urethra	23	7.66
Anus	6	2
Rectum	3	1

(4.48%) and dysuria (1.49%) were less common. The average duration of symptoms for all patients was 6 months (median 6 months; SD= 17.16). When comparing the duration of symptoms between younger and older women, average duration of symptoms was 7 months (average 21; SD= 20.45) for younger women (<50 years old) and 6 months (average 11; SD= 16.13) for older women (≥ 50 years). Illiterate women and those with only basic school education levels had symptoms for about 13 months, while women with high school education, college or higher had symptoms for 9 months.

The most common tumor localization was the labia minora (39.97% of cases), followed by labia (31.06%), clitoris (23.16%) and perineum (6.80%). Most tumors (72.20%) affected the vulva unilaterally. About 20% of the tumors were bilateral, 4.74% were located centrally, and 2.72% affected the vulvar midline.

Table 3 shows data regarding the invasion of adjacent sites From

the 50 tumors available on our study, 15% had invaded the vagina, 7.66% the urethra, 2% the anus and 1% the rectum.

Figure 4 shows FIGO staging in which stages IB and IIB were the most common: 57.09% of the tumors were stage IB and 22.14% stage IIB. Survival curves showed a significant difference between survival rates of patients with early tumors (FIGO I and II) and those of patients with late tumors (FIGO III and IV), as shown in figure 2c ($p=0.0005$)

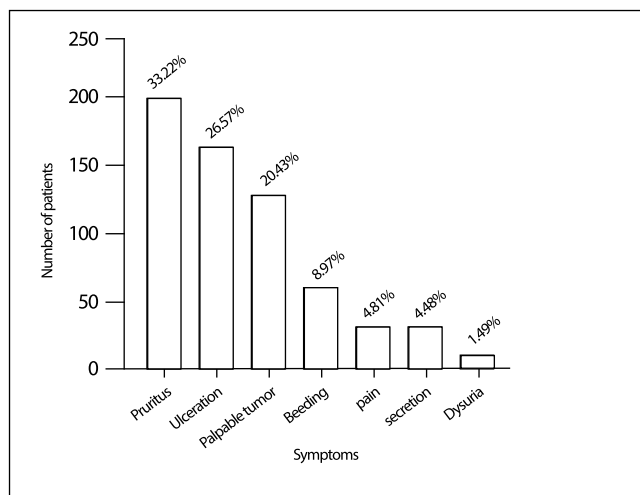


Fig. 3. Most common symptoms by patients with vulvar SCC (NICRH, Bangladesh 2015–2018) of which pruritus was most frequently mentioned

Table 4. Treatment features of the patients with vulvar SCC (2015–2018, NICRH, Bangladesh)

Clinicopathological features	N	%
Type of surgery		
Wide local excision	5	10
Partial vulvectomy	2	4
Modified radical vulvectomy	43	86
Radiotherapy		
No radiotherapy	2	4
Adjuvant radiotherapy	45	90
Lymphadenectomy		
Yes	40	80
No	10	20

A wide range of clinicopathological aspects were addressed in this study such as treatment of the tumors with chemo/radiotherapy, types of surgery performed, lymph-adenectomy, complications of the treatment, recurrence and status of the patients. These data are shown in table 4. All the patients were treated surgically. Modified incision

Radical vulvectomy was most frequently performed (86 %), followed by wide local excision (10%). Ninety percent of the patients receive radiotherapy and lymphadenectomy was performed in 80 %.

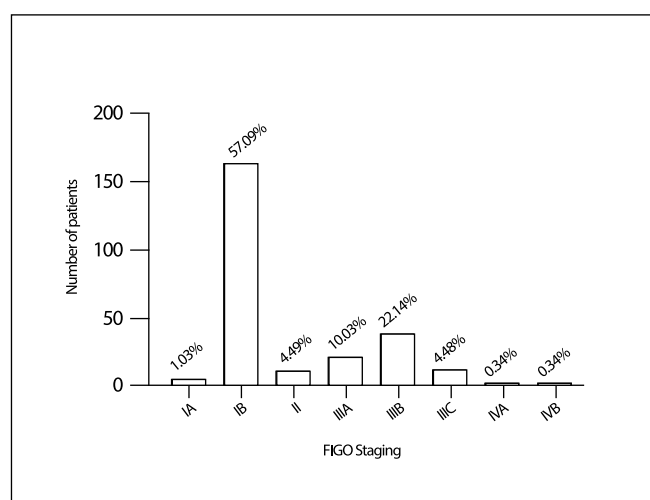


Fig. 4. FIGO staging for vulvar SCC from 2015 to 2018. Different FIGO staging and the proportion of tumors included in each stage are shown.

Patient Outcome

Data on patient outcome are shown in table 5. Recurrence was observed in 30 patients (60%), with local recurrence being the most common. Lymph node recurrence was found in 30.08%.

DISCUSSION

Our study found that the median age of onset for vulvar carcinoma was 70 years, which agrees with other studies in the literature that give the average age of onset as the seventh and eighth decades. We also found that the incidence increased with age, as has been suggested by other authors^{6,13-16}. However, our patients ranged in age from 15 to 98 years. Some studies have reported that tumors found in younger women are directly related to

HPV infection, vulvar dysplasia and tobacco use, in contrast to the older age group in which causal factors are suggested to be p53 mutations, chronic inflammation and vulvar dystrophy⁶⁻¹⁷.

Assuming clinical importance, our findings would differ from other studies in which the younger women had a worse survival¹⁸⁻¹⁹. However, our results are consistent with the fact that vulvar tumors associated with HPV infection, which has been shown to be an independent predictor of better survival, have a better prognosis compared to tumors with p53 mutations, which is the most commonly found associated factor in women over 50 years¹⁸.

Table 5. Outcome of the patients with vulvar SCC (2015-2018, NICRH, Bangladesh)

Outcome	N	%
Complications		
No	30	60
Yes	20	40
Most common complications		
Seroma	13	26
Wound infection	5	10
Wound breakdown	2	4
Lymphedema	17	34
Recurrence		
No	20	40
Yes	30	60
Type of recurrence		
Local	30	60
Lymph node recurrence	5	10
Distant	10	20
Locoregional + distant	5	10

Our study had a significant number of illiterate patients or patients with only a few years of formal education. This may be reflected in the average number of pregnancies reported (6 per women) and the lack of oral contraceptive use (only in 5.15%). We did find a difference in the duration of symptoms, which averaged 13 months for those with less formal education compared to 9 months for those patients with a higher educational level. Similarly, we found a lower survival rate for women in the illiterate group (fig. 2).

Women with low levels of formal education seem to have less access to information on sexual behavior, hygiene and sexually transmitted disease, particularly HPV, which is known to be a high-risk factor for the development of vulvar cancer in this group of women. Not only has prophylactic administration of quadrivalent HPV vaccine been shown effective in preventing high-grade vulvar and vaginal lesions in women naïve to HPV16 or HPV18 infections, but it also has been shown to prevent infection and lesions of these specific HPV types in women in the older age groups^{24,25}. A generalized lack of specific information on the part of physicians was high-lighted by a recent American study, evaluating doctors from different specialties. Nearly all of them (97.8%) thought that cervical cancer was prevented by the HPV vaccine, but only 27.8% were aware that this vaccine also prevents vulvar cancer²⁶.

A recent Brazilian study²⁷ showed that the 79 interviews with

health professionals informed that they had a good general knowledge about HPV, but many did not know that vaccines were available against many of the HPV groups. Thus, it seems that not only patients but also health professionals could benefit from continuing educational efforts as well as preventative programs.

Our examination of the patients' medical records showed that most of them were in the older age group, reported only one sexual partner during their lifetimes (90%), in general did not use oral contraceptives, and claimed not to use alcohol or tobacco. It could be that this is a reflection of the cultural inhibitions possibly present in their lives. However, many times the records lack information on these subjects, and thus our results could be biased in terms of underreporting.

Surgery is the most common treatment for vulvar carcinoma^{28,29}, and many different types of procedures have been advocated over the course of time^{13,28,30,31}. Current FIGO recommendations state that in situ (FIGO stage 0) and FIGO stage IA (≤ 2 cm) tumors may be treated by superficial partial vulvectomy, FIGO stages IB (stromal invasion ≤ 1.0 cm) and II (≤ 2 cm) may be treated with partial vulvectomy and lymphadenectomy, and FIGO stage III (any size with adjacent spread) and IVA (tumor invasion to other organs) may be treated with radical (or en bloc) vulvectomy and lymphadenectomy^{30,32}. Modified radical vulvectomy was performed in 86% of our patients. Even though this procedure was introduced to decrease the morbidity and mortality rates compared to classical radical vulvectomy (en bloc), complications and recurrences are still a concern. Forty percent of our patients had complications from surgery, Lymphedema being the most common, followed by infection and seroma. Psychosexual problems such as fear, distortion of body image and depression were not evaluated in this study, but are described in the literature, especially among younger patients¹⁴.

In our study, 30 patients (60%) had recurrent disease. This figure is a bit higher than that reported by Coulter and Gleason²⁹, who found a recurrence rate of about one third. Their study showed that the size of the lesion, close margins of resection (<1 cm) and lymph node status at primary surgery were the main predictors of recurrence²⁹. We found local recurrence in 60% of our patients. Nodal metastases occurred in 10% of our patients, while the literature cites 11–38%^{32–35}. Nodal recurrence in primary vulvar carcinoma seems principally related to the depths and size of the tumor as well as vascular invasion²⁹. Distant metastatic disease was found in 20% of our study patients. Corresponding literature rates are 8–37%^{32–34}.

However, it has been shown that long-term follow-up of these patients is required, as recurrences can be seen many years after the primary therapy³⁰.

The main limitations of this paper should be clarified: the fact

that vulvar carcinoma is a rare tumor, leading to a small number of cases being evaluated; retrospective study of patients who underwent surgical procedure; medical records without full information (partially completed by the physician or noncollaborative patient); limited published data available on vulvar carcinoma (scarce literature leads us to a more speculative discussion and comparison with other studies performed in other countries).

In conclusion, our study is only 50 cases of different places of Bangladesh vulvar carcinoma to the world literature. Although most of our patients were over 50, we had 1 patient aged 15 years, which highlights the increasing incidence of this disease in younger women. We feel this aspect will become more important with time. We also found that women with low educational levels have a significantly lower survival. This highlights the need for more effective socio-educational policies, particularly here in Brazil. Ideally, randomized controlled clinical trials would be of great help, due to the worldwide rise in incidence of this cancer. However, a basic regular gynecological exam with educational reinforcement remains a very important part in the diagnosis of early and more potentially curable, vulvar cancer.

Disclosure Statement

No conflicts of interest reported.

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Autism and zinc deficiency in early development

Mechanistic link found between zinc, autism risk genes and abnormal neuronal connections associated with autism spectrum disorders

Source: Frontiers

Summary: Autism has been associated with zinc deficiency in infancy. While it is not yet known whether zinc deficiency in early development causes autism, scientists have now found a mechanistic link. Their study connects zinc, autism risk genes and abnormal neuronal connections associated with autism spectrum disorders.



The emergence of autism in children has not only been linked to genes encoding synaptic proteins -- among others -- but also environmental insults such as zinc deficiency. Although it is unclear whether zinc deficiency contributes to autism, scientists have now defined in detail a possible mechanistic link. Their research shows how zinc shapes the connections or 'synapses' between brain cells that form during early development, via a complex molecular machinery encoded by autism risk genes. Published in *Frontiers in Molecular Neuroscience*, the findings do not directly support zinc supplementation for the prevention of autism -- but extend our understanding of its underlying developmental abnormalities, towards an eventual treatment.

Zinc and autism risk genes

"Autism is associated with specific variants of genes involved in the formation, maturation and stabilization of synapses during early development," says study senior author Dr Sally Kim of Stanford University School of Medicine.

"Our findings link zinc levels in neurons -- via interactions with the proteins encoded by these genes -- to the development of autism."

Kim and colleagues found that when a signal is transferred via a synapse, zinc enters the target neuron where it can bind two such proteins: Shank2 and Shank3. These proteins in turn cause changes in the composition and function ('maturation') of adjacent signal receptors, called 'AMPA's', on the neuron's surface at the synapse.

A mechanistic link

Through an elegant series of experiments, the paper describes the mechanism of zinc-Shank-mediated AMPAR maturation in developing synapses.

"In developing rat neurons, we found that Shank 2 and 3 accumulate at synapses in parallel with a switch to mature AMPARs. Adding extra zinc accelerated the switch -- but not when we reduced the accumulation of Shank 2 or 3," explains Dr Huong Ha -- the study's lead author, a former Stanford graduate student.

"Furthermore, our study shows mechanistically how Shank2 and 3 work in concert with zinc to regulate AMPAR maturation, a key developmental step."

In other words, zinc shapes the properties of developing synapses via Shank proteins.

"This suggests that a lack of zinc during early development might contribute to autism through impaired synaptic maturation and neuronal circuit formation," concludes co-senior author Professor John Huguenard, also of Stanford University School of Medicine.

"Understanding the interaction between zinc and Shank proteins could therefore lead to diagnostic, treatment and prevention strategies for autism."

Will zinc supplements help prevent autism?

"Currently, there are no controlled studies of autism risk with zinc supplementation in pregnant women or babies, so the jury is still out. We really can't make any conclusions or recommendations for zinc supplementation at this point, but experimental work in autism models also published in this *Frontiers Research Topic* holds promise," points out Professor Craig Garner of the German Centre for Neurodegenerative Diseases, also co-senior author.

Taking too much zinc reduces the amount of copper the body can absorb, which can lead to anemia and weakening of the bones. Furthermore, zinc deficiency does not necessarily imply a dietary deficiency -- and could result instead from problems with absorption in the gut, for example.

"Nevertheless, our findings offer a novel mechanism for understanding how zinc deficiency -- or disrupted handling of zinc in neurons -- might contribute to autism," adds Garner.

Story Source:

Materials provided by Frontiers. Note: Content may be edited for style and length.
<https://www.sciencedaily.com/releases/2018/11/181109073034.htm>

How too much salt can cause inflammation

New research, published in the journal *Nature Immunology*, now shows how a high intake of salt may cause inflammation in multiple sclerosis.

Multiple sclerosis (MS) is an autoimmune disorder in which the body's immune system destroys the protective coating around neurons called myelin.

This neurological disease affects around 400,000 people in the United States and approximately 2.5 million adults worldwide. Generally, women are at a higher risk of developing the condition than men.

While researchers do not yet know what causes MS, an interplay between genetic predisposition and environmental factors is likely to be key.

For instance, researchers have so far identified 233 haplotypes that underpin MS. A haplotype is a set of genetic variants that can be found on the same chromosome and that is inherited from one parent.

As for environmental factors, studies have found that vitamin D insufficiency, smoking, obesity, and a high dietary intake of salt all correlate with a higher risk of MS. Some studies have zoomed in on the effect of a high salt intake on a model of MS and found that it exacerbates brain inflammation, while others

have found that it boosts the number of pro-inflammatory cells. However, until now, the precise molecular mechanism behind this effect that salt has on MS was not known. New research finds a molecular pathway that explains how a high-salt environment might potentially trigger the autoimmune disorder.

Tomokazu Sumida, an associate research scientist in the Hafler laboratory at the Yale School of Medicine in New Haven, CT, is the first author of the new paper.



One recent study reveals how excessive salt consumption may trigger inflammation in people with MS.

Social media use increases depression and loneliness, study finds

Date: November 8, 2018

Source: University of Pennsylvania

Summary: Facebook, Snapchat, and Instagram may not be great for personal well-being. The first experimental study examining use of multiple platforms shows a causal link between time spent on these social media and increased depression and loneliness.

The link between the two has been talked about for years, but a causal connection had never been proven. For the first time, University of Pennsylvania research based on experimental data connects Facebook, Snapchat, and Instagram use to decreased well-being. Psychologist Melissa G. Hunt published her findings in the December *Journal of Social and Clinical Psychology*.

Few prior studies have attempted to show that social-media use harms users' well-being, and those that have either put participants in unrealistic situations or were limited in scope, asking them to completely forego Facebook and relying on self-report data, for example, or conducting the work in a lab in as little time as an hour.

"We set out to do a much more comprehensive, rigorous study that was also more ecologically valid," says Hunt, associate director of clinical training in Penn's Psychology Department. To that end, the research team, which included recent alumni Rachel Marx and Courtney Lipson and Penn senior Jordyn Young, designed their experiment to include the three platforms most popular with a cohort of undergraduates, and then collected objective usage data automatically tracked by iPhones for active apps, not those running the background.

Each of 143 participants completed a survey to determine mood and well-being at the study's start, plus shared shots of their iPhone battery screens to offer a week's worth of baseline social-media data. Participants were then randomly assigned to a control group, which had users maintain their typical social-media behavior, or an experimental group that limited time on Facebook, Snapchat, and Instagram to 10 minutes per platform per day.

For the next three weeks, participants shared iPhone battery screenshots to give the researchers weekly tallies for each individual. With those data in hand, Hunt then looked at seven outcome measures including fear of missing out, anxiety, depression, and loneliness.

"Here's the bottom line," she says. "Using less social media than you normally would leads to significant decreases in both depression and loneliness. These effects are particularly pronounced for folks who were more depressed when they

came into the study."

Hunt stresses that the findings do not suggest that 18- to 22-year-olds should stop using social media altogether. In fact, she built the study as she did to stay away from what she considers an unrealistic goal. The work does, however, speak to the idea that limiting screen time on these apps couldn't hurt. "It is a little ironic that reducing your use of social media actually makes you feel less lonely," she says. But when she digs a little deeper, the findings make sense. "Some of the existing literature on social media suggests there's an enormous amount of social comparison that happens. When you look at other people's lives, particularly on Instagram, it's easy to conclude that everyone else's life is cooler or better than yours."

Because this particular work only looked at Facebook, Instagram, and Snapchat, it's not clear whether it applies broadly to other social-media platforms. Hunt also hesitates to say that these findings would replicate for other age groups or in different settings. Those are questions she still hopes to answer, including in an upcoming study about the use of dating apps by college students.

Despite those caveats, and although the study didn't determine the optimal time users should spend on these platforms or the best way to use them, Hunt says the findings do offer two related conclusions it couldn't hurt any social-media user to follow.

For one, reduce opportunities for social comparison, she says. "When you're not busy getting sucked into clickbait social media, you're actually spending more time on things that are more likely to make you feel better about your life." Secondly, she adds, because these tools are here to stay, it's incumbent on society to figure out how to use them in a way that limits damaging effects. "In general, I would say, put your phone down and be with the people in your life."

Melissa G. Hunt is the associate director of clinical training in the Department of Psychology in the School of Arts and Sciences at the University of Pennsylvania.

Rachel Marx and Courtney Lipson graduated from the University of Pennsylvania in 2018.

Jordyn Young is a member of the University of Pennsylvania Class of 2019.

Story Source:

Materials provided by University of Pennsylvania. Note: Content may be edited for style and length.

<https://www.sciencedaily.com/releases/2018/11/181108164316.htm>

Vagus nerve stimulation can reverse brain inflammation after surgery, mice study shows

Reviewed by James Ives, MPsychOct 12 2018

For adults over age 65, surgical complications can dampen not only their physical health but also their mental sharpness, with more than half of high-risk cases declining into delirium.

In research published this week in the journal *Brain Stimulation*, Duke University scientists show in a mouse model that a current treatment for seizures can also reverse brain inflammation, such as inflammation after surgery, and the subsequent confusion or cognitive decline that results.

The therapy involves minimally invasive stimulation of the vagus nerve using small electrical pulses comparable to a cell phone's vibrations.

The scientists used a Doppler ultrasound to guide the placement of a needle that delivers the electrical pulse, avoiding nearby delicate structures such as the carotid artery. Researchers hope to refine the technique into a completely non-invasive approach to preventing cognitive decline when seniors and other at-risk patients have surgery.

"Delirium is now recognized as the most common complication in older adults after surgery," said Niccolò Terrando, Ph.D., associate professor of anesthesiology at Duke and the study's senior author. "For most patients, it lasts a few days and resolves on its own. For some, it can lead to severe complications and even contribute to long lasting cognitive deficits, like dementia."

Terrando noted that these cognitive complications have a huge impact on quality of life and can be expensive, with health care costs for delirium reaching \$164 billion a year according to the American Society of Anesthesiologists.

"So far, there is no therapy for this kind of cognitive complication after surgery," Terrando said. Anti-inflammatory drugs have many side effects and work broadly, he said, and they don't adequately target the inflammation in the brain that scientists believe triggers cognitive complications.

Related Stories

- Three-pronged therapy triggers axons to regrow after spinal cord injury in rodents
- Modified T lymphocytes prevent nerve cell damage in encephalitis
- Damage to small nerves shown to be cause of chronic pain following knee surgeries

The vagus nerve helps the brain communicate with the heart, lungs, gut and other parts of the body. Vagus nerve stimulators have been surgically implanted in epilepsy patients for more than 20 years to reduce seizures.

In recent years, U.S. doctors have also prescribed at-home,

non-invasive stimulators for severe headaches. However, there is not substantial evidence that the devices are stimulating the vagus nerve and not other structures near it, said Warren M. Grill, Ph.D., professor of biomedical engineering at Duke.

For the experimental model, mice with inflammation received one nerve-stimulating treatment lasting several minutes. The researchers monitored for signs of vagus nerve activation, such as a slower heart rate and twitching of muscles around the larynx, and found improved cognitive outcomes and reduced brain inflammation after this treatment.

"This minimally invasive approach is already exceedingly benign, but in the long term it would be desirable to have an entirely non-invasive approach and we are beginning that work," Grill said.

<https://www.news-medical.net/news/20181012/Vagus-nerve-stimulation-can-reverse-brain-inflammation-after-surgery-mice-study-shows.aspx>

Could it be possible to eliminate clogged arteries?

Published Sunday 14 October 2018
By Monica Beyer

A new clinical trial to study a potential way of reducing the risk of early-onset atherosclerosis may be on the way.



Atherosclerosis can lead to a range of cardiovascular problems.

After evaluating previous research, a report published in the Journal of the American Heart Association concludes that a clinical trial might pave the way for a new treatment to help reduce the early onset of atherosclerosis.

According to lead author Dr. Jennifer G. Robinson, a professor of epidemiology and director of the Prevention Intervention Center at the University of Iowa in Iowa City, the key may be targeting B lipoproteins in young and middle-aged adults.

These blood proteins (also called apolipoprotein B) include low-density lipoprotein (LDL), or the "bad," cholesterol. Scientists think that LDL and other B lipoproteins are among the leading causes of atherosclerosis.

Preventing atherosclerosis

"Lowering them may have a big impact on making atherosclerosis go away," says Dr. Robinson. "If this works, you could completely eliminate heart attacks and strokes within a generation, because you can't have a heart attack or stroke unless you have atherosclerosis."

The potential study aims to determine whether it is possible to reverse atherosclerosis in high-risk adults aged 25–55 using medications known as statins and PCSK9 inhibitors over a 3-year period. Both statins and PCSK9 inhibitors work to lower LDL cholesterol in the blood.

"The idea is to get the cholesterol very low for a short period of time, let all the early cholesterol buildup dissolve, and let the arteries heal," says Dr. Robinson, confirming that this method has been successful in animal studies. "Then patients might need to be re-treated every decade or two if the atherosclerosis begins to develop again."

"Once you know what causes something, you can come up with a hammer for it and eliminate it. We're not the first ones to think of this idea. This would be the culminating study of decades of research by thousands of people."

Dr. Jennifer G. Robinson

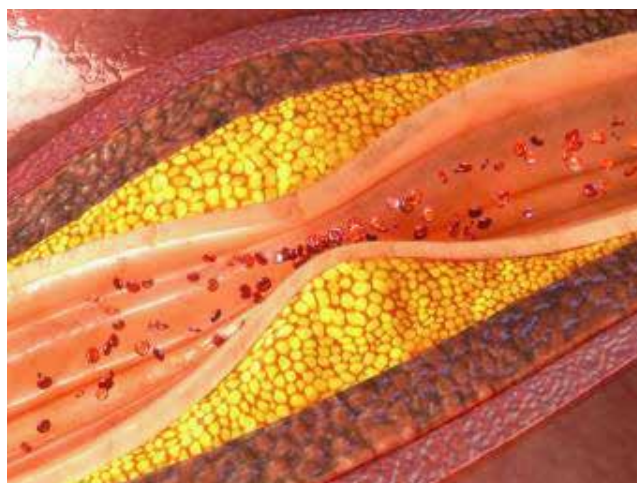
Dr. Robinson continues, "But I'm excited about this, and I think it's really time to pursue this hypothesis."

How atherosclerosis affects your health

Atherosclerosis, wherein plaque builds up in the arteries, can prevent oxygen-rich blood from traveling through the blood vessels to supply the rest of the body.

Plaque is made up of different substances in the blood, such as fat, cholesterol, and calcium. Over time, this plaque begins to harden, and when it does, it narrows the arteries.

This means that a person does not get as much oxygen-rich blood as they need, which can have serious consequences, including heart attacks and strokes. It can also lead to death.



Reversing atherosclerosis with one shot

Injecting synthetically designed nanofibers could be an innovative way to break up arterial plaque.

Read now

There are some risk factors for atherosclerosis that people can try to control themselves, including unhealthy blood cholesterol levels. High levels of LDL and low levels of high-density lipoprotein, or "good," cholesterol are among the leading causes of the disease.

Other risk factors include high blood pressure, smoking, insulin resistance, diabetes, being overweight, and a lack of physical activity. An unhealthful diet can also be a factor, particularly for people who eat a lot of foods that are high in saturated fats, trans fats, cholesterol, sodium, and sugar.

Potential study limitations

A new way to combat early-onset atherosclerosis would be welcome, especially as heart disease is so widespread and a leading cause of death for people in the United States. The Centers for Disease Control and Prevention (CDC) note that about 1 in 4 deaths are a result of heart disease.

However, Dr. John Wilkins, a cardiologist and assistant professor at Northwestern University Feinberg School of Medicine in Chicago, IL — who has conducted studies on B lipoproteins but was not involved in this study — thinks that it might be difficult to convince healthy adults to take medications to keep atherosclerosis at bay.

He also notes that this type of clinical trial may be hard to do as it would involve tracking people for 20 or 30 years, which could prove difficult.

Overall, the study is promising, and as Dr. Robinson says, it could lead to big changes in how doctors and their patients fight heart disease in the future. Reducing or eliminating atherosclerosis in people is an excellent goal, and while a clinical trial has not started yet, it is definitely a good place to start.

<https://www.medicalnewstoday.com/articles/323296.php>

Can Injecting Millions of Stem Cells into the Brain Treat Parkinson's Disease?

By Rachael Rettner, Senior Writer

Source: Frontiers

Summary: Autism has been associated with zinc deficiency in infancy. While it is not yet known whether zinc deficiency in early development causes autism, scientists have now found a mechanistic link. Their study connects zinc, autism risk genes and abnormal neuronal connections associated with autism spectrum disorders.



A new experimental therapy for Parkinson's disease that involves injecting millions of special stem cells into the brain of patients with the condition is currently being tested in a clinical trial.

The study, which began in October, is conducted by researchers at Kyoto University in Japan. So far, researchers have started to treat one man in his 50s, according to AFP.

Although previous studies have tested stem cell therapies for Parkinson's, the new study is the first to use so-called induced pluripotent stem cells, or iPSCs. These are "adult" cells (like blood or skin cells, as opposed to embryonic cells) that have been reprogrammed so that they resemble cells in early development, and they have the potential to form any cell type in the

body.

For the study, the researchers used iPSCs to create "dopaminergic progenitor" cells, or the cells that give rise to brain cells that produce dopamine, a brain chemical that is needed to control muscle movement. In Parkinson's disease patients, the brain cells that produce dopamine die off, leading to symptoms such as tremors and difficulty with walking, movement and coordination. [10 Things You Didn't Know About the Brain]

In the new trial, the researchers hope to show that these transplanted stem cells will help replace the lost dopamine-producing cells and restore dopamine production, according to The Michael J. Fox Foundation.

For the treatment, the researchers injected 2.4 million stem cells into the left side of the man's brain, in an operation that took 3 hours, according to AFP. The patient will now be monitored for side effects, and if no problems occur, the researchers will inject another 2.4 million stem cells into the right side of his brain.

The researchers plan to enroll a total of seven patients in the trial and to track the patients for two years.

The iPSCs were derived from donors, so the patients will need to take drugs to suppress their immune system to prevent rejection of the transplanted cells, according to Kyoto University.

Originally published on Live Science.

<https://www.livescience.com/64053-parkinsons-disease-treatment-stem-cells.html>

Common biomarker of kidney disease may also indicate COPD

A commonly used biomarker of kidney disease may also indicate lung problems, particularly COPD, or chronic obstructive pulmonary disease, according to new research published online in the American Thoracic Society's American Journal of Respiratory and Critical Care Medicine.

In "Albuminuria, Lung Function Decline, and Risk of Incident COPD: the NHLBI Pooled Cohorts Study," Elizabeth C. Oelsner, MD, MPH, and coauthors report a link between albuminuria, the amount of the protein albumin in urine, and COPD. The researchers conducted their study by pooling information from 31,877 participants (average age: 60 years) from six cohort studies funded mainly by the National Heart, Lung, and Blood Institute.

Albuminuria indicates damage to the single layer of cells lining blood vessels, known as the endothelium, in the kidney. Previous studies have shown that this damage is associated with microvascular (small vessel) dysfunction throughout the body, including the lungs. However, according to the authors of the current study, no large-scale, prospective study has tested whether albuminuria is associated with the development of COPD.

"The pulmonary microvasculature is critical to gas exchange and known to be impaired in patients with COPD, especially those with emphysema," said Dr. Oelsner, Herbert Irving Assistant Professor of Medicine at Columbia University. "We wanted to test whether albuminuria, a non-invasive and commonly used clinical test, could serve as a marker for increased risk of developing chronic lower respiratory diseases, such as COPD and asthma."

The researchers excluded participants who had been diagnosed with COPD or asthma upon enrollment in the studies. Participants were followed for changes in lung function over a median of 6 years and for respiratory hospitalizations and mortality over a median of 15 years.

The study found for each standard deviation increase in albuminuria, there was a:

- 15 percent increase in those who developed moderate-to-severe COPD;
 - 26 percent increase in COPD hospitalizations and deaths; and
 - 3 percent greater decline in FEV1 (the amount of air that can be forcibly exhaled in one second) and an 11 percent greater decline in the ratio between FEV1 and FVC (the total amount of air that can be forcibly exhaled after taking the deepest breath possible). Both FEV1 and FEV1/FVC are important measures of lung function.
- The researchers found that these associations remained significant even after taking into account smoking history,

diabetes, hypertension and cardiovascular disease. Interestingly, while smoking is known to cause both endothelial damage and COPD, the results were found to be similar in never-smokers. The study did not find a significant association between albuminuria and asthma.

• The authors said that their findings suggest that endothelial damage in the lungs may play an important role in the development and progression of COPD. They added that the mechanisms behind that damage and behind microvascular dysfunction may present promising targets for new therapies designed to prevent or treat COPD.

• Dr. Oelsner noted that a clinical trial is currently being conducted to test whether angiotensin II receptor blockers (ARBs), which have been shown to prevent progression in kidney disease, may also slow progression of emphysema.

• "Our study helps to explain why COPD patients often have a constellation of vascular problems, including heart and kidney disease," Dr. Oelsner said. "This makes it all the more important for clinicians to encourage avoidance of exposures like smoking and treatment of diseases like hypertension and diabetes that cause endothelial dysfunction."

<https://www.news-medical.net/news/20180928/Common-biomarker-of-kidney-disease-may-also-indicate-COPD.aspx>

Medical Services Department (MSD) of Orion Pharma Ltd. successfully arranged momentous number of Scientific Seminar, Round Table Meeting and Clinical Meeting in different venues in all over the Country.

SCIENTIFIC SEMINAR

Dhaka Medical College and Hospital, Dhaka

A scientific seminar has been organized in Dhaka Medical College and Hospital, Department of Surgery, Unit VI on 6th November, 2018. It was a wonderful discussion on **PERIOPERATIVE NUTRITIONAL MANAGEMENT** in the presence of Programme chairperson, Associate Prof. Dr. Mohiuddin Matubber. The session was ended with a exciting raffle draw and refreshment. OPL was scientific partner of this great event.



Sylhet MAG Osmani Medical College and Hospital, Sylhet

A Scientific Seminar was arranged on 11th November, 2018 by the Department of Psychiatry, Sylhet MAG Osmani Medical College & Hospital. It was a informative discussion on **OVERVIEW ON OCD AND ITS MANAGEMENT**. Prof. Dr. RKS Royle, Head, Department of Psychiatry was the Chairperson of programme. All members of the department were present in the program. It was concluded with a luscious refreshments sponsored by OPL.



Khulna Medical College and Hospital, Khulna

A Program was arranged by the Department of Gastroenterology of KMCH on 08th November, 2018 in the Seminar Room of Khulna Medical College Hospital, Khulna in association with Orion Pharma Ltd. The program was presided by the Prof. Dr. Abdul Ahad, principal & Head, Dept. of Gastroenterology, KMCH. About 90 Doctors was attended the session.

Shaheed Taj Uddin Ahmed Medical College and Hospital, Gazipur

A scientific seminar has been organized by Shaheed Taj Uddin Ahmed Medical College and Hospital, Gazipur, Dept. Of Pediatrics on 18th November, 2018. It was a very updated scientific discussion on **CHILDHOOD BLEEDING DISORDER AND UPDATE** in the presence of Programme chairperson, Asst. Prof. & Head, Department of Pediatrics Dr. Md Amjad Hossain Khan. The session was ended with cultural festive environment. OPL was scientific partner of this great event.



Mugda Medical College and Hospital, Dhaka

On 3rd October, 2018 a Scientific Seminar was arranged by the Mugda Medical College and Hospital on **ROLE OF CALCIUM IN PREGNANCY**. Prof. Dr. Nahid Yesmin, Head, Department of Obs & Gynae, Mugda Medical College and Hospital enlightened the seminar as the chairperson. Orion Pharma Ltd. proudly coordinated the programme as scientific partner.



ROUND TABLE MEETING

Centre for the Rehabilitation of the Paralysed (CRP), Savar

On 13th September, 2018 A RTM has been organized by CRP, Savar. Dr. Rashedul Karim, Register, CRP, Savar was the keynote presenter of the meeting. Dr. Sayed Uddin Helal, MS (Neuro), Consultant-Neurosurgeon & Head of the Dept. was the Chairperson of the program. About 15 Consultants attended the session & enjoyed delicious lunch sponsored by OPL.



M Abdur Rahim Medical College and Hospital, Dinajpur

A RTM was arranged on 29th October, 2018 by the Department of Cardiology, M Abdur Rahim Medical College, Dinajpur. Dr. Sharier Kabir, Asst. Prof. was the Chairperson and Key note Speaker of the Program. All Doctors of the department were present in the program. It was concluded with a luscious refreshments sponsored by OPL.



National Institute of Cardiovascular Diseases and Hospital, Dhaka

On 07th November, 2018 A RTM has been Organized by NICVD, Dhaka. Prof. Dr. Amal Kumar Choudhury, Interventional Cardiologist, NICVD was the Chief Guest & Keynote presenter of the Program. About 35 Consultants attended the session & enjoyed delicious lunch sponsored by OPL.

Diabetic Hospital, Naogaon

A RTM was arranged on 26th November, 2018 by Diabetic Hospital, Naogaon. Dr. Md. Ishaque Ali Akando, In Charge, Diabetic Hospital, Naogaon was the Chairperson of the program. About 15 senior doctors was enjoyed the session followed by delicious dinner sponsored by OPL.



National Institute of Cancer Research and Hospital, Mohakhali, Dhaka

On 11th October, 2018 A RTM has been organized by NICRH, Mohakhali, Dhaka. Dr. Moshir Rahman, Asso. Prof. was the Chairperson & keynote presenter of the seminar. About 22 Consultants attended the session & enjoyed delicious lunch sponsored by OPL.

Khulna Medical College & Hospital, Khulna

A RTM was arranged on 15th November, 2018 by the Department of Pediatrics of Khulna Medical College & Hospital, Khulna. Prof. Dr. Abdullah Al Mahbub was the Chairperson & Keynote Speaker of the conference. All members of the department were present in the program. It was concluded with a luscious refreshments sponsored by OPL.

Thana Health Complex, Nababgonj

A RTM was arranged on 27th November, 2018 by the Thana Health Complex, Nababgonj. Dr. Md. Shohidul Islam, UH & FPO was the Chairperson & Keynote Speaker of the conference. All Hospital Doctors were present in the program. It was concluded with a luscious refreshments sponsored by OPL.

<http://journal-index.org/ISSN-validator/issn-validator.php>



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Calcium supplements may contain high concentration of lead (Pb).



According to **ACOG (American College of Obstetricians and Gynecologists)** recommendation, elevated lead levels in pregnancy have been associated with:



**Spontaneous
Abortion**



**Low Birth
Weight**



**Impaired
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