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Contents

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Contents

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Editorial

Bronchorrhoea- an emerging respiratory symptom

Bronchorrhoea 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, 4, 5] It can also be caused by non-malignant conditions like chronic bronchitis, asthma, and endobronchial tuberculosis. There are three postulated pathophysiological mechanisms for bronchorrhoea:

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 secre-tion- this can be mediated by receptors for prostaglandins (PGE2, PEF2α) or secretin in the bronchial epithelium.
3. Excessive transudation of plasma prod-ucts into the airway.[6]

Bronchorrhoea has negative impact on both survival and quality of life. It can cause excessive cough, sleep disturbance and dyspnoea. When severe, it may lead to respiratory failure, dehydration and electrolyte disturbance.

The management of bronchorrhoea 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 chemo-therapy
2. Anticholinergic agents
3. Macrolides
4. Pulsed methylprednisolone
5. Inhaled indomethacin
6. Gefitinib (EGFR-TKI)
7. Octreotide

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- Type manuscripts in British English in double-spaced paragraph including references, figures with legends and tables on one side of the page.
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- Assemble manuscript in following order:

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(2) Then next page with author designations and place of work.
(3) Abstract (structured) within 250 words.
(4) Main text which includes Introduction, Materials and methods, Results, Discussion, Conclusion, Acknowledgments (if any) and contributions of the authors in that specific study.
(5) References;
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(7) Figures with legends

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Text page must include:

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- Limit use of acronyms and abbreviations. Abbreviations must be defined at the first mention.
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The Following are typical main headings:

i. **Introduction**
ii. **Materials and Methods**
iii. **Results**
iv. **Discussion**
v. **Conclusion.**

Introduction

Summarize the rationale for the study with pertinent references. The purpose (s) of the study should be clearly elicited.

Materials and Methods

Identify type of study and describe the study subjects and methods used with methods of statistical analysis. Cite reference (s) for standard study and statistical methods. Describe new or modified methods. Give proper description of the apparatus (with name and address of manufacturer) used. ***Generic name of drug must be given. Manuscripts that describe studies on humans must indicate that the study was approved by an institutional Ethical Committee and that the subjects gave informed consent.***

Results

Present only important results observations in logical sequence in the text, tables or illustrations with relevant statistics.

Discussion

Emphasize new and important results and the conclusions that follow including implications and limitations. Relate observations to other relevant studies.

Conclusion

Link the conclusion with the goals of the study, but avoid unqualified statements and conclusions not adequately supported by data. State new hypothesis when warrented.

Acknowledgments

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References

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1. World Health Organization: WHO Recommendations: Low Birth Weight: preventing and managing the Global Epidemic. Geneva, World Health Org, 2000 (Tech.Rep.Ser., no.894).
2. Rashid M. Food and Nutrition. In : Rashid KM, Rahman M, Hyder S, eds. Textbook of community Medicine and Public Health. 4th ed RHM Publishers Dhaka: Bangladesh, 2004; p. 156-160.
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Each table must be typed and inserted with in results. Table number should be followed by a roman brief informative title. Provide explanatory matter in footnotes. For footnotes use symbol in this sequence; *, **, +, ++, etc.

Figures

Original figures having good quality must be submitted indicating figure number, short figure title at the bottom of figure. Any abbreviation or symbols used in the figures must be defined in the figure or figure legend.

North Bengal Medical College Journal
Vol 3 No 1 January 2017

Original Article

Methicillin-Resistant *Staphylococcus aureus* Prevalence Among Healthy School Children of Rajshahi (Bangladesh)

Md. Mizanur Rahman,[1] Md. Shah Alam,[2] Sabera Gul Nahar,[3] Rezowana Sharmin,[4] Tapas Kumar Paul,[5] Mst. Shamima Akter Banu,[6] Sharmina Aftab[7]

Revised : April 20, 2016 Accepted : May 26, 2016

Abstract

Introduction: *Staphylococcus aureus is an important cause of superficial and deep life threatening infections and its antibiotic resistance is a menace. Now it is a global challenge, specially Methicillin resistant S. aureus (MRSA).*

Methods: *This cross-sectional study was carried out to observe nasal carriage of S. aureus and MRSA among healthy school children of different areas of Rajshahi from January 2012 to December 2012. Three hundred students were enrolled for this study and data were collected with a pre-design data sheet.*

Results: *Out of 300 samples, 86 (28.67%) showed the growth of S. aureus and 11(12.79%) isolates were MRSA. There was no significant differences among sexes, age sub-groups and different localities in colonization of S. aureus ($p>0.05$). S. aureus isolates indicated a high rate of resistance to cotrimoxazole 76 (88.37%) and vancomycin 86 (100%) was the only antibiotic against which all the isolates were sensitive.*

Conclusion: *This study revealed that children under 12 years of age are potential carriers of S. aureus, particularly MRSA. It is recommended to conduct regular screening for MRSA surveillance and maintain rational use of antibiotics to minimize carriage and drug resistance.*

Key words: *S. aureus, MRSA, Nasal carriage*

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Introduction

Staphylococcus aureus is an established cause of superficial and deep life threatening infections[1] and its antibiotic resistance is a menace. It colonizes in the skin and mucosal surfaces of healthy individuals, but it is an important human pathogen causing both nosocomial and community acquired infections[2] and infections caused by it is a global challenge. It has the ability to develop resistance to many effective antibiotics due to production of penicillinase, an enzyme that destroy the β-lactum antibiotics. Methicillin is a Penicillinase -resistant penicillin was introduced in Europe in 1959 and in the United States in 1961 and the first cases of Methicillin resistant *S. aureus* (MRSA) were reported in the United Kingdom in 1961 followed by in other European countries, Japan and Australia.[3] The first report of MRSA in the United States appeared in 1968.[4]

Widespread occurrence of MRSA eventually leads to the emergence of multi-drug resistant *S. aureus* which in turn limits treatment options. Methicillin resistance *S. aureus* is a major health problem which can cause both asymptomatic colonization and infection, ranging from minor skin infection to life-threatening condition such as bacteremia and sepsis.[5] This bacteria is transmitted mainly through person to person contact[6] and colonize on multiple body sites. The anterior nares are the most frequent carriage site as this area is well ventilated and usually remains moist.[7] MRSA have become a serious health problem all over the world. The incidence and prevalence of MRSA varies widely between countries, geographical regions, hospitals and even wards in the same hospitals. In Turkey, the prevalence of MRSA in the community is 0.3%,[8] in India 3.89 %,[9] in Chicago, USA 2.5%[10] and in Taiwan 13.23%.[11]

Materials and Methods

This study enrolled 300 healthy school children aged 6 to 12 years. Specimens were obtained from anterior nares with sterile swabs and plated on Blood agar and Nutrient agar plates. Agar plates were incubated at 37°C for 24 hours. The yellow or golden coloured colonies were subcultured on mannitol salt agar and selected for the catalase and tube coagulase test. Mannitol fermenting, catalase and tube coagulase positive isolates were identified as *S. aureus.*[12]

Identified bacteria were tested for antimicrobial susceptibility testing using modified Kirby-Bauer technique on Mueller-Hinton agar and using commercially available antimicrobial discs.[12] The susceptibility test of *S. aureus* were tested against cloxacillin, ampicillin, ciprofloxacin, gentamicin, cotrimoxazole and vancomycin. All *S. aureus* isolates were tested to detect MRSA using oxacillin (1µg) disc. The inoculum size was adjusted with 0.5 McFarland's standard and incubating at 35°C for 24 hours. A zone of inhibition less than 10 mm or any discernable growth within zone of inhibition was indicative of

methicillin resistance. On the other hand a zone of inhibition equal to or more than 13 mm were taken as sensitive.[13]

Results

Among 300 school children, 142 (47.33%) were male and 158 (52.67%) were female. Out of 300 samples studied 86 (28.67%) showed the growth of *S. aureus* and 11 (12.79%) isolates were found to be MRSA. There was no significant sex and age sub-groups difference in colonization of *S. aureus* ($p>0.05$), although the rate was slightly higher among girls and age sub-group 6-8 years 36 (36.67%) (Table I). No significant difference in carriage rate was observed among different areas of schools, but slightly higher in schools of rural area and MRSA in slum area. (Table II). *S. aureus* isolates indicated a high rate of resistance towards cotrimoxazole 76 (88.37%) followed by ampicillin 66 (76.74%), cloxacillin 57 (66.28%), ciprofloxacin 41 (47.67%) and gentamicin 39 (45.35%). No resistance was found against vancomycin (Figure 1).

Table I: Nasal colonization in different age group and sex

Age group(yrs)	Male		Female		Total	
	S. aureus	**%**	***S. aureus***	**%**	***S. aureus***	**%**
06-08	15 (42)	35.71	18 (48)	37.5	33 (90)	36.67
09-10	13 (44)	29.55	16 (48)	33.33	29 (92)	31.52
10-112	12 (56)	21.43	12 (62)	19.35	24 (118)	20.34
Total	**40 (142)**	**28.17**	**46 (158)**	**29.11**	**86 (300)**	**28.67**

Table II: Nasal colonization in different community

Area	Nasal swab	*S. aureus*	%	MRSA	%
Rural	100	30	30	4	13.33
Slum	100	29	29	4	13.79
Urban	100	27	27	3	11.11
Total	**300**	**86**	**28.67**	**11**	**12.79**

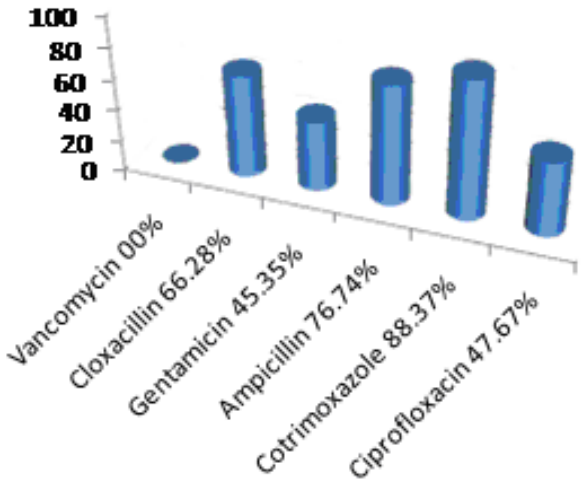

Figure 1: Drug resistance pattern of *Staphylococcus aureus*

Discussion

In our study, *S. aureus* was isolated in 28.67% from healthy school children that is nearly similar with the study of Saxena S et al.[14] in east Delhi, India. Hussein FM et al.[10] in Chicago, USA and Wen-Tsung L et al.[11] in Taiwan and their observations were 29.4%, 24.4% and 25% respectively. Our finding is dissimilar with the Barrett FF et al.[4] and Ramana KV et al.[15] in India and O'Brien FG et al.[16] in two communities in Australia. All *S. aureus* isolates are (100%) sensitive to vancomycin which is consistent with the finding of Shams-uzzaman AK et al.[17] in Bangladesh. Resistance of other drugs to *S. aureus* are variable such as gentamicin (45.35%), ciprofloxacin (47.67%) cloxacillin (66.28%), ampicillin (76.74%) and co-trimoxazole (88.37%).

Out of 86 (28.67%) *S. aureus*, MRSA were 11 (12.79%). Now a days MRSA is increasing in hospitals of all sizes, health care centers, different population groups and various communities all over the world.[18] Our study is nearly similar with the study of Wen-Tsung L et al.[11] in Taiwan and Harputluoglu U et al.[19] in Turkey and their findings were 13.2% and 15% respectively. Our study were dissimilar with the study of Ramana KV et al.[15] in India, Palavecino E[3] in Turkey, Hussein FM et al.[10] and Alfaro C et al.[20] in USA. Their observations were 19%, 0.3%, 2.55% and 22% respectively. This dissimilarity may be due to different geographical location, antibiotics consumption, immunological status, nutritional status and personal hygiene.

Conclusion

Our results suggests that healthy school going children under 12 years of age are potential carriers of *S. aureus* and in particular MRSA. The relatively high

proportion of MRSA and the associated antibiotic resistance in this study emphasizes the need for local or country based surveillance to characterize and monitor MRSA and to develop strategies that improve MRSA treatment and control.

Contribution of the Authors

First author designed and conducted the study and wrote the manuscript. Second and third authors critically reviewed the manuscript. Others helped in data collection and statistical analysis.

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Original Article

Effect of Single Instillation of Intravesical Mitomycin-C following Transurethral Resection of the superficial Transitional cell Carcinoma of the Urinary Bladder

Sheikh Mohd. A. Hakim,[1] A.B.M. Golam Robbani,[2] Md. Shah Alam,[3] Md. Shaharul Alam Mondol[4]

Revised : June 02, 2016 Accepted : August 19, 2016

Abstract

Introduction: *We analyzed the impact of a single instillation of mitomycin-C in patients with low risk superficial urinary bladder cancer with short-term follow-up.*

Methods: *This comparative interventional study was conducted on 60 patients with low risk superficial urinary bladder transitional cell carcinoma (TCC), admitted to the Urology unit in Rajshahi Medical College Hospital, Rajshahi during the period from July, 2008 to June, 2010. Patients with muscular invasion, Grade-III tumour or bladder carcinoma in situ (CIS) on pathological examination were excluded from the study. After complete transurethral resection of the bladder tumour (TURBT), patients were divided into two arms : First group who had received no instillation of mitomycin-C (i.e. non-mitomycin-C or control group) and a second group with a single immediate intravesical instillation of 40 mg mitomycin-C (i.e. mitomycin-C or study group). Recurrences were considered early if they occurred within the first 12 months of follow up.*

Results: *Follow-ups were conducted on 3rd, 6th, 9th and 12th month (i.e. 3 monthly) following transurethral resection. Following intervention, there was no recurrence in 3rd and 9th month. Recurrence free rate was observed as 86.66% in mitomycin-C group and 80% in non-mitomycin-C group on 6th month (i.e. recurrence rate in mitomycin-C group 13.34 % and non-mitomycin-C group (20 %) of follow-up. On the 12th month, 90% and 83.33% of recurrence free rate was observed in mitomycin-C group and non-mitomycin-C group respectively (i.e. recurrence rate in mitomycin-C group (10 %) and non-mitomycin-C group (16.67 %). Overall, the recurrence rate in mitomycin-C group was 23.33 % and in non-mitomycin-C group was 36.67%.*

Conclusion: *These data confirm the positive effect of a single immediate mitomycin-C instillation in patients with low risk superficial transitional cell bladder carcinoma. This benefit is limited to early recurrence and is not maintained with long-term follow-up. This study also suggests that, cell implantation as a mechanism of early recurrence can be controlled or minimized with a single mitomycin-C instillation.*

Key words: *Bladder cancer, Mitomycin C, Recurrence*

North Bengal Med. Coll.J. 2017; 3 (1) : 12-19

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Introduction

Urinary bladder cancer continues to be a significant health problem for the mankind. Ninety percent of bladder cancers are transitional cell carcinoma (TCC) with the remainder being squamous cell carcinoma and adenocarcinoma.[1] Approximately 75-85% of new bladder TCC is superficial i.e. confined to the mucosa or lamina propria.[2] Recurrence, rather than progression of superficial bladder cancer after primary transurethral resection (TUR), is common. With no adjuvant treatment, there is a 70% chance of recurrence of superficial tumours within 5 years of resection.[3] This level of recurrence might seem alarmingly high and out of proportion to the acceptable recurrence rates of other tumours. Superficial bladder TCC can be fully resected via transurethral route in the first instance. Yet the question arises that why the recurrence rates are so high. Theories regarding the aetiology of tumour recurrence include - reimplantation of cells liberated at transurethral resection, inadequate resection of the residual tumour and diffuse field change giving rise to new tumours.[1] As recurrence of superficial bladder transitional cell carcinoma is such a common phenomenon, it necessitates repeated and often prolonged cystoscopic follow-up.

The administration of one instillation of intravesical mitomycin-C immediately after transurethral resection of superficial transitional cell carcinoma of urinary bladder has been demonstrated to decrease the risk of early recurrence.[4,5] The mechanism by which post TUR intravesical mitomycin-C reduces recurrence is thought to involve destruction of the liberated tumour cells in the bladder and a direct ablative effect on any viable residual tumour cells at the resection site. Instillation within 24 hours of transurethral tumour resection provides superior protection from tumour recurrence. Therefore, it appears that, tumour recurrence can be reduced simply by mitomycin-C instillation close to the time of surgery, possibly by preventing seeding or implantation of tumor cells at the time of resection.[6] On the other hand, various intravesical immunotherapies (such as BCG and Interferon Alfa 2b) and chemotherapies (such as Thiotepa, doxorubicin, epirubicin, mitomycin-C etc) have been used. BCG carries a greater risk of both the local and systemic effects. Interferon Alfa 2b is not specifically approved for superficial bladder cancer and it is costly also. Thiotepa is absorbed due to its low molecular weight and causes blood dyscrasias. doxorubicin, epirubicin and mitomycin-C are of equal efficacy. But a single mitomycin-C instillation is an inexpensive approach with minimal local and systemic side effects in comparison to doxorubicin and epirubicin. These are the rationalities for the use of mitomycin-C than the other intravesical agents.

It can be concluded that, transurethral resection of bladder tumours followed by optimal use of immediate post operative intravesical mitomycin-C is feasible way to reduce short-term recurrence of superficial bladder cancer than the transurethral resection alone. In this study, we reported single insertion of mitomycin-C following transurethral resection of bladder tumour.

Materials and Methods

This study was conducted on 60 patients with superficial transitional cell carcinoma of urinary bladder admitted into the urology unit in Rajshahi Medical College Hospital during the period from July, 2008 to June, 2010. A hospital based comparative interventional study was performed in patients with primary transitional cell carcinoma of urinary bladder. The patients were free of urinary infection and had a normal upper urinary tract on ultrasonography and /or excretory urography. Patients with muscle invasive or Grade III tumours or bladder carcinoma in situ (CIS) on pathological examination and abnormal upper urinary tract on ultrasonography and / or IVU were excluded from the study. After complete transurethral resection (TUR) of tumour, each patient was numbered serially. Of them, the odd number of patients were not instilled with intravesical mitomycin-C (i.e. non-MMC or control group) and the even number of patients were instilled with intravesical mitomycin-C (i.e. MMC group or study group). Thus all the selected patients were divided into two groups :

First group - had no post TUR instillation of intravesical mitomycin-C (i.e. non-mitomycin C or control group). Second group - had a single dose of 40 mg mitomycin-C (i.e. mitomycin-C group or study group) diluted in 40 ml distilled water which were instilled when haematuria ceased, usually within 6-24 hours of transurethral resection. The instillation was retained for 2 hours with catheter clamping and then the bladder was irrigated with saline if needed.

Patients were evaluated with bladder ultrasound and cystoscopy at 3, 6, 9 and 12th months (i.e. every three months for one year). At each cystoscopy, any tumour or abnormal looking urothelium were resected and the resected tissue was sent for histopathological examination to confirm the recurrence. Recurrences were considered early if they occur within the first 12 months of follow up. Ethical clearance from the ethical committee of Rajshahi Medical College was taken to carry out this study. After explanation of the study purpose, an informed consent was taken from the patient.

All clinical information including history, physical findings and investigation reports were collected and recorded in a pre-designed data collection sheet. Comparison between numerical data was performed using the unpaired students' 't' test while comparison between categorical data was done using the Chi square test. The Data was analyzed and compiled by SPSS II. Values less than or equal to 0.05 was considered as significant *p* value.

Results

The main objective of this study is to know and compare the effect of single intravesical instillation of mitomycin-C (MMC group) within 24 hours of transurethral resection with that of control group. Distribution of respondents in terms of different parameters is shown in tabulated form and statistical analysis is done to show the significance of intervention in both groups. The results obtained in follow up cystoscopies were compared in both groups and analyzed to see statistical significance.

Table I: Recurrence status at 3rd, 6th, 9th and 12th month of follow up cystoscopy (n-60, MMC Group-30 and non-MMC Group-30)

Modality of Treated Groups	3rd Month Recur-rence	6th Month Recurrence				9th Month Recur-rence	12th Month Recurrence			
		No no.(%)	Yes no.(%)	Total			No no.(%)	Yes no.(%)	Total	
MMC Group	0	26 (86.66)	4 (13.34)	30	χ^2-0.154 df-1 p-0.690	0	27 (90.00)	3 (10.00)	30	χ^2-0.108 df-1 p-0.742
Non MMC Group	0	24 (80.00)	6 (20.00)	30		0	25 (83.33)	5 (16.67)	30	
Grand Total	**0**	**50 (83.33)**	**10 (16.67)**	**60 (100)**		**0**	**52 (86.67)**	**8 (13.33)**	**60 (100)**	

At 3rd month: the study shows no recurrence in follow-up cystoscopy in both MMC immediate single dose group and non-MMC group. At 6th month: the table shows the number of recurrences of superficial bladder cancer following transurethral resection of bladder tumor (TURBT) and MMC chemotherapy seen in follow-up cystoscopy at 6th month. In MMC immediate single dose group it was 4 and in non-MMC group it was 6 (Table I). This result is statistically insignificant (p>0.05). At 9th month: the table also shows that, recurrence of superficial bladder tumor seen in 4 cases of MMC immediate single dose group and 6 cases of non-MMC group on follow-up cystoscopy at 6th month, when they were resected at 6th month, further recurrence at 9th month was not seen. At 12th month of follow-up cystoscopy: the Table II shows the number of recurrence in MMC immediate single dose group was 3 and in non-MMC group was 5. The difference is not significant in statistical analysis (p>0.05).

Table II: Distribution of recurrence number in relation to tumour size among the respondents in 6th and 12th month of follow up cystoscopy

Modality of treated Group	6th month				12th month			
	Primary tumor size (cm)	Patients no. (%)	Recurrence no. (%)	Overall recurrence no.(%)	Primary tumor size (cm)	Patients no. (%)	Recurrence no. (%)	Overall recurrence no.(%)
MMC group	<2	6 (20.0)	0	4 (13.33)	<2	26 (86.67)	0	3 (10.00)
	≥ 2	24 (80.0)	4 (13.33)		≥ 2	4 (13.33)	3 (10.00)	
Non-MMC group	<2	9 (30.0)	0	6 (20.0)	<2	23 (76.67)	1 (3.33)	5 (16.67)
	≥2	21 (70.0)	6 (20.0)		≥2	7 (23.33)	4 (13.33)	

At 6th month of follow up: it was seen that, there was no recurrence of tumor when the size of the primary tumor was < 2 cm in both groups of patients. Four cases (13.33%) of recurrences were seen out of 24 having primary tumor size ≥ 2 cm in MMC immediate single dose group. Six cases (20.0%) of recurrence out of 21 belonged to same size were seen in non-MMC group (Table II). The difference in recurrence among the groups was insignificant ($p>0.05$). At 12th month of follow up: the study shows no recurrence of tumor where size of the primary tumor was <2 cm. Three recurrences were seen when the primary tumor was > 2 cm in MMC immediate single dose group. In non-MMC group 1 recurrence was seen where the size of primary tumor was < 2 cm and 4 recurrences when the primary tumor size was ≥ 2 cm (Table II). Here the difference in recurrence among the groups was statistically significant ($p<0.05$).

Table III: Distribution of number of recurrence in relation to grade of the tumour among the respondents at 6th and 12th month

Modality of treated Group	6th month				12th month			
	Primary tumour Grade	Patients no. (%)	Recurrence no. (%)	Overall recurrence no.(%)	Primary tumour Grade	Patients no. (%)	Recurrence no. (%)	Overall recurrence no.(%)
MMC group	I	19 (63.33)	1 (3.33)	4 (13.33)	I	17 (56.67)	1 (3.33)	3 (10.00)
	II	11 (36.66)	3 (10.00)		II	13 (43.33)	2 (6.67)	
Non-MMC group	I	14 (46.66)	2 (6.67)	6 (20.00)	I	18 (60.00)	1 (3.33)	5 (16.66)
	II	16 (53.33)	4 (13.33)		II	12 (40.00)	4 (13.33)	

At 6th months of follow up: recurrence was seen in 1 case of Grade I and 3 cases of recurrence were seen in case of Grade II in MMC immediate single dose group. In Non-MMC group, 2 cases in Grade I and 4 cases in Grade II were found to recur (Table III). Histopathologically, there was no progression of the grade of recurrent tumors.

At 12^{th} months of follow up: 1 recurrence were found in case of Grade I and 2 recurrences in Grade II in MMC immediate single dose group. One recurrence was seen in Grade I and 4 recurrences were found in case of Grade II in non-MMC group (Table III).

Discussion

It is well known that, the multifocal field changes in the urothelium and the implantation of tumor cells following transurethral resection contribute to the high incidence of recurrence of bladder tumors. It seems futile to rely solely on transurethral resection alone. Intensive topical chemotherapy initiated shortly after surgical resection might reduce the likelihood of the recurrences by destroying viable tumor cells. Anti-neoplastic agents administered transurethrally, place a high concentration of drug in contact with the neoplastic cells and urothelium. It acts by exerting a cytotoxic action on microscopic foci of carcinoma, carcinoma in situ, floating malignant cells, thus diminishing the number and/or frequency of new recurrences, while minimizing systemic toxicity.[7] Regimens based on chemotherapeutic drugs have often been established on empirical basis, which compromises between potential toxic effect and aimed benefit.[4] In USA, the choice of drug is BCG, occasionally Thiotepa but in Japan and Europe the choice of' treatment is mitomycin C and Doxorubicin.[8] The dose of mitomycin C therapy was used in different strength in different studies. In an experimental study, it was seen that mitomycin C when administered at a concentration of 1 mg/ml, it induces apoptosis and necrosis of tumor cells.[9] Keeping in this view, the present study was conducted to observe and compare the efficacy of post TURBT single immediate dose of mitomycin C to that of conventional non-MMC group treatment in preventing the recurrence of superficial bladder transitional cell carcinoma. Bivariate analysis of different factors having prognostic importance has been identified. These include previous recurrence rate (<1 per year or $\geq$ 1 per year), size of the tumor (up to 2 cm or more than 2 cm.), tumor grade (Grade I or II). Considering the above factors good prognostic group in relation to low rate of recurrence and progression was identified. These are the size of the tumor <3 cm, grade of the tumor I or II. In this study, mean size was 2.075 (± 0.567) cm and 2.231 (±.642) cm in MMC immediate single dose group and non MMC group respectively. The distribution of grade of the tumor in both groups (I & II) were statistically insignificant when compared in between groups. The important variables which influence the recurrence and outcome of treatment (tumor size and grade) were same in this study and both groups of patients included in this study were of low risk group. After dividing the respondents into two groups by random sampling intervention was done. Table I showed no recurrence in all patients of both groups at third month of follow-up. In current literature negative cystoscopy at third month of follow-up, following TURBT was considered as a good predictor of prognosis.[10]

Solitary recurrences were seen at 6th month of follow-up cystoscopy. This study showed that the number of recurrence was 4 in MMC immediate single dose group and was 6 in non MMC group. The difference of recurrences in both groups are not significant (p>0.05). Overall tumor free rate

was 86.66% in MMC immediate single dose group and 80.0% in non MMC group. The result of the study is similar to other studies.[4,11] The recurrent tumors were resected. After taking biopsy, the base of the tumors were fulgurated. No intervention was made. There was no evidence of progression in the specimen, confirmed by histopathological report. These patients having recurrence at 6th month were scheduled to follow at 9th month. No recurrence of tumor in above group of patients at 9th month of follow-up.

In the 12th month follow-up, it was seen that 3 cases in MMC immediate single dose group and 5 cases in non MMC group were recurred, with recurrence free rate of 90% and 83.33% respectively. The result of the present study was similar with the other studies.[4,11,12] The recurrent tumors were resected. After taking biopsy, the base of the tumor was fulgurated. No intervention was made. There was no evidence of progression in recurrent tumors, confirmed by histopathological report. The difference of recurrence among the groups is not significant ($p>0.05$). It is established that the tumor size and grade are intimately related to the recurrence. These are considered as prognostic factors in study of Parmar MKB et al.[10]

In this study, follow-up of each patient was done for 1 year after initial TURBT. The analysis confirms the positive effect of a single immediate mitomycin-C instillation in patients with low risk superficial bladder cancer.

Conclusion

This study confirms the positive effect of a single immediate mitomycin-C instillation in patients with low risk superficial bladder cancer. This benefit is limited to early recurrence and is not maintained with long-term follow-up. Overall, mitomycin-C is perceived to be very well tolerated but some respondents need to reassess their usage of mitomycin-C for high-grade superficial tumours and CIS. Thus, this approach is an alternative to observation or intravesical chemotherapy, sparing patients a significant number of transurethral resections during the first 12 months postoperatively. This study also suggests that, cell implantation as a mechanism of early recurrence can be controlled or minimized with a single mitomycin-C instillation. In this way, single instillation of intravesical mitomycin-C immediately following transurethral resection of transitional cell carcinoma of urinary bladder reduces the risk of early recurrence.

Contribution of the Authors

First author was the principal researcher, second author was the guide of this research work, third and fourth authors did the statistical analysis and computer composing.

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Original Article

Early Post Operative Complications following Abdominal Surgery. A Prospective Study in a Tertiary level Hospital

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Abstract

Introduction: *Postoperative complications are a significant source of morbidity and mortality. A major factor affecting hospital cost is complications following surgery.*

Methods: *This observational study was carried out to evaluate the incidence of early Postoperative complications following abdominal surgery, admitted in Rajshahi Medical College Hospital during the period of six months enrolling 96 patients of post abdominal surgery complications above the age of 12 years selected by purposive sampling.*

Results: *In this study a total number of 96 out of 3613 patients with a mean age of 39.44 years (±15.18) and a range of 12-72 years, admitted with postoperative complications were included. The incidence was 2.66%. The age group of most of the patients is 21-30 years (28.1%) among the study population. In this study 26 patients were primarily operated by specialist surgeon (27.08%), 66 by non specialist surgeon (68.75%) and 4 by non doctor (4.16%). Among the complications, following appendicectomy was highest observed 27.1% and next common complication following lower uterine caesarean section (12.5%) and then cholecystectomy (11.5%). Most of the patients referred from private clinics (83.3%) whereas from Govt. hospital only (16.7%). In most of the clinic post operative care conducted by person other than nurse and doctor (44.8%). Missed diagnosed case was 7.3%. Grade llla and Grade lllb (25.0% and 29.2% respectively) complications are more than Grade l and Grade ll (18.8% and 11.5% respectively). About 46.9% patients had a total hospital stay of about two weeks and 13.5% had more than two weeks.*

Conclusion: *When a patient undergone an operation he or she hopes for the most advanced care. Training of the surgeon, hospital volume and learning curve are becoming more important to maximize patient safety.*

Key words: *Postoperative complications, Abdominal surgery, Appendicectomy*

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Introduction

Postoperative complications are a significant source of morbidity and mortality. The rising cost of health care is given increasingly importance worldwide. A major factor affecting hospital cost is complications following surgery.[1] Admitted patients with postoperative complications in the tertiary level hospital are not uncommon in our country. Most of them admitted with early complications.[2] Arrangement of operation theatre complex in hospitals or clinics, proper sterilization and utilization of the surgical equipment, surgical expertise, surgical judgment and operative decision making, the nature and site of the disease for which surgery was performed are also important. The likelihood of developing post-operative complications depends on age, general condition of the patient, presence of other co-morbidity, type and duration of anesthesia, surgical site, and urgency of the procedure and so on. Experience of surgeon is dependent on training, repetitions (learning curve) and on case load of the surgeon and of the hospital. It is established that the incidence of postoperative complications is highest for emergency procedure, intermediate for urgent operations and lowest for elective or planned intervention.[3] The postoperative period can again be divided into three phases; (1) an immediate or post-anesthetic phase; (2) intermediate phase; and (3) a convalescent phase. The first two phases are encompassing the hospitalization period. The convalescent phase is a transition period from the time of hospital discharge to full recovery.[4] The early postoperative period can purposively be defined as the time from awakening after surgery until discharge from hospital.[5] So the early postoperative period encompasses the immediate and intermediate phases of postoperative period. But the highest incidence of post-operative complications is between 1 and 3 days after the operation.[6]

In our perspective various types of abdominal operation are being done in primary and secondary level hospitals and private clinics where there is lack of specialist or trained surgeon and trained anaesthetist. The early postoperative complications following abdominal surgery are potentially life threatening and needs proper management to recovery. To reduce these complications, it is important to establish the risk factors that increase their incidence using multivariate analysis. Due to limitation of resources, appropriate clinical assessment and monitoring in the primary and secondary health care centre to manage these complications they are often admitted into tertiary level hospitals. The aim of this study was to find out the incidence of admission and pattern of postoperative complications. It will give the massage to both the people and health department about the current surgical care status of primary and secondary health care facilities of private and government hospitals in our country.

Materials and Methods

This observational study was conducted over a period of six months on the patients with early postoperative complications following abdominal operation admitted in the surgery department of Rajshahi Medical College Hospital. In this study, we selected 3613 patients admitted during the period of April, 2013 to September, 2013 in the surgery department of RMCH. About 96 patients were admitted with early postoperative complications. Among the admitted patients with both medical and surgical complications developed in early postoperative period discharged or referred from any primary or secondary hospitals or clinics were included.

- Data collection by structured questionnaire containing all the variables of interest.
- Proper history taking.
- Clinical examinations and
- Relevant investigations were done.

A good clinical history and proper physical examination was performed on all the subjects admitted. Clinical history was focused on present complaints and about index operation. Special attention is to be given on preoperative assessment, presence of any co-morbidity, quality of surgeon, level of hospital or clinic, anaesthetic and postoperative care of index operation. Physical examination was started from vital signs and detailed abdominal and systemic examination were carried out and systematically recorded on a proforma. Routine and special investigations were done according to need. All the patients were categorized into 5 groups and classified according to severity. Patients with medical problem were managed with the consultation of relevant discipline. After proper counseling and taking consent, reoperation was done if required for purpose of diagnosis and treatment of all surgical problems. Immediate outcome of management was monitored and recorded. Finally all data obtained were entered into the database and analysis was made by statistical package for social science (SPSS) using appropriate statistical test or method. All the procedure of study was done after taking informed written consent from the patient/legal guardian. Keeping compliance with Helsinki Declaration for medical research involving human subject 1964, patients and legal guardians of the patient were informed verbally about the study, the underlying hypothesis and right for the participant to withdraw from the project at any time, for any reason, what so ever. Written consent was obtained from each subject.

Results

The total admitted patients with postoperative complications and other variables were analyzed. The mean age of the patients was observed 39.44 (± 15.2) with a range of 14-72 years. The incidence of postoperative complications were observed highest among female followed by male patients as 58.75% (n-56) and 41.25% (n-40) respectively (Figure 1).

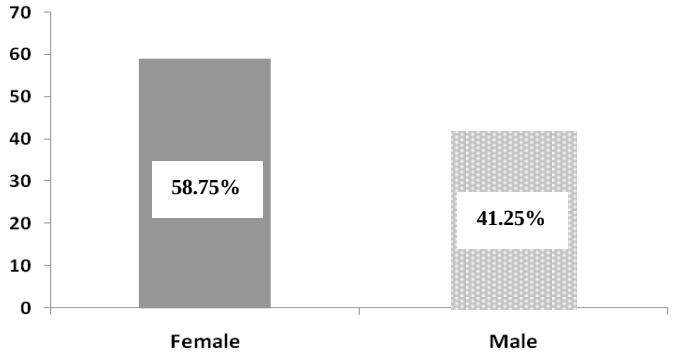

Figure 1: Incidence of the postoperative complications among different sexes

The age group of most of the patients developed complications were 21-30 years (28.1%) among the study population and the second highest were observed within 31-40 years (25.0%) as shown in Table I.

Table I: Age group distribution of the patients

Years	No. of patients	Percentage (%)
12-20	7	7.3
21-30	27	28.1
31-40	24	25
41-50	12	12.5
51-60	13	13.5
61-70	12	12.5
>70	1	1.0
Total	96	100

The admitted patients with complications grading from grade-l, grade II, Grade IIIa, Grade-lllb, grade-lVa, Grade-lVb and Grade-V were seen about 18.8%, 11.5%, 25.0%, 19.2 %, 6.2%, 2.1% and 7.3% respectively (Table II).

Table II: Classification of complications following operations

Grade	Number of cases	Percentage (%)
Grade l	18	18.8
Grade II	11	11.5
Grade IIIa	24	25
Grade IIIb	28	29.2
Grade IVa	6	6.2
Grade IVb	2	2.1
Grade V	**7**	7.3
Total	**96**	**100**

Among the complications following operation of different systems most likely was the wound infection (10.4%) of gastro-intestinal tract, but the pyoperitoneum was (9.4%). On the other hand, pelvic abscess and fecal fistula were 8.3% and 8.3% respectively.

Table III: Complications following operations performed in different hospitals

Types of complications	Number of patient	Percentage (%)
Wound infection	10	10.4
Pyoperitoneum	9	9.4
Pelvic abscess	8	8.3
Fecal fistula	8	8.3
Burst abdomen	7	7.3
Missed diagnosis	7	7.3
Sub-hepatic abscess	6	6.3
Paralytic ileus	6	6.3
Haemoperitoneum	5	5.2
Clot retention	4	4.2
Fecal peritonitis	4	4.2
Biliary peritonitis	3	3.1
Urinary fistula	2	2.1
Renal failure	2	2.1
Aspiration depression	2	2.1
Respiratory depressio	2	2.1
Foreign body	2	2.1
VVF	2	2.1
Peniculitis	1	1
Atelectasis	1	1
Ml	1	1
CCF	1	1
Hypotension	1	1
RVF	1	1
Cardiac arrest	1	1
Total	**96**	**100**

The complications were aroused after performed the different types of index abdominal hepatobilliary, renal and gynaecological operations. The highest complications (27.1%) were observed after appendicectomy followed hepatobilliary operations likely cholecystectomy (Table IV).

Table IV: Incidence of different types of index operations

System	Name of Operation	Number of Cases	Percentage %	Total
GIT	Appendicectomy	26.0	27.1	
	Resection & anastomosis of gut	5.0	5.2	37
	GIT Perforation repair	6.0	6.2	
HB & PS	Cholecystectomy	11.0	11.5	11
Renal	Protatectomy	6.0	6.2	10
	Removal of renal stone	4.0	4.1	
Gynae & Obs	VH	9.0	9.4	31
	TAH	8.0	8.3	
	LUCS	12.0	12.5	
	Tubectomy	2.0	2.1	
Others	Herniotomy & Herniorrhaphy or	5.0	5.2	7
	Plasty	2.0	2.1	
	Multiple operation			
	Total	**96**	**100**	

The postoperative complications developed from both emergency and elective surgical operations were observed about 60% and 40% respectively (Figure 2).

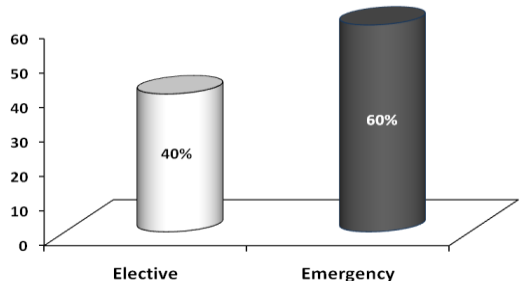

Figure 2: Bar diagram showing the index operations

The operations were performed in the different level of hospitals of the country. Most of the patients (80 cases) were undergone operations in the private clinic or hospitals where as a few cases were done in the government specialized hospitals where (Table V).

Table V: Institutions of index operation

	Level of hospital			
	Tertiary	**Secondary**	**Primary**	**Total**
Govt. Hospital	2	12	2	16
Private clinic or /Hospital	0	14	66	80
Total	**2**	**26**	**68**	**96**

The different types of surgeons were directly involved in the operations in different places of the country. Highly skilled, trained, postgraduate surgeons, medical graduate (MBBS) and medical assistants were played a role in the surgical treatment. The mostly the youngest, medical graduates surgeons were highest in numbers (69.79%) as compared to the specialized surgeons (Figure 3).

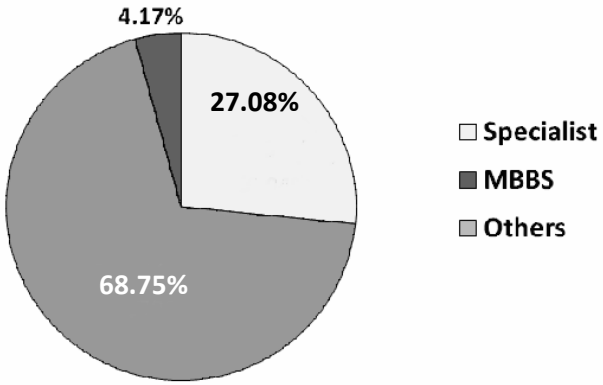

Figure 3: Pie diagram of level of surgeon

The different category of medical staffs were likely doctors, specialized nurses, and medical assistants and others were involved in postoperative complications following different operations (Table VI).

Table VI: Person who conduct the postoperative periods in managing patients

	Number of patients	Percentage (%)
Doctors	30	31.2
Nurses	23	24
Others	43	44.8
Total	**96**	**100**

In this study, the management of the complications, about 79.2% (n-76) patients could be managed in surgery department with the help of specialists likely blood transfusion, anesthesia and medicine. But about 19.8% (n-19) patients were transferred to other discipline likely ICU, nephrology, cardiology and respiratory medicine department and 1.0% (n-1) patient was referred to higher special centre for better management. About 40.6% (n-39) patients were managed conservatively, 59.4% (n-57) patients were needed reoperation, but about 19.8% (n-19) patients had developed further complications. Of the total number of patients, 83 (83.3%) recovered completely, while 9 patients disabled and 7 patients were died (Table VII).

Table VII: Consequences of patient management in RMCH

Consequences of Management	Number of patients	Percentage (%)
Complete recovery	80	83.3
Disabled	9	9.4
Died	7	7.3
Total	96	100

The overall mortality was observed about 7.3%. The patients were undertaken their postoperative management care in the hospitals ranging from within a day to 1 month or more (Table VIII).

Table VIII: Total staying of patients in hospital (RMCH)

Number of Days	Patients	Percentage (%)
1-7	31	32.3
8-15	45	46.9
16-30	13	13.5
>30	7	7.3
Total	**96**	**100**

Discussion

A significant proportion of patients had been admitted in Rajshahi Medical College Hospital with early postoperative complications in every year. They were referred either from surgeon or from private clinics or government hospitals of primary and secondary level. Among the admitted patients in surgery department about 2.66% were with postoperative complications following abdominal surgery. Female were predominant than male and most of the cases were of younger age (about 53.1%). A

total number of 96 out of 3613 patients with a mean age of 39.44 years (±15.18) and a range of 14-72 years admitted with complications. The mean age 39.44 indicates most of the patients are young.[7]

This study revealed that 66 patients were primarily operated by non-specialist surgeon (MBBS), 26 patients by specialist and 4 patients operated by non-doctor respectively. These second and third category surgeons avoid to perform operation of aged patients and patients having co-morbidity. In this study, patients with postoperative complications following appendicectomy was observed about 27.1%. The rate is high and second most common following lower uterine caesarean section (12.5%) then cholecystectomy (11.5%).[8]

Patients admitted into Rajshahi Medical College Hospital with early postoperative complications following abdominal surgery are mainly referred from private clinics (83.3%), where as from government hospital only 16.7%. In a study in Vienna, Coelho JC[8] reported that appendicectomy done in public hospital developed complications about 36%, on the other hand in private hospital developed complications about 22%.

Preoperative management is a very essential tool for the successful outcome of postoperative patients. Faulty care in either sides may produce unsatisfactory results irrespective of the standard of surgery. In this study it was shown that in most of the clinic postoperative care conducted by person other than Nurse and doctor (44.8%).[9]

In this study, we observed pyoperitoneum in 9.4% and haemoperitoneum in 5.2% cases but those were not properly evaluated preoperatively. Missed diagnosis was a problem for postoperative surgical complications. In our study, 7.3% patients were admitted with postoperative complications that were undergone abdominal surgery as missed diagnosed case.[10]

In classification of postoperative complications shown Grade-llla (25%) and Grade lllb (29.2%) respectively were more than Grade-l (18.8%) and Grade-ll (11.5%) respectively. But the mortality rate was 7.3%. In Switzerland, Dindo D et al.[1] studied with 6336 patients where they rescored complications were in Grade I 45%, Grade ll in 25%, Grade llla 4.8%, Grade lllb 24%, Grade IVa 9.7%, Grade IVb 4.2%. The mortality rate of Grade V was 7.3%. That study differ from present study in case of Grade-l and Grade-ll complications as because those types of complications were minor variety and can possible to manage in primary and secondary health care centre. Whereas the mortality of both study was same.[1]

About 46.9% patients had a total hospital stay of about two weeks and 13.5% patients had more than two weeks. This increased length of stay in hospital increases total hospital cost. Nadia AK et al.[11] shown that postoperative complications were associated with substantial increases in total hospital cost and length of stay (LOS), even after adjusting for type of surgery, urgency of surgery, and preoperative patient is comorbid conditions. It was reported increases in hospital costs and LOS with several postoperative complications in a study of 1,008 surgical patients.[12]

In our perspective, many of operations were done by non-specialist surgeons, even some were done by non-doctors personnel like nurse, medical assistant, village doctors, health assistant, and quack etc. These types of personnel are not recommended for doing surgery but they invariably doing so, even some kind of major surgery. As they do not know details about the postoperative complications and their managements, they referred patients to tertiary level hospital like Rajshahi Medical College Hospital.

Conclusion

When a patient undergone an operation, he or she hopes for the most superior care. Patients trust their lives in the hands health care workers, and their expectations should be taken seriously. Specifically, surgeons and other health care providers should ensure that all safeguards are taken before, during and after procedures to prevent any postoperative complications. Training of the junior surgeon, hospital volume and learning curves are becoming more important to maximize patient safety, evaluate surgeon expertise and calculate cost effectiveness. In addition, standar-dization of postoperative care is essential to minimize postoperative complications.

Contribution of the Authors

First author was the principal researcher. Others helped for data collection, computer composing, and statistical analysis.

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Original Article

Role of Modified Alvarado Score in the Management of Acute Appendicitis

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Abstract

Introduction: *This study was carried out in Rajshahi Medical College Hospital, Rajshahi to evaluate the role of modified Alvarado score in the diagnosis of acute appendicitis.*

Methods: *It was a cross-sectional study. A total of 227 cases having features of appendicitis, admitted in the surgery unit of Rajshahi medical college hospital, were selected for our study.*

Results*: About 221 (97.4%) of patients complained sudden onset of anorexia. The second leading symptom was nausea and vomiting 214 (94.3%). About 186 (82%) of the patients had history of onset of pain around umbilicus. Pain shifting to right iliac fossa was complained by 78% of the patients. The affected patients exhibited tenderness in right lower quadrant (RLQ), positive cough test, muscle guard/rigidity, rebound tenderness, Rovsing's signs and leukocytosis 220 (96.9%), 215 (94.7%), 215 (94.7%), 210 (92.5%), 206 (90.7%) and 157 (69.2%) were found respectively. The patients with score (8-10) along with history of pain migrating to right iliac fossa and associated with tenderness indicate high possibility of acute appendicitis. While patients with score (1-4) are unlikely to have appendicitis and could be discharged home safely.*

Conclusion: *Modified Alvarado score (8-10) along with history of pain migrating to right iliac fossa and tenderness in right lower quadrant indicate high probability of acute appendicitis and should be operated immediately, while patients with score (1- 4) are unlikely to have appendicitis and could be sent home safely. Patients with score (5- 7) may have variable outcome and further decisions should be taken according to guidelines of disease.*

Key words: *Acute appendicitis, Alvarado score, Rovsing's sign*

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Introduction

Acute appendicitis is a common cause of abdominal pain for which a prompt diagnosis is very essential to reduce both morbidity and mortality.[1] Fitz R,[2] a Harvard pathologist, described first time the classical signs and symptoms of acute appendicitis. It is rare in infancy and old age, but is common in children, teenagers and young adults.[3] Much effort has been directed towards early diagnosis and intervention as approximately 7% of population suffers from this disease during their life time.[4] Delay in the diagnosis definitely increases the morbidity, mortality and the cost of treatment.

In the recent years, to diagnose acute appendicitis and to reduce the incidence of negative appendicectomy without increasing the risk of gut perforation, various scoring systems have been developed to evaluate the patients with suspected acute appendicitis for observation and/or surgery.[5] Many of them are difficult and complex to apply in clinical setting, but the Alvarado Score (after the name of Alfredo Alvarado, an American surgeon) is simple, effective and can easily be applied.[6]

The Alvarado Score was based on a retrospective analysis of 305 patients and subsequently validated by prospective studies in adults.[1] This score comprises 10 points and consists of 3 symptoms, 3 signs and 2 laboratory tests. According to this score patients are categorized into 4 groups and patients with score 9-10 are considered cases of acute appendicitis with high probability.

Several modifications were done in Alvarado score, but Al-Fallouji MAR[7] has modified the Alvarado score into a more practical, reliable and easy for junior doctors. The modified Alvarado score was based on a prospective assessment of appendicitis patients to design a more clinically oriented and more practical score. Improvement in clinical performance with their use has increased the diagnostic accuracy from 58% to 78% with a drop in perforation rate from 27% to 1.25%.[8] This study was carried out with an aim to evaluate acute appendicitis by using modified Alvarado score to increase diagnostic accuracy and cost effective treatment for the poor patients like those in our country.

Materials and Methods

This cross-sectional study was conducted in the Department of General Surgery, Rajshahi Medical College Hospital, Rajshahi over a period of one year from January to December 2008. Clinically suspected cases of acute appendicitis admitted in the general surgery units of Rajshahi Medical College Hospital, Rajshahi were the study population. A total of 227 cases of suspected acute appendicitis, selected purposively, were included in the study.

Selection criteria for the admitted patients must have fulfilled the criteria likely pain in

the right iliac fossa and/or periumbilical pain, tenderness in right lower abdomen, tenderness in Mcburney's point, and modified Alvarado score with 5 – 10.

Exclusion criteria of the patients of this study were such as those patients aged less than 12 years old, patients with lump or abscess in the right iliac fossa, ultrasonography suggestive of pelvic pathology in female patients and modified Alvarado score having in between 1–4.

The modified Alvarado score (MAS) consists of 3 symptoms, 4 signs and 1 laboratory test were shown in table I. According to this score, patients with score 8-10 were diagnosed as having acute appendicitis and patients with score <8 as probable appendicitis or other acute abdomen cases or normal appendix (Table II). All cases underwent open appendisectomy and the resected specimens were sent for histopathological diagnosis. Then the diagnoses made by MAS were compared against histopathological diagnoses and sensitivity, specificity, positive predictive value (PPV), negative predictive values (NPV) of MAS were computed. All variables data were collected by using a structured questionnaire containing all the variables of interest and analyzed using SPSS (Statistical Package for Social Sciences) version 22.

The key variables of our interest of this study were modified Alvarado score and histopathological diagnosis of resected specimen of vermiform appendix. To calculate modified Alvarado score consists of 3 symptoms (migratory pain in right iliac fossa, anorexia and nausea/vomiting), 4 signs (tenderness in RLQ, rebound tenderness in right iliac fossa). Elevated temperature >37.3^{0}C/> 99.14^{0}F and Rovsing's sign/cough test/rectal tenderness) and total count of WBC were studied in each patient and recorded. Besides these, age, sex and other pertinent clinical variables were studied by Alvarado A and Al-Fallouji MAR.[6,7]

Results

A total of 227 clinically suspected cases of appendicitis was included in the study to evaluate the role modified Alvarado score (MAS) in diagnosing acute appendicitis. The mean age was 24.9 years with the lowest and highest ages were 13 and 54 years respectively. The age distribution of the patients were observed over 69 (30%) of the patients were < 20 years, 101 (44.5%) in 20 – 30 years, 37 (16.3%) in 30 – 40 years and 20 (8.8%) in 40 or above 40 years old (Table I).

Table I: Distribution of patients by age (n - 227)

Age (years)*	Frequency	Percentage
< 20	69	30.4
20 – 30	101	44.5
30 – 40	37	16.3
≥ 40	20	8.8

* mean age ± SD = 24.9 years**;** range = 13 – 54 years**.**

More than half, 119 (52%) of the patients were male and the rest were female, having male to female ratio of roughly 1:1 (Figure 1).

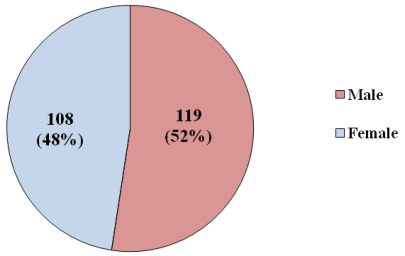

Figure I: Distribution of patients by sex

In our study, we observed 221 (97.4%) of patients complained of sudden onset of anorexia. The second leading symptom was nausea & vomiting 214 (94.3%). 186 (82%) of the patients had history of onset of pain around umbilicus. Pain shifting to right iliac fossa was complained by 187 (78%) of the patients. The affected patients exhibited tenderness in right lower quadrant (RLQ), positive cough test, muscle guard/rigidity, rebound tenderness, Rovsing's signs and leukocytosis were found 220 (96.9%), 215 (94.7%), 215 (94.7%), 210(92.5%), 206 (90.7%) and 157 (69.2%)) respectively. The peroperative findings of resected appendices were observed in 131 (57.7%), 41 (18.1%), 40 (17.6%) and 15 (6.6%) as inflamed, gangrenous, normal and perforated respectively (Table II).

Table II: Distribution of patients by per-operative findings of appendix (n-227)

Peroperative findings	Frequency	Percentage
Normal	40	17.6
Inflamed	131	57.7
Gangrenous	41	18.1
Perforated	15	6.6

Histopathological diagnosis of the resected specimens revealed that 177 (78%) patients had appendicitis and the rest 50 (22%) were with normal appendices (Figure 2).

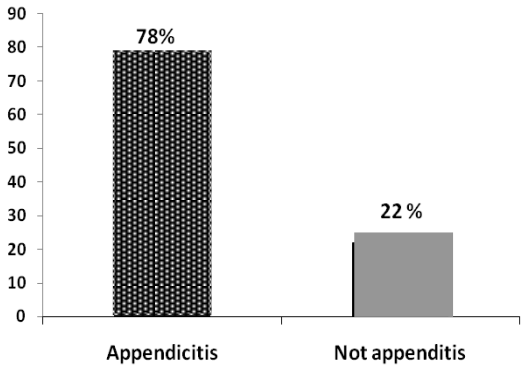

Figure 2: Distribution of patients by histopathological diagnosis

Discussion

Appendicitis is the most common surgical disease for hospital admission and emergency surgery. Delay in diagnosis definitely increases the morbidity, mortality and cost of treatment. In equivocal cases aggressive surgical approach 'when in doubt

take it out' has resulted in increased negative appendicectomy which has been reported in various series from 8-33%.[9-11] Efforts must be made to avoid unnecessary appendicectomy of otherwise normal appendix and to increase the diagnostic accuracy of whatever tool used to diagnose the diseased appendix.

In this study, the sensitivity of modified Alvarado score in correctly diagnosing appendicitis of those who have the disease was high while the specificity of the score in ruling out of those who do not have the disease was low. Fenyo G[12] reported in his study that a sensitivity of 90.2% and specificity of 87.0% with negative laparotomy rate of 17.5%. In a prospective study of 215 adults and children in Cardiff, use of the Alvarado score decreased an unusually high false-positive appendisectomy rate of 44% to 14%.[1] However, 7.5% patients with low scores were subsequently shown to have appendicitis. In relatively small study of 49 consecutive patients from Newcastle region, the overall sensitivity of the score was 87.5%, but its specificity was poor,[13,14] however, reported a low sensitivity (66.7%) and high specificity (83.3%) with a negative appendicectomy rate of 32.3%. Keeping consistency with these findings, our results showed that the modified Alvarado scoring system has a low sensitivity and high specificity.

The data clearly show that the specificity and hence the ability of the modified Alvarado scoring system to exclude true negatives (i.e., patients who do not have appendicitis) remains reasonably high. In contrast, the sensitivity shows the ability of the score to detect true positives those have appendicitis. Hence, as a clinical aid for diagnosing cases of acute appendicitis among patients complaining of right iliac fossa pain it is not as useful as its ability in avoiding unnecessary surgery in patients who do not have acute appendicitis. As a result, the negative appendectomy rate can be lowered by the use of the Alvarado scoring system. However, to be sure that patient does not have appendicitis, some steps need to be followed.[7] Accordingly patients with score 1-4 are unlikely to have acute appendicitis and can be discharged home safely thus reducing unnecessary admission, a cost-effective policy that can prevent wastage of money, staff time and effort that can be spent on urgent efforts. Patients with score 5-7 (in more than 80% cases) are unstable group of patients. They must be re-scored subsequently until they switch into score 8 and consequently operated on or they may pass into a lesser score (in less than 20% cases) due to the underlying normal or resolving appendicitis and therefore can be discharged home. Persistent score 7 after 24 hour is better to operate. Patients with score 8-10 must be operated on immediately because their probability of being appendicitis is about 67-90%. [1, 13]

By adopting this safe policy, one can obviate nearly 30% of negative laparotomy and thus the old policy 'when in doubt take it out' would be replaced with policy 'observe and conserve'. The results of the regression

analysis of the parameters in the Alvarado score show that migration of pain is the single most important symptom pointing towards a diagnosis of acute appendicitis.

Conclusion

Though the function of appendix is still not clear, but it can be used for reconstructive surgery, such as replacement of damaged common bile duct and right ureter, for appendicecostomy to divert faecal effluent in distal colonic obstruction and as a caecal reservoir with appendicular conduit in bladder reconstruction. Therefore, every effort should be made to preserve healthy appendix for future reconstructive surgery.

Contribution of the Authors

First author was the main researcher. Next two were responsible for data collection, drafting work or revising it critically for intellectual content. Others were responsible for statistical analysis and computer composing.

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Original Article

A Study on Synthesis, Characterization and Toxicity of Silver Nanoparticles

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Abstract

Introduction: *Nanoparticles are increasing attention for the wide range of new applications in various fields of technology. Silver nanoparticles possess unique properties which find tremendous applications such as antimicrobial, anticancer, larvicidal, catalytic, and wound healing activities.*

Methods: *This quasi experimental study was designed to synthesize silver nanoparticles (AgNPs) from silver nitrate ($AgNO_3$) solution using glucose as reducing agent and starch as capping agent during the period of July 2014 to June 2015. The characterization of nanoparticles was carried out using UV-Vis spectroscopy. The harmful effect of AgNPs was investigated using Brine shrimp (Artemia salina) in various micro molar concentrations (0.01µmol, 0.1µmol, 10 µmol, 25µmol, 50 µmol). The LD_{50} and mortality rate was also evaluated.*

Results: *The AgNPs containing colloidal solution showed distinctive color change and a sharp peaked surface plasmon resonance at 420 nm. Maximum mortality rate was observed at 50 µmol (61%). The LD_{50} value was obtained at 1.62 µmol which signifies high toxicity of silver nanoparticles to Artemia salina.*

Conclusion: *This study established that, the chemical synthesis guided AgNPs are small, spherical and have toxic effect on Artemia salina.*

Key words: *Silver nanoparticles, Brine shrimp, Cytotoxicity*

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Inroduction

Nanoparticle may be defined as particles of controlled size with at least one dimension less than 100 nm.[1] That is nanoparticles are the particles between 1 to 100 nm that behave as a whole unit in respect of its transport and properties. Nanoparticles are now being developed for a variety of biological applications such as medicines, antimicrobial agents, wound dressings, drug targeting and deliveries. Development of newer drug delivery system based on nanotechnology methods is being tried for conditions like cancer, diabetes, fungal infections, viral infections and gene therapy.[2] Nanotechnology has also found its use in diagnostic medicine as contrast agents like fluorescent dyes and magnetic nanoparticles.[3] Among metal nanoparticles silver have received considerable attention due to their attractive properties like size and shape depending optical, electrical and magnetic properties which can be incorporated into antimicrobial application, biosensor materials, cosmetic products and electronic components.[4] β-d-Glucose as reducing agent is renewable, inexpensive and nontoxic.[5] Starch capped nanoparticles can be radialy integrated into systems relevant for pharmaceuticals and biomedical applications.[6] The increase of manufacture and consumption of products containing silver nanoparticles can lead to metallic nanoparticles release in the environment if waste is not properly disposed. On the other hand, concentration of these nanoparticles is increasing in aquatic environment and can strongly affect and damage the biota.[7] Therefore, it is thought worthwhile to study the synthesis of AgNPs in a simple method using glucose as reducing substance and starch as stabilizing agent with gentle heating. Brine shrimp lethality study was also determined in order to observe cytotoxic effect of AgNPs.

Materials and Methods

This study was carried out in the department of Pharmacology, Rajshahi Medical College, Rajshahi during the period July 2014 to June 2015. Silver nitrate ($AgNO_3$), β-d glucose, starch were purchased from local market. All glass wares and instruments (conical flasks, measuring cylinders, beakers, petri plates and test tubes, micropipettes etc.) were purchased from local market. Deionized water was used throughout the experiment.

Preparation of Silver Nanoparticles

For synthesis of silver nanoparticles 200 µl of 0.1 M silver nitrate and 500 µl of 0.1M glucose were placed into the conical flask using 1000 µl micropipette. Then 10 ml of 0.2% starch was added into the flask. The mixtures of solutions were gently heated in a hot plate for 10 minutes. A change in color of the solution was obtained from colorless to yellow indicating the formation of silver nanoparticles.

UV-Vis Spectral Analysis

UV-Vis spectroscopy was used to analyze the presence of silver nanoparticles using MODEL 340 Spectrophotometer (SEQUOIA TURNER CORP). The scanning range for the samples was 200-800 nm. Baseline correction of the spectrophotometer was carried out by using a blank reference. Ultraviolet–visible spectroscopy (UV-Vis) refers to absorption spectroscopy or reflectance spectroscopy in the ultraviolet-visible spectral region. It is the measurement of light passing through a sample (I), and compares it to the intensity of light before it passes through the sample (I_0). The ratio I / I_0 is called the transmittance and usually expressed as a percentage (% T). The absorbance A is based on the transmittance: A = - log (%T).

Brine Shrimp Cytotoxicity Assay

Brine shrimp *Artemia salina* cysts were purchased and maintained in the laboratory conditions and were used for cytotoxicity assay. Briefly, *Artemia salina* cysts of 1 gm were aerated in 1 L capacity of glass jar containing 3.8 % of saline water (3.8 gm commercial salt in 100 ml of distilled water). The jar was aerated constantly for 48 hrs at room temperature (25-29 °C). After hatching, active free-floating young nauplii were collected from bright illumination and were used for the bioassay. Parallel negative control (without AgNPs) was also included for the experimental set up. Five test samples containing 0.01 µmol, 0.1 µmol, 10 µmol, 25 µmol, 50 µmol were prepared. 10 nauplii transferred to each test petridis (10 petridis for each test sample) using pipette. Then 1ml of nano solution and artificial sea water was added to make the final volume 5 ml. The experimental set up was allowed to remain 48 hrs in darkness. Survivors were counted with a magnifying glass after 48 hours. Percentages of mortality at each dose and control were determined. The results were calculated as means ± standard deviation (SD). LD_{50} for tested concentration of Brine Shrimp cytotoxicity assay along with 95% confidence limit were determined using probit analysis. Percentage of mortality was calculated by the following formulae: % mortality (number of dead *Artemianauplii* / initial number of lice *Artemianauplii*) × 100.

Results

When solution of glucose and starch was gently heated with aqueous solution of the $AgNO_3$, the color from colorless solution mixture started turning yellow just after 2-3 minutes of heating and after 10 minutes it became yellowish brown. On the other hand, control solution (deionized water, glucose and starch) did not develop color after heating.

The UV-Vis absorption spectra of the Ag NP were shown in Figure 1. UV-Vis spectroscopy allows high quality character-ization of the AgNPs. Absorption spectra of Ag nanoparticles formed in the reaction media had a sharp peak and absorbance maxima at 420 nm which indicates that size of synthesized AgNPs were below 30nm. The absorption range of prepared silver

nanoparticle solution was checked on 1st, 3rd and 45th day. There was no significant change observed in peak position for 3rd and 45th day. The control solution did not develop SPR peak observed in UV-Vis spectra confirming absence of nanoparticles.

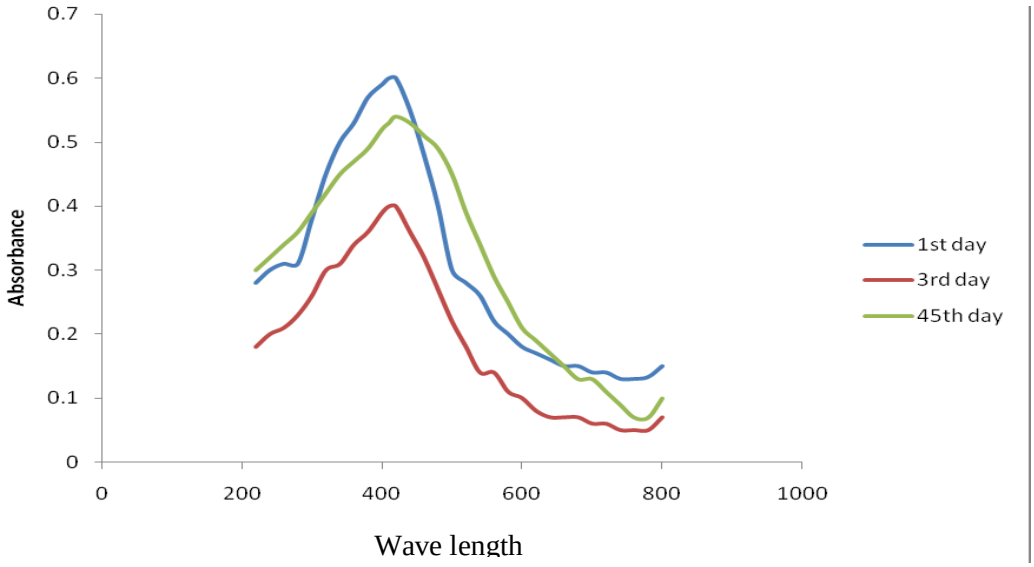

Figure 1 : UV-Vis absorption spectra of silver nanoparticles

The brine shrimp lethality assay was also performed to determine the cytotoxicity of AgNps, which could also provide an indication of possible toxicity of the test materials. It was demonstrated that early developmental stages of *Artemia* was highly vulnerable to toxins. The lethality was found to be directly proportional to the concentration of NPs. The results were found to be in such a way that in the control the mortality was about 0%. In minimum concentration of 0.01µmol the mortality was 37% and as the concentration increased to 0.1µmol, 10 µmol, 25 µmol and 50 µmol the mortality was increased to 39%, 50%, 56% and 61%. Maximum mortality rate was observed at 50µmol. While LD_{50}-48 hours was obtained at 1.62 µmol (.275 mcg/ml) as shown in Table I.

Table I: LD_{50} value of AgNPs

Test sample	LD_{50}-48 hours (µmol)	95% confidence limit		Regression equation	λ^2 (df)
		lower	upper		
AgNPs	1.62	6.826	386.17	Y= 4.673±.147	.20 (3)

(AgNPs= Silver nanoparticles, µmol= Micromol, LD_{50}= Median lethal dose (dose at which 50% of shrimp nauplii died), λ^2= Chi-square, df = degree of freedom).

Discussion

At the macroscale, silver always looks like silver. But it is well known that silver nanoparticles exhibit yellowish color in aqueous solution due to surface plasmon vibration.[8] In the silver nanoparticles, electrons oscillate collectively. These oscillations affect how light interacts with the nanoparticles. The specific oscillations depend on the particles size and shape. So particles of different sizes have different colors. The appearance of yellowish color in the solution suggests the formation of silver nanoparticles. Our observation is in agreement with the other studies reported earlier.[9-10]

UV-vis spectroscopy is one of the most widely used techniques for characterization of silver nanoparticles. The absorption phenomenon shown by the nanoparticles is due to surface plasmon resonance. In the present study, silver nanoparticles exhibited a single and well defined peak in the absorbance spectrum with maximum absorbance at 420 nm which corresponds to characteristic surface plasmon resonance of AgNPs. Only a single SPR band is expected in the absorption spectra of spherical nanoparticles, whereas anisotropic particles could give rise to two or more SPR bands depending on the shape of the particles. On the other hand, relatively narrow peak indicates that AgNPs were within a narrow size distribution.[11] Therefore; the overall findings concluded that synthesis of silver nanoparticles using glucose as reducing agent and starch as capping agent were spherical and roughly spherical in shape and having narrow size. The sharp narrow plasmon peak at 420 nm observed in this study was similar to an previous report[5] who found the surface plasmon absorbance spectrum of SNPs formed in aqueous starch dispersion at 419 nm and 90% of those particles were in the size range from 1 to 8 nm, which was further confirmed by TEM study.

In the present study, toxicity of silver nanoparticles (SNPs) was observed using brine shrimp lethality bioassay and the mortality rate of brine shrimp was found to be increased with increased concentration of nanoparticles. The highest mortality was found at 50 µmol and LD_{50}-48 hours was observed at 1.62 µmol (0.275 mcg/ml) indicates high toxicity to the *A. salina.* In another similar study,[7] evaluating toxicity of PVA (polyvinyl alcohol) stabilized silver nanoparticles to algae and micro crustaceans showed the LD_{50} 48 hours was 0.55 mcg/ml which was also much higher than our study. The possible mechanism of toxicity effect of silver nanoparticles on brine shrimp was the nanoparticle aggregates at elevated levels in guts of *Artemia salina* resulting lack of food uptake since the guts were completely filled with the aggregates of silver nanoparticles.[12]

Therefore, the overall findings concluded that synthesis of silver nanoparticles using

glucose as reducing agent and starch as capping agent were spherical and roughly spherical in shape and having narrow size range and highly stable. The synthesized silver nanoparticles using glucose and starch have potential harmful effects on aquatic invertebrates. Taking into account the mobility of SNPs into the cell and their fate in a bioprocess or even in the environment, other cytotoxicity tests and specific bioassays might be performed on cell lines for further studies.

Conclusion

Nanotechnology stands for an important scientific advancement and can contribute with several benefits for human. In the present study, silver nanoparticles were successfully obtained from reduction of silver nitrate solution using glucose as reducing agent and starch as capping agent. UV-vis spectroscopy suggested the formation of uniform and spherical silver nanoparticles. The uncontrolled and unobserved release of these nanoparticles, either as by products or medical wastes, could have a large negative consequence on the aquatic, terrestrial organisms and also on humans. So, brine shrimp lethality assay was performed to investigate the toxicity of silver nanoparticles. AgNPs produced by using glucose and starch showed significant toxicity against *A. salina*. Silver nanoparticles produced by the method reported in this study using glucose as reducing agent and starch as capping agent have promising applications in biomedical, dental and pharmaceutical fields. Hence, effects and fates of this promising technology need further studies to evaluate the potential risks of nanoparticles on environment.

Contribution of the Authors

First author was the principal researcher. Second and third authors did the statistical analysis and computer composing. Fourth author was the supervisor of the research work.

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Review Article

Snake Bite in Bangladesh

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Abstract

Snake bite is a common public health problem in Bangladesh. Incidence is about 8000 per year with 20% death due to snake bite. Rapid diagnosis of acute hemorrhagic disorders, neurorespiratory, renal, and hemodynamic failure subsequent to snake bite and their rapid interventions saves life. Due to strong believes of public on traditional treatment and lacks of awareness of scientific treatment by medical professional, the patient's do not get appropriate uniform treatment. Hospital treatment based on scientific knowledge, including early administration of the appropriate dose of potent snake antivenom along with adjuvant treatment, proper care of the wound, correcting electrolyte imbalance, tissue oxygenation and maintenance of adequate nutrition may help rapid recovery. In this study, incidence of clinical effects of different types of snake bite and the management guideline for medical professionals are described.

Key words: Antisnake venom, Cobra, Krait snake bite, Viper

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Epidemiology

Snake envenoming is a disease of poverty.[1] Envenoming by poisonous animals (snakes, scorpions, wasps, ants and spiders) is an occupational hazard, often faced by farmers, plantation workers, fisherman, hunters of tropical & subtropical countries.[2] Open-style sleeping on floor, also expose people to bites of from nocturnal snakes in south Asia. A previous survey in Bangladesh covering a larger area conducted in 1995-1996 estimates an incidence of 4.3 per 1000,000 populations with 20% mortality rate.[3] Snake bite is significantly the most important cause of envenoming.

Eventually, the reliable figures on incidence, morbidity, and mortality are scarce in our country due to poverty, inadequate healthcare facilities regarding species specific anti venom production in snake bites management. This study aims at summarizing and discussing clinical features, diagnosis and treatment of snake bites envenoming to awareness of medical personnel in Bangladesh.

Snakes in Bangladesh

There are 82 species of snakes in Bangladesh of which 28 are venomous. Most of the snakes are non-venomous, like worm snakes, pythons, wolf snakes, rat snakes etc. The major families of poisonous snakes are elapid which includes common cobra, king cobra and common krait, banded krait, viperidae (Russell's viper), Saw scalded vipers and *hydrophidae* (sea snakes).

Mode of action of venom

A pair of salivary glands secrete a powerful multipurpose enzyme fluid (venom) that flow at the time of envenoming through the channeled or grooved teeth called fangs. Most snakes inject 10% of the available venom in a single strike except the Russell's viper which injects 75% of stored venom in one single bite due to big long sharp curved fangs.[4]

Venom is a cocktail of 20 or more components including proteins, enzymes, polypeptide toxins, non-toxic nerve growth factors, hyaluronidase, metalase, lipids, free amino acids, nucleotides, carbohydrates, biogenic amines, various activators and inactivators of physiological process. Elapid venom is mainly neurotoxic and sea snake venom myotoxic. [5]

Clinical features and Diagnosis

Some people who are bitten by snakes may develop quite striking symptoms and signs, even when no venom has been injected. Anxious people may hyperventilate so that they develop pin and needle sensation in the extremities, spasm of their hands and feet and dizziness. Others may develop vasovagal shock after the bite or suspected bite with faintness and collapse with profound slowing of the heart. Others may become highly agitated and irrational and may manifest a wide range of misleading symptoms.[6]

Bite by venomous snake must leave fang marks, these are usually two but only one may be evident if the bite is sideways on. In contrast bites by non-poisonous snakes produce a characteristic U shaped set of teeth marks. [7]

Management

Regarding management, first aid is to be given at the time when bite occurs. If one can locate the bite site, remove the surface deposited venom by clean cloth or cotton, keep the extremity at approximately heart level, immediately apply a broad firm bandage on the bitten area and around the limb, with pressure equal to that one can easily put and remove the finger underneath the bandage. As much as of the limb should be bandaged as possible.[9,10] Victims should not be allowed to walk, do not incise at the site of the bite, if the victim is found unconscious, without respiration, healthcare worker, resuscitator or anyone can start mouth-mouth breathing and others measures of resuscitation.

In Bangladesh, we have polyvalent antivenom which acts against Cobra, Common Krait, and Russel's viper. It should be given if signs of systemic poisoning (e.g. ptosis or haemorrhagic signs) develop after snake bite. Its use should be considered in all patients with extensive tissue damage because of the risk of systemic poisoning.

Anti venom accelerates dissociation of the toxin-receptors complexes and reverses the paralysis. On arrival of the patient, 100 ml (10 Vial) Anti snake venom(ASV) is added to 200 cc. of normal saline and given to the patient over 30-50 minutes. One should sit by the side of the victim for easy diagnosis and treatment of anaphylaxis. Within 30 minutes after initial dose of ASV, if there is no improvement of neurological manifestations one can repeat the dose of ASV and no more than total 20 vials of ASV is to be administered. ASV neutralizes circulating venom only and not the toxin fixed in the tissues, the toxins action at tissue level may be antagonized by nesotigmine-atrophine therapy in case of elapid bite and heparin along with supportive fibrinogen transfusion in case of viper bite. When antivenom is not available, local infiltration of carbolic soap around the site of the bite in case of elapid snakes and heparin in case of vipers is recommended. Before discharge, envenomed victims should be closely observed daily for minimum 3-4 days.[8]

Basic cardiopulmonary resuscitation to all patients found unconscious at home and not breathing should start receiving chest compressions and mouth to mouth respiration en-route to the hospital. Endotracheal intubation and ventilation indicated if victim has pooling of saliva, unable to lift the neck from pillow, signs of respiratory failure like abdominothoracic respiration, signs of cerebral hypoxia. At the periphery, one can do endotracheal intubation, or if not possible a laryngeal mask can be put directly over larynx and ambu bag ventilation.[10]

Conclusion

Ultimately death by venomous snake bite makes a family economically deprived. Our researchers should make attempts to prepare venomous toxoid to immunize the risky population against venomous snake toxins. Antivenom producers should prepare a new kit for detecting venom antigen in blood and to prepare antivenom from venoms obtained from snakes caught from relevant areas of the country. As a result, the attending physician will get utmost satisfaction when the victim of snake bite recovers.

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Case Report

A Teenage Girl with Nonfunctioning Adrenocortical Carcinoma- A Rare Case

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Abstract

Adrenocortical carcinomas (ACs) are uncommon malignancies that can have protean clinical manifestations. A majority of cases are metastatic at the time of diagnosis, with the most common sites of spread being the local periadrenal tissue, lymph nodes, lungs, liver, and bone. Detection of tumors at an early clinical stage is crucial for curative resection. The present case was a 15 years old girl presented with abdominal distension and discomfort at Department of Surgery of Shaheed Ziaur Rahman Medical College and Hospital, Bogra, Bangladesh. The data were collected by history taking, clinical examination, laboratory investigations, trans-abdominal ultrasonographic examination, Computed Tomography of abdomen and by histopathological study of the excised surgical specimen. From histopathological report the case was finally diagnosed as adrenocortical carcinoma. This case report emphasize the significance of thorough evaluation of all women presented with vague abdominal pain. Although this condition is rare, it is potentially dangerous in its massive form and hormonal effect as the prevalence is more in female than male..

Key words: *Nonfunctioning adrenocortical carcinoma, Teenage girl, CT scan*

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Introduction

Adrenocortical carcinomas are rare aggressive tumors. Their annual incidence is approximately one to two per million among the population of the United States of America.[1] Approximately 60% of adreno-cortical carcinomas are functional tumors.[2] The female-to-male ratio for ACs is approximately 2.5-3:1. The accumulation of data, especially in international registries, revealed the incidence of adrenal tumors to be higher in female individuals than had previously been thought, particularly in those aged 0-3 years and those over 13 years. Nonfunctional ACs are distributed equally between the sexes. AC occurs in 2 major peaks: in the first decade of life and again in the fourth to fifth decades. While, functional tumors are more common in children, however, nonfunctional tumors are more common in adults. Based on data from the International Pediatric Adrenocortical Tumor Registry, the median age at which children develop adrenal carcinomas is 3.2 years; 60% are younger than four years, and 14% are older than 13 years.[2-4] Patients with active endocrine tumors often present with cushing's syndromes alone (45%), a mixed cushing's and commonly present with an enlarging abdominal mass and abdominal or back pain or with an incidental finding on radiographic imaging called an "adrenal incidentaloma". Laboratory investigations include the following serum glucose, serum cortisol, serum adrenal androgen, urine adrenal hormone, urine vanillylmandelic acid (VMA) and urine homovanillic acid (HVA) levels. Imaging studies include Xray abdomen in erect posture, ultrasonography, Computed tomography (CT) scanning and magnetic resonance imaging (MRI) but CT, MRI are the imaging studies of choice in AC. The typical imaging feature is characterized by mass with irregular edges in adrenal region. The presence of contiguous adenopathy serves as corroborating evidence. Some of the macroscopic features of an AC that suggest malignancy include a weight of more than 500 g, the presence of areas of calcification or necrosis, and a grossly lobulated appearance.[5-8] Histological findings also include numerous mitoses, scant cytoplasm, and none of the rosettes observed in neuroblastoma. When feasible, total resection remains the management modality of choice for the definitive treatment of AC. It also remains the only potentially curative therapeutic modality. While open laparo-tomy for adrenalectomy represents the standard of care, several reports suggest a role for laparoscopic resection if the adrenal tumor is small and there is no preoperative evidence of metastatic disease. Medical care in patients with AC, which can be supportive or adjuvant to surgical resection,

encompasses treatment of endocrine excess syndromes, use of mitotane or several multiagent chemotherapy regimens, treatment with prevention of potential complications, strategies for palliative and terminal care issues, including symptom relief and management.[1, 3, 9-11] A variety of staging system has been used for ACs. The Union of International Cancer Control (UICC) proposed the first TNM classification of malignant tumors for AC in 2003. However, an analysis based on data from the German AC Registry revealed several shortcomings of this classification system. Therefore, ENSAT developed a revised staging system. The superiority of the ENSAT staging system over the 2004 UICC/American Joint Committee on Cancer Classification System for prognostication was confirmed in a recent North American study. Estimated five-year disease-specific survival rates of patients with stage-1 and stag-4 cancer in the studies were 82% and 13%, respectively.[9,10] Nowadays, adreno-cortical cancer is often diagnosed after a great delay, when the cancer is very advanced. The only potentially curative treatment for ACC is surgical resection,[11] which is technically possible in most patients with stage-1 and 2 diseases. The most important predictor of survival in patients with adrenal cancer is adequacy of resection. Patients who undergo complete resection have five years actuarial survival rates ranging from 32% to 48%, whereas median survival is less than one-year in patients who undergo incomplete excision. Other treatment options include treatment with mitotane, an adrenocorticolytic drug, as well as adjuvant chemotherapy and palliative irradiation.

Case Report

A 15 years old girl with a history of abdominal pain and swelling in epigastric, left hypochondriac, and left lumbar region was admitted in surgery ward at Shaheed Ziaur Rahman Medical College Hospital, Bogra, Bangladesh. The swelling presents for last four months with occasional abdominal pain which was dull aching, non-radiating and aggravates by taking food. She had early satiety and nausea for same duration. The patient had no previous medical diseases or surgical operations. Her menarche commenced at the age of 12-years with irregular cycle, duration and heavy flow. But she had no menstruation for the last two years. She denied uses of any medications. Her bladder and bowel habit were normal. General examination revealed, the patient was anxious looking, below average nutrition, anaemic, blood pressure 90/60 mm of Hg with all other parameters were normal. Her weight was 35 kg, height was 140 cm and the secondary sex characteristics were well developed. On abdominal examination, left flank was full

with a lump which was globular in shape, smooth regular surface, hard in consistency, non-tender, moved with respiration and not fixed with overlying skin. Pelvic and digital rectal examination revealed normal. She had no lymphadenopathy or hepatosplenomegaly and no clinical signs of hormonal excess. The patient was advised for all relevant laboratory investigations, hormonal evaluations, ultrasonography of whole abdomen and CT scan of abdomen. She had raised ESR (60 mm in 1st hour), Hb-7.0 g/dl and hyponatremia (Na-130 mmol/L). Others laboratory findings with hormonal evaluation revealed normal. Ultrasonography of whole abdomen revealed a retroperitoneal mass inseparable from left kidney and spleen was not identified (Figure 1).

Figure 1: Ultrasonography revealed heterogeneous mass with central necrosis in left adrenal region

CT scan of abdomen showed a retroperitoneal mass originated from upper pole of left kidney pushing the left kidney downwards, spleen laterally, stomach medially and as suggested mass arising from left adrenal gland with differential diagnosis of enlarged lymph node (Figure 2).

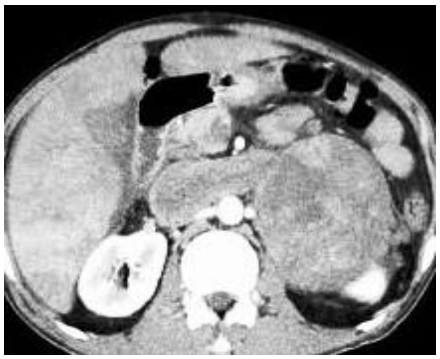

Figure 2: **CT scan revealed heterogeneous enhancing mass lesion with central necrosis in left adrenal region pushing the left kidney downwards**

During operation, left subcostal incision was given and a mass which measured about 12×15 cm (Figure 3) was removed. The mass was sent for histopathological examination, the features of that mass were consistent with adrenocortical carcinoma. After operation the patient was managed postoperatively with all subsequent measures.

Figure 3: Tumor after resection

Discussion

Approximately 60% of adrenocortical carcinomas are functional tumors.[2] Patients with active endocrine tumors often present with Cushing's syndromes alone (45%), a mixed Cushing's and virilization syndrome

(25%), or virilization alone (<10%).[3] Conversely, patients with nonfunctioning tumors more commonly present with an enlarging abdominal mass and abdominal or back pain. Our present case presented as nonfunctional tumour with abdominal pain which was dull aching, non-radiating and aggravates by taking food, early satiety and pain and swelling in epigastric, left hypochondriac, and left lumber region. Patient had no lymphadenopathy or hepato-spleenomegally and no clinical signs of hormonal access. The accumulation of data,[2-6] especially in international registries, revealed the incidence of adrenal tumors to be higher in female individuals than had previously been thought, particularly in those aged 0-3 years and those over 13 years. Present case was 15 years old girl and age-gender demography was comparable with previous studies. A hormonal work-up for functional ACs is widely mandatory; however, the question whether to perform this evaluation in apparently asymptomatic patient has been debated.[4] Plasma metanephrine level or urinary metanephrine and catecholamine levels may be measured to exclude pheochromocytoma. Plasma aldosterone and rennin levels may be measured in patients with hypertension and/or hypokalaemia. In present case laboratory investigations were within normal limit. In this study ultrasonography revealed a retro-peritoneal mass inseparable from left kidney but spleen was not identified. CT scan of abdomen showed a retro-peritoneal mass originated from upper pole of left kidney pushing the left kidney downwards, spleen laterally, stomach medially and as suggested mass arising from left adrenal gland with differential diagnosis of enlarged lymph node. Previous studies[3,4,7] revealed CT scanning can detect adrenocortical mass and also distinguish adenomas from ACs.[3,4,7] The size of adrenal mass visualized on imaging studies was the single most important criterion to help diagnose malignancy. In the series reported by Copeland PM,[5] 92% of adrenal tumors were greater than 6 cm in diameter. MRI was complementary to CT in that local invasion and involvement of the vena cava were more readily identifiable. A fine-needle aspiration biopsy cannot distinguish a benign adrenal mass from a metastatic tumor. Capsular or vascular invasion was the most reliable sign of cancer. In the absence of these findings, the Weiss histopathological system is the most commonly used method for assessing the likelihood of malignancy because of simplicity and reliability.[6,7] Immunohis-tochemistry is also helpful in rendering the diagnosis.[5, 8]

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Case Report

Pregnancy with Ruptured Caesarean Scar Mark

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Abstract

Ruptured uterus is an unpredictable condition to both obstetrician and mother as because it increases morbidity and mortality of mother and foetus. It is not uncommon in our country due to increased prevalence of scar rupture following increased incidence of caesarean section over the years. Ruptured uterus usually occurs beyond 28th weeks of pregnancy. Small rupture to the wall of the uterus in early months is called perforation, either instrumental or due to perforating hydatiform mole. But scar rupture in early months of pregnancy (18wks) is rare and carries grievous consequences to both mother and foetus. Here one case report of pregnancy with scar rupture has been presented that was diagnosed after laparotomy. Diagnosis before rupture by clinical suspicion and ultrasonography, resuscitation and laparotomy is necessary to prevent catastrophe.

***Key words**: Pregnancy, Scar rupture, Laparotomy*

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Introduction

During the past few decades the prevalence has been found to be almost static where as improved obstetric care reduces the rupture from obstructed labour but there has been increased incidence of caesarean section over the years. Incidence of scar rupture is about 0.2-1.5% in the former and about 4-9% in later.[1] The lower segment scar is at greater risk, when the scar integrity is weakened by puerperal sepsis, placental implantation over the scar, high parity, multiple pregnancy, large foetus, hydramnios. Hysterectomy scar behaves like that of classical scar. Myomectomy scar hardly ruptures as wound heals well because the uterus remains quiescent following the operation.

Case Report

A 25 years old female G4P2A1 with 18 weeks of pregnancy, hailing from Dhangara, Raiganj, Sirajganj got admitted in North Bengal Medical College Hospital (NBMCH) on 03.09.2016 with complaints of severe lower abdominal pain for one day. The lady had a previous Intra Uterine Foetal Death (IUD) spontaneously on home delivery or normal vaginal delivary (NVD) at full term about 11 years back. Then her 2nd issue was delivered by lower segment caesarean section (LSCS) about 9 years back. An abortion (spontaneous) occured at 12 weeks about 2 years back. According to the patient's statement, she was a regularly menstruating women with average flow and duration. Her LMP was on 26.04.2016 and accordingly her expected date of delivery (EDD) on 03.02.2017. Her pregnancy confirmed by early ultrasonogram. It was her planned pregnancy but she was on irregular antenatal check up. Her pregnancy was uneventful up to 18 weeks. Then she developed sudden lower abdominal pain for 1 day, which was confined to hypogastrium. Pain was not associated with per vaginal bleeding and not radiated to back or thigh. She had no complaints of dysuria, frequency, excessive vaginal discharge or itching. For this reason she got herself admitted into this hospital for further management. With due consent and maintaining adequate privacy, examination was done on 03.09.2016, found her anxious but cooperative. She was an average body built, mild anaemic and non icteric. She was normotensive (BP-120/80 mm of Hg) pulse was 78 beat/min, temperature was normal and oedema was absent. Breast showed pregnancy changes. Cardio-respiratory systems were found normal.

Abdominal examination revealed that abdomen was uniformly enlarged. Symphysio fundal height (SFH) was 18 weeks size, which corresponds with her gestational age. Foetal movement was present. Tenderness present on scar margin. Per vaginal examination revealed that there was no per vaginal bleeding and no any other significant abnormalities. Routine

investigation was done. Her blood group was A positive (+ve), Hb%-11gm/dl, RBS-4.5mmol/l, HBsAg positive, VDRL nonreactive. Ultrasonogram of pregnancy profile revealed a significant information about her pregnancy. It was 18 weeks pregnancy, the foetus was alive, the placental location was fundal, amniotic volume was normal but amniotic sac was protruded through the uterine scar which looks growth like structure outside the anterior uterine wall (Figure 1 & 2). Repeat ultrasonogram was done for reconfirmation by another sonologist which revealed same reports. After counselling the patient's guardian about the fate of the case and she was taken for immediate laparotomy followed by hysterotomy. On opening the abdomen, scar margin of previous lower segment caesarean section (LSCS) was found ruptured and amniotic membrane bulging through the ruptured scar of uterine wall. Her postoperative period was uneventful and she was discharged on 5th post operative day in good condition.

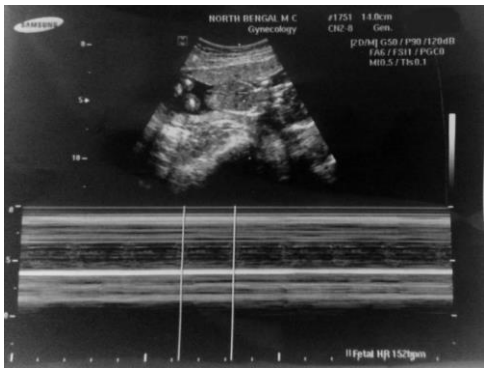

Figure 1: Ultrasonogram of 18 weeks live pregnancy

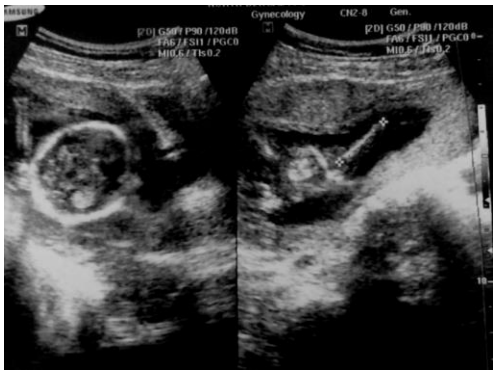

Figure 2: Repeat ultrasonogram of 18 weeks live pregnancy

Discussion

The prevalence of reptured uterus varies from 1:2000 to 1:200 deliveries.[1] The identification or suspicion of uterine rupture is a medical emergency and must be followed by an immediate and urgent response from the obstetrician. An emergency laparotomy is usually required to save the patient's life. A complete uterine rupture is very unlikely now a days. There is no clear cut predictive indicator for rupture uterus. However several factors are responsible for weak scar such as – infections are found to be responsible factors for higher maternal C/S complications.[4,5] Other predisposing foctors involved are improper haemostasis at the time of surgery, imperfect co-optation of uterine margins at the time surgery, extensions of the angles of uterine incision, over distension of the uterus. When uterine rupture is diagnosed or strongly suspected, surgery is necessary. Previously most cases of uterine rupture was

managed with hysterectomy. Now-a-days most cases are managed by controlling the bleeding surgically and repairing the defect.

To identify the previous caesarean scars the following investigations can be done.

- Hysterogram in interconceptional period. Radiographic imaging of the uterus which shows uterine defects in the lateral view (wedge depression >5mm).
- Ultrasound imaging use for visualisation of scar defects and measurement of scar thickness that depends on the quality of ultrasound and skills of the sonologist.
- MRI.

According to study by Rozenberg P et al.[2] cut off value of 3.5 mm, on ultrasound measurement of scar thickness at 36 weeks of gestation was observed to show negative predictive value of 99.3% for scar rupture.[2] Different studies showed different cut off values for estimating the strength of the scar.[3] Therefore presently there is no clear cut off value of scar thickness to indicate the strength of the scar. Risk of rupture is high (9%) when the full thickness was less than 2.3mm. TVS (Trans vaginal sonogram) seems to be more accurate than trans abdominal sonography, yet it is not commonly used.[3]

Conclusion

Early diagnosis of scar dehiscence or rupture is needful for prompt laparotomy and resuscitation to reduce morbidity and mortality in mother and foetus.

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