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Review Article

Case Report

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ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 12 Number 1

Morphological study on age related changes of uterus

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Abstract

The uterus is an essential principal accessory female reproductive organ whose function is to receiving and rearing an egg within its mucosa, nourishes and protects the embryo, and expels it at the proper time. Uterus related clinical conditions such as leiomyomas also known as myomas or fibroid and carcinoma cervix are major medical conditions within aging population. Detailed morphological knowledge is essential for proper diagnosis and management of uterine diseases. It was a descriptive type of study carried out between July 2006 to June 2007. Present study was performed on 50 autopsied human uterus of age ranging from 1 to 65 years. The samples were collected from unclaimed dead bodies that were under examination in the morgue of Department of Forensic Medicine of Sylhet M A G Osmani Medical College, Sylhet. The samples were divided into four age groups. Group A (1-12 years), Group B (13-24 years), Group C (25-46 years) and Group D (46-65 years). All samples were studied morphologically. Statistically significant positive correlation was found between age and weight, length, breadth, thickness of uterus. In conclusion, there were changes in the morphology of uterus in relation to age.

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Introduction

The uterus is an essential principal accessory female reproductive organ whose function is to receiving and rearing an egg within its mucosa, nourishes and protects the embryo, and expels it at the proper time[1].

The uterus-a thick walled, pear shaped, hollow muscular organ-lies in the lesser pelvis normally with its body lying on the top of the urinary bladder and its neck(cervix) between the urinary bladder and rectum[2]

Benign tumors and tumor-like conditions occur more commonly in the uterus than perhaps in any other organ. Neoplasm's of the uterus are all leiomyomas[3] which may be found in nearly one woman in three over the age of 30 years. These are also among the commonest large solid benign neoplasm, being exceeded in size only by giant lipomas[4].These benign tumours arise from the uterine myometrium or, less commonly from the cervix. They are composed not only of smooth muscle but of various amounts of elastin, collagen and extra cellular matrix proteins.

Uterine leiomyomas, also known as myomas or fibroids. They are estimated to be present in at least 20% of all woman of reproductive age and may be discovered incidentally during routine annual examination. Leiomyomas are more common in African American than in white woman[5]

Thus even the term fibroid is inactive by histological criteria. It is extraordinary that a tumor present in the uterus of up to 77% of patients requiring hysterectomy[1] has not been

given higher priority in medical research. Uterine fibroids have been a low-priority area when compared with cancer research and poorly funded-surprisingly given that they are the most common neoplasm which any woman is likely to develop.
The morbidity and mortality associated with uterine diseases affect an increasing number of women and is a major medical condition within our aging population. Disease can be defined and measured only in terms of deviation from normal structure and function. A clear conception on the anatomy of uterus is a prerequisite for the diagnosis and treatment of uterine diseases.
The situation in developing countries like Bangladesh is more gloomy. There is no adequate data regarding the above mentioned diseased. So considering the above aspects, investigation regarding anatomical changes of the uterus in relation to age may lead to valuable information which may cause dramatic modification in both medical and surgical treatment of uterine disorders.

Materials and Methods

The samples of human uterus were collected from unclaimed dead bodies that were under examination in the morgue of the department of forensic Medicine of Sylhet M.A.G Osmani Medical College from September 2006 to March 2007. After legal formalities the samples were collected within 24-36 hours of death without any sign of putrefaction. All the samples were collected from medicolegal cases. During collection appropriate age and cause of death were noted from morgue's record. The samples were brought to the department of Anatomy, Sylhet M.A.G Osmani Medical College. The samples were tagged immediately, which was bearing a code number for subsequent identification. Soon after collection each sample was gently washed in tap water on a dissection tray. Blood and blood clots were removed as per as possible. Then the samples were fixed in 10% formal saline solution. The collected samples were divided into four groups.

Result

Table -1

Age distribution in different group

Group Age	Age limit(Years)	No of samples
A	1-12	7
B	13-24	15
C	25-45	19
D	46-65	9

Variable studied

1. Weight of uterus
2. Length of uterus

Measurement procedure:

1. Weight of uterus; The surface of the each uterus were dried with blotting paper. Then the organ was weighted by means of an analytical balance in gms.

Length of uterus: Length of the uterus was measured from the external os to the fundus of the uterus. Measurement was done with the help of a slide caliper graduated in cm

Weight of the Uterus:

The mean ±SD weight of the uterus was19.36 ± 5.86 gm in group A (1-12 years), 54.33 ± 11.98gm in group B(13-24 years), 66.07 ± 14.56gm in group C (25-45 years) and 46.33 ± 9.03 gm in group D (46-65years).
The highest mean weight was found in group C and the lowest mean weight was found in group A. The mean difference in weight between the four group were significant ($p<0.001$) positive correlation was present between age and weight of the uterus($r = +0.243$ $p<0.001$) (Table II , fig 1 & 3).

Length of the uterus:

The mean ±SD length of the uterus was was3.41 ± .78 cm, in group A (1-12 years), 6.57 ±.59 cm in group B(13-24 years), 7.46 ±.55 cm in group C (25-

45 years) and 6.25 ± .59 cm in group D (46-65years).

The highest mean length was found in group C and the lowest mean length was found in group A. The mean difference in length between the four groups were significant($p < 0.001$) positive correlation was present between age and length of the uterus($r = +0.381$ $p < 0.001$) (Table II , fig 2 & 4).

Table- II

Weight and length of uterus in different study group

Group (n)	Weight(in gm) mean ± SD (range)	Length(in cm) mean ± SD (range
A	19.34 ± 5.86	3.41 ± .78
(7)	(11.5 - 29.5)	(2.1 - 4.4)
B	54.33 ± 11.98	6.57 ± .59
(15)	(34 - 88)	(5.9 - 8.2)
C	66.07 ± 14.56	7.46 ± .55
(19)	(45.5 - 115.5)	(6.5 - 8.3)
D	46.33 ± 9.03	6.25 ± .59
(9)	(36 - 68)	(5.6 - 7.4)

	P value
A vs B	< 0.001***
B vs C	< 0.05*
C vs D	< 0.001***
A vs D	< 0.001***

Group A : Age 1-12 years
Group B : Age 13-24 years
Group C : Age 25-45 years
Group D : Age 46 -65 years
SD = Standard deviation
*** = Significant
(In unpaired Student's 't'test of significance of difference between groups)

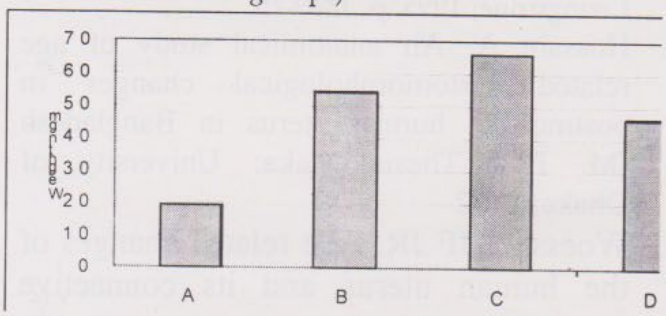

Fig: 1 weight of the uterus in different age groups

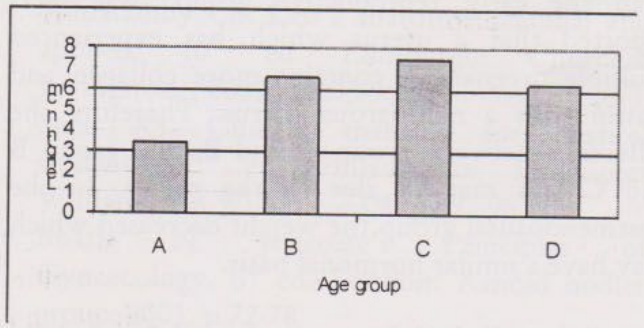

Fig: 2 length of the uterus in different age groups

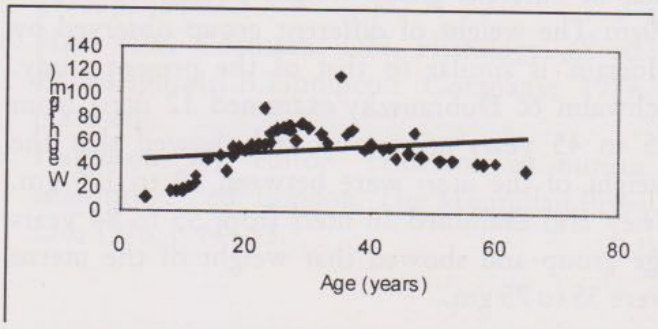

Fig:3 Relationship between age and weight (n=50)

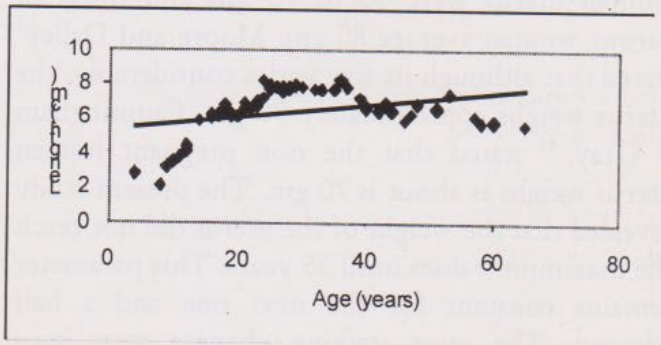

Fig:4 Relationship between age and length (n=50)

Discussion

Weight of the uterus

The uterine weight in the childhood was remarkably lower than that of adult series and it was similar to findings of Williams et al[6] who observed the average weight in premenercheal group 14 to 17 gm. After that the weight of the uterus increased abruptly by three and a half fold, which was also supported by findings of Woessner[8] and Hossain[7] .Such abrupt changes might be due to the hormonal influences on the uterus. In the middle aged group the weight was a little greater

than the early reproductive group. Woessner[8] reported that a uterus which has experienced multiple pregnancies contains more collagen and elastin than a nulliparous uterus. Therefore the difference between group A and B, and group B and C was may be due to the parity. In the postmenopausal group the weight decreased which may have a similar hormonal basis.

Hossain[7] studied 40 human uterus of Bangladeshi people ranging from 1 to 65 years. He observed that in different group weight ranged from 5 to 70gm The weight of different group observed by Hossain[7] is similar to that of the present study. Schwalm & Dubrauszky[9]examined 12 uteri from 25 to 45 years age group and showed that the weight of the uteri were between 70 to 100 gm. They also examined 16 uteri from 55 to 84 years age group and showed that weight of the uterus were 35 to 75 gm.

Langlois P[10] stated weight of the non-parous woman uterus were 50 to 70 gm and those of parous woman average 80 gm. Moore and Dalley[2] stated that although its size varies considerably, the uterus weighs approximately 90 gm. Cunningham F Gray [11] stated that the non pregnant human uterus weight is about is 70 gm. The present study revealed that the weight of the uterus did not reach the maximum values until 35 years. This parameter remains constant for the next one and decayed. The most striking ch beyond 46 years wher nt a postmenopausa[1] pported by Woessner[8]

Lengt'

The l observed by Bloom and Creis ily D[13]7cm. Sinnatamby[14] and Snel at's[16] 8-9cm. Woodburne T[17] and Willia at 7.5cm.

Hossain[7] studied 40 human uterus of different age groups the average mean(±SE) length of the uterus were 3.6 ± 0.27cm from 1to 12 years age group,6.87 ± 0.24cm from 13 to 24 years age groups,7.42 ± 0.21cm from 25 to 45 years age groups and 6.51 ± 0.30cm from 46 to 65 years age group respectively.

So the findings of the present study are similar to the findings of Hossain[7] but the values were little less than the above mentioned author and it may be due to racial variation and was also somewhat shrinkage due to fixation.

The average length of the uterus in the group A was much less than the group B and C.The length of the uterus than abruptly increases in the early reproductive group B and than gradually increases in the late reproductive period group C. In postmenopausal group D, the length was somewhat shorter than group B and C.

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ORIGINAL ARTICLE

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Correlation of pre operative serum level of CA 125 with FIGO stages of ovarian carcinoma

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Abstract

The present study was carried out with an aim to evaluate the correlation of preoperative serum CA 125 level with FIGO stages in ovarian carcinoma. Comparative Cross Sectional Study was done during the period of January, 2010 to December, 2010 in the Department of Pathology, SOMCH. Total 40 patients were selected from the indoor of Gynaecology and Obstetrics department in SOMCH & JRRMC on the basis of fulfilling inclusion and exclusion criteria. For staging purpose post surgical specimens were collected from the same study subject. Among the total 40 cases of ovarian carcinoma, 11 cases were staged as FIGO stage-I, 05 cases were stage-II, 23 cases were stage-III, and 01 case was stage-IV. The highest numbers were found as FIGO stage-III. In the case of CA 125, the lowest level was found 11.49 U/ml and highest level was found 498 U/ml. The mean (±SD) was 115.50 (±67). The mean values of serum CA 125 in stage-I, stage-II, stage-III and stage-IV were 42.72 U/ml, 71.40 U/ml, 149.43 U/ml, 498.00 U/ml respectively. Phi (φ) coefficient correlation test (r_φ) was done for the CA 125 mean levels and for the CA 125 positive cases with FIGO stages to see their correlation. The test was found significant. The preoperative assessment of serum CA 125 levels can predict the FIGO stages of the ovarian carcinoma before operation. As a result, the clinician can make a plan of treatment of the patient preoperatively and could be helpful for better management.

[OMTAJ 2013; 12(1)]

Introduction

Ovarian carcinomas comprise a diverse group of neop[illegible] range of morphological cha[illegible] manifestations, genetic alter[illegible] behavior than any other organ in[illegible] arian carcinoma accounts for the greatest number of deaths from malignancies of female genital tract and is the 5th leading cause of cancer fatalities in women[1-2]. According to the annual report (2005) of National Institute of Cancer Research and Hospital, Dhaka that the total prevalence of ovarian cancers were 3.8%[7].

The single most important prognostic indicator of ovarian cancer is the extent of the tumor at the time of diagnosis, the stage. 'The International Fedaration of Gynaecology and Obstetrics' (FIGO), is the widely accepted staging system for ovarian carcinoma[8].

With the bless of modern sciences, we use tumor markers for the staging correlation. At present serum CA125 is the gold standard tumour marker for this disease[4]. CA125 levels correlate with the widely used FIGO staging system. CA125 is elevated in approximately 50% of ovarian cancer patients with FIGO stage I, 70% of FIGO stage II, 90% of FIGO stage III and more than 95% of the FIGO stage IV[3-6]. Hence, staging of ovarian carcinoma assumes prime

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importance for patients who may receive chemotherapy or neoadjuvant therapy prior to resection of the tumor and in those who present with metastases[5].

Materials and Methods

This was a Simple Cross sectional Comparative study carried out in the department of Obstetrics and Gynaecology of SOMCH and JRRMC during the study period from January 2010 to December 2010 were included as the study population. Patients were enrolled on the basis of history, physical examination and fulfilling the inclusion and exclusion criteria. After proper explanation of the procedures to the patient, information were obtained by brief history with particular reference. Post surgical specimen was collected from the same study patient. The specimens were examined in the Department of Pathology M A G Osmani Medical College, Sylhet under p mass was examined with partic size, shape, number, consistency. On fluids and solidity are examined meticulously. Three representative tissue blocks of 3-5 mm thickness were taken from the specimens. For microscopic examination routine paraffin sections were stained with haematoxylin and eosins staining method.

The estimation of serum CA125 test was done by ELISA method in the immunological Laboratory of the department of Microbiology, M A G Osmani Medical College, Sylhet. The serum was preserved in micro-centrifuged tube at -20° C for analysis. All data were analysed by computer with the help of using SPSS version 17.0. Quantitative data was analyzed by mean and standard deviation (SD). Qualitative data was summarized by ratio and percentage. Correlation between FIGO stages of ovarian carcinoma and levels of serum CA125 were done by Phi (φ) coefficient correlation test (r_φ). p value < 0.05 was considered as significant and p value > 0.05 was considered as non-significant.

Prior to the commencement to the study, the research protocol was approved by the "Ethical Clearance Committee" of Sylhet M A G Osmani Medical College.

Results

Among the total 40 cases of ovarian carcinoma, 11 cases were staged as FIGO stage-I, 05 cases were stage-II, 23 cases were stage-III, and 01 case was stage-IV. The highest numbers were found as FIGO stage-III. It may be due to when the patient attended the physician, they produce themselves in worsen condition due to social barriers and maltreatment by local quacks. Of the total 40 cases of ovarian carcinoma, preoperative serum CA 125 values of all cases were estimated. In the case of CA 125, the lowest level was found 11.49 U/ml and highest level was found 498 U/ml. The mean (±SD) was 115.50 (±67). The mean values of serum CA 125 in stage-I, stage-II, stage-III and stage-IV were 42.72 U/ml, 71.40 U/ml, 149.43 U/ml and 498.00 U/ml respectively. The elevated (cut off value 35 U/ml) preoperative serum CA 125 levels were observed in 63.6% cases of FIGO stage I, in 80.0 % cases of FIGO stage II, in 86.9 % cases of FIGO stage III and in 100 % cases of FIGO stage IV. So the preoperative serum CA 125 had been increased with progressive FIGO stages in ovarian carcinoma. The results are shown in the following tables (Table I Table II).

FIGO stage	NO	Mean	Standard deviation
Stage-I	11	42.72	4.406
Stage-II	05	71.40	6.580
Stage-III	23	149.43	32.379
Stage-IV	01	498.00	11.676
Total	40	115.50	67.127

Table-I: Correlation of CA 125 means with FIGO Stages of ovarian carcinoma.

Serum CA 125	FIGO stage							
	Stage I		Stage II		Stage III		Stage IV	
	No.	%	No.	%	No.	%	No.	%
≤35 U/ml	4	36.4	01	20.0	03	13.1	0	0
>35 U/ml	7	63.6	04	80.0	20	86.9	01	100
Total	11	100.00	05	100.00	23	100.00	1	100.00

Table-II Correlation of CA 125 positive cases with FIGO stage of Ovarian carcinoma.

Phi (φ) coefficient correlation test (r_φ) was done for the CA 125 mean levels and for the CA 125 positive cases with FIGO stages to see their correlation. The

'p' values were 0.013 and 0.014 respectively in which both were <0.05. The Correlation was observed in both the instances were significant.

Discussion

The present study was designed with the aim to evaluate the correlation of preoperative serum level of CA125 with FIGO stages of ovarian carcinoma. In the present study, FIGO staging was determined from plain X-ray of whole abdomen, ultrasonography, ascitic fluid study, operative findings, gross and histopathological findings of tumor and lymph nodes status. Among the total 40 cases of ovarian carcinoma, 11 cases were stage-I (27.50%), 05 (12.50%) cases were stage-II, 23 (57.50%) were stage-III, and 1 (2.50%) case was stage-IV. The highest numbers were found as FIGO stage-III (57.50%) lesion which is similar to other authors[10-11].

In the present study, the mean preoperative CA125 levels were found according to the FIGO staging as follows: 42.72 U/ml in stage-I, 71.40 U/ml in stage-II, 149.43 U/ml in stage-III and 498.00 U/ml in stage-IV. It denotes that the mean CA125 level increases with the progressive FIGO stages of ovarian carcinoma. These findings are correlated well with other authors[10-11]. Based on the fact that, CA125 a cell surface bound mucin that is shed by proteolytic cleavage. It binds mesothelin that is found on the surface of peritoneal mesothelial cells as well as on ovarian surface epithelium.

In the present study, the CA 125 positive (cut off value 35 U/ml) cases were found as follows: 63.6% in stage-I, 80.0% in stage-II, 86.9% in stage-III and 100% in stage-IV. These observations are consistent with the studies done by others[11-12-13].

In conclusion, in the present study, our observations were that the preoperative serum CA125 levels correlates with FIGO stages and increases with progressive FIGO stages in ovarian carcinoma. The preoperative assessment of serum CA 125 levels can predict the FIGO stages of the ovarian carcinoma before operation. As a result, the clinician can make a plan of treatment of the patient preoperatively and could be helpful for better management.

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ORIGINAL ARTICLE

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A comparative study on the effect of oral clindamycin and azithromycin in treatment of chronic acne vulgaris

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Abstract

A prospective comparative study was conducted in the department of Dermatology and Venereology, Sylhet MAG Osmani Medical College and hospital, during the period from January 2010 to December 2010 with a view to find out efficacy and safety of clindamycin and azithromycin in the treatment of chronic acne vulgaris. Sixty five, aged and sex matched diagnosed chronic acne vulgaris patients were randomly distributed into two groups, clindamycin-group (n=35) and azithromycin- group (n=32). Clindamycin group was treated with clindamycin 300mg 12 hourly for 8 weeks and azithromycin group was treated with azithromycin 500 mg once daily for 3 consecutive day in a week for 8 weeks. Each patient was followed up every 2 weeks for 8 weeks period.

The numbers of inflammatory lesions (red papules and pustules) were counted on one side of the face at baseline and every follow up visits and the efficacy of both drugs was assessed by changing of lesion count and reducing the percentage of reduction of lesion count in different followed up.

The mean lesion count decreased at baseline and end of treatment were 29.5 ± 11.6 and 5.8 ± 5.5 respectively in clindamycin group and 28.9 ± 11.3 and 7.2 ± 6.6 respectively in azithromycin group. The reduction of lesion count lesion from baseline to end point of treatment was significant in both groups ($p<0.001$); but it was not significant between the groups ($p>0.05$).

The percentage reduction of lesion count was 29.9% at 2nd week; which decreased to 79.1% at the end of 8th week in the clindamycin group whereas 21.2% and 74.8% respectively in the azithromycin group. The percentage reduction of lesion count from 2nd week to end point of treatment was significant in both groups ($p<0.001$); but it was not significant between the groups ($p>0.05$).

At the end of 8th week of treatment the response was good in 66.7%, moderate in 18.2%, poor in 12.1% and no response in 3.0% of patients in clindamycin group; and it was 56.2%, 25.0%, 15.6% and 3.1% respectively in azithromycin group. The difference between groups statistically was not significant ($p=0.852$).

Regarding adverse effects, clindamycin group and azithromycin group experienced some form of adverse effects but did no vary significantly ($p=0.710$).

The present study showed that both clindamycin and azithromycin were equally effective drugs in treatment of chronic acne vulgaris with similar safety profile.

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Introduction

Acne vulgaris is a chronic inflammatory disease of pilosebaceous follicles characterized by comedones, papules, pustules and nodules. It is a common dermatological disorder in individuals aged 13-35 years which mostly involves face and trunk and lesions may vary in number during the natural course of the disease.[1,2].

The mechanisms of developing acne involve excessive sebum production, increased proliferation of keratinocytes, bacterial colonization and inflammatory reactions and it is enhanced by follicular rupture and subsequent leakage of lipids, bacteria, and fatty acids into dermis [3].

The choice of acne therapy is largely determined by the severity and extent of the disease. Patients with mild acne usually require topical treatment alone [4].Those with more extensive acne should be prescribed topical agents in conjunction with appropriate oral therapy [5]. Oral therapies included-antibiotics, clindamycin, aziyhromycin, tetracycline, doxycycline, erythromycin, cotrimoxazole, and minocycline;

Azithromycin is a macrolide that inhibits atypical intracellular pathogens, gram-positive and gram negative aerobic bacteria, including P acnes [6]. Clindamycin is a chloride-substituted derivative of lincomycin, is active against anaerobic infections [7] and has shown marked improvement, reducing colony counts of P acnes [8] to decrease the percentage of surface lipid free fatty acids the suspected inciting agents in the inflammatory phase of the disease and great promise in the treatment of acne [9].

Recent research has been focused to establish the role of azithromycin due to its safety, effectiveness and excellent patient compliance [10]and clindamycin is effective, popular [8]and most helpful alternative drug in the treatment of acne vulgaris [11].

With this view, we aimed to perform a comparative study on the effect of oral clindamycin and azithromycin in the treatment of chronic acne vulgaris.

Material and Methods

A prospective comparative clinical study was done to compare the efficacy and safety of oral clindamycin and azithromycin in the treatment of moderate to sever chronic acne vulgaris. The severity of acne vulgaris was estimated by counting number of inflammatory lesions (red papules and pustules) on the face at the initiation of the study. Based on inflammatory lesion count on half of face, acne was categorized into four groups[12] as:

1. Mild: lesion count 0-5 inflammatory lesions.
2. Moderate: Between 6 and 20 inflammatory lesions.
3. Severe: Between 21 and 50 inflammatory lesions.
4. Very severe: More than 50 inflammatory lesions.

The study was conducted on 70 male, female, age ranged 15to 35 years patients of moderate to severe acne, in the department of dermatology and venerology, MAG Osmani Medical College Hospital, during the period from January 2011-december 2011.

Study procedure:

After selection of the study population, Informed written consent was obtained from the patients after full explanation of the details of the disease process, options of treatment, ultimate outcome, possible side effects and complications and chances of recurrences and above all the purpose of the study. Study population were divided into group-A treated by clindamycin,300mg 8 hourly for 8 weeks and group-B treated by azithromycin 500mg thrice weekly for 8weeks and both groups were followed up 2 weekly for a period of 8 weeks.

The efficacy was assessed by counting the number of inflammatory lesions (red papules and pustules) on the face at every follow up visits.The percentage reduction of inflammatory lesion counts was calculated by comparing the count of one side of face at each follow up visits. The treatment outcome was determined by the percentage reduction of inflammatory lesion counts, e.g- a reduction of 80% or more was labeled as good, 50–79% as moderate, 20–49% as poor, and a reduction less than 20% as no response [13].

Safety and Tolerability of the drugs was assessed by the adverse events like nausea, epigastric pain, vomiting, anorexia, diarrhoea, constipation, weight loss, headache, bloody or tarry stool (pseudomembranous colitis), itching, skin rash and photosensitivity.

Results

The study was conducted on 65 male, female patients (33 in clindamycin and 32 in azithromycin treated group) with male, female ratio 46.2:53.8. In the clindamycin treated group (Group-A) 54.5% was male and 45.5% was female, while in Azithromycin treated group(group-B) 37.5% male and 65.2% female.

Age of the study patients ranged from 16 to 25 years. Mean age of clindamycin group (Group-A) was 22.24 $\pm$ 4.37 years with range of 17 to 33 years and mean age of azithromycin group was 22.03 $\pm$ 5.42 years with age range of 16 – 35 years. Sex –age comparison showed that in this study was age and sex matched. Out of 65 patients, 51 patients aged 16 to 25 years, suggesting acne is an early age disease.

The duration of acne vulgaris in the clindamycin group ranged from 9 months to 9 years and in the azithromycin group 4 months to 7 years. The mean duration of acne vulgaris of the patients in both groups was almost equal($z=1.054; p>0.05$).

Severity of acne vulgaris was moderate in 16 patients and severe in 17 patients in the clindamycin group whereas in the azithromycin group 17 and 15 patients repectively. The study groups were matched in term of severity ($p=0.708$).

The efficacy of both drugs was assessed by Change of lesion count and the percentage reduction of lesion count in different followed up interval presented in table-I and figure I.

Table- I showed the change in lesion count at different time interval in course of treatment. In the clindamycin group, the mean lesion count was 29.5 $\pm$ 11.6 before the initiation of treatment which decreased steeply to 21.8 $\pm$ 10.2 at 2nd week, 15.3 $\pm$ 8.7 at 4th week; 9.4 $\pm$ 7.6 at 6th week and 5.8 $\pm$ 5.5 at 8th week. In the azithromycin group, mean lesion count was 28.9 $\pm$11.3 before the initiation of treatment which decreased steeply to 22.8 $\pm$ 9.8 at 2nd week, 17.3 $\pm$ 8.8 at 4th week; 11.6 $\pm$ 8.1 at 6th week and 7.2 $\pm$ 6.6 at 8th week. Reduction of lesion count in both clindamycin and azithromycin treated group as estimated at the end of 2nd, 4th, 6th and 8th weeks as compared to baseline was significant ($F=231.473$; $p<0.001$). But when the lesion count of the two treatments were compared, there were no significant differences in lesions count estimated at baseline, at 2nd, 4th, 6th and 8th weeks.

Table-I: Change of lesion count at different follow up

Study group	Lesion count (mean± SD) at					†P value
	Baseline	2nd wk	4th wk	6th wk	8th wk	
Clindamycin (n=33)	29.5 ±11.6	21.8 ±10.2	15.3 ±8.7	9.4 ±7.6	5.8±5.5	<0.001
Azithromycin (n=32)	28.9 ±11.3	22.8± 9.8	17.3± 8.8	11.6± 8.1	7.2±6.6	
*P value	0.831	0.664	0.376	0.248	0.371	

Figure-I showed the percentage reduction of lesion count at different follow up interval. In the clindamycin group, percentage reduction of lesion count was 29.9% at 2nd week;48.3% at 4th week; 68.1% at 6th week and 79.1% at 8th week as compared to baseline. In the azithromycin group, the percentage reduction of lesion count was 21.2% at 2nd week; 42.6% at 4th week; 56.3% at 6th week and 74.8% at 8th week as compared to baseline. Percentage reduction of lesion count in both clindamycin and azithromycin treated groups as estimated at the end of 2nd, 4th, 6th and 8th weeks as compared to baseline was significant (†$p<0.001$). But when the effectiveness of the two treatment groups

were compared, there were no significant differences in percentage decrease in lesion counts estimated at the end of 2nd, 4th, 6th and 8th weeks.

Figure-I:

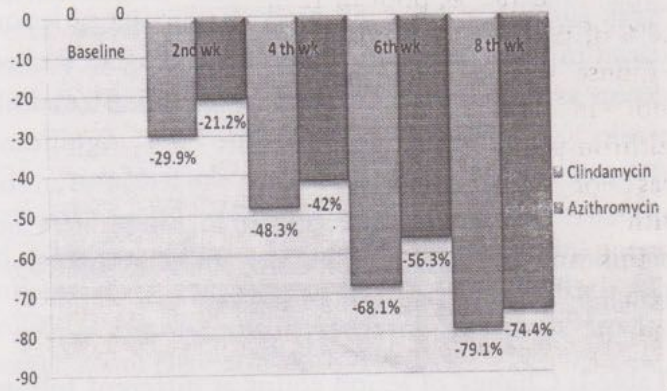

Table II showed that the response At the end of 4th week of treatment the response was good in 6.1%, moderate in 39.4%, poor in 48.5% and no response in 6.1% of patients in clindamycin group whereas, the response was moderate in 43.8%, poor in 50.0% and no response in 6.2% in azithromycin group. At the end of 4th week of treatment the response did not differ significantly (p=0.681).

And at the end of 8th week of treatment was good in 66.7%, moderate in 18.2%, poor in 12.1% and no response in 3.0% of patients in clindamycin group; whereas the response was good in 56.2%, moderate in 25.0%, poor in 15.6% and no response in 3.1% in azithromycin group. The difference between groups was not significant (p=0.852).

Table-II: Distribution of patients on response of treatment at the end of 4th and 8th week.

	At 4th week		At 8th week	
Response	Clin (n=33)	Azith(n=32)	Clin (n=33)	Azith(n=32)
No response	2 (6.1)	2 (6.2)	1 (3.0)	1 (3.1)
Poor	16 (48.5)	16 (50.0)	4 (12.1)	5 (15.6)
Moderate	15 (39.4)	14 (43.8)	6 (18.2)	8 (25.0)
Good	2 (6.1)	0 (0.0)	22 (66.7)	18 (56.2)

In this study, the clindamycin group adverse effects were nausea (12.1%), epigastric pain (9.1%), photosensitivity (3.0%), itching (3.0%) and diarrhoea (3.0%); while in the azithromycin group, nausea (9.4%), epigastric pain 3(9.4%), diarrhoea (3.1%), constipation (6.2%) and anorexia (6.2%). No difference in adverse effects of treatment between the groups

Discussion

Acne commonly afflicts young adults, especially women, and remains a major cause of visits to the physician's office. Effective treatment is essential to prevent facial deformity and physical scarring. Systemic antimicrobial therapy, aimed to reduce inflammatory papules and cysts, often leads to adverse effects, e.g, gastrointestinal symptoms, headaches, and vulvovaginal candidiasis. For the least 30 years, oral broad-spectrum antibiotics, such as tetracyclines and macrolides, have been used for the treatment of inflammatory acne without an officially approved indication. Because the short half-life, commonly prescribed antimicrobials necessitates administration several times a day. A drug with prolonged action would permit less frequent dosage and thus improve patients compliance. Such an agent, would be safe, cost-effective, well tolerated, effective in the treatment of acne [6].

Macrolide antimicrobials (like erythromycin) exert a broad spectrum of activity against a number of common microbial pathogens and are well absorbed orally. Azithromycin, a macrolide antibiotic, effectively inhibit intracellular pathogens as well as Gram-positive and Gram-negative aerobic and anaerobic bacteria. Azithromycin that affinity for inflammatory tissue, and exhibit antimicrobial activity, including Propionibacterium acnes, which is inhibited in vitro at minimum inhibitory concentrations for 90% of isolates of 0.15 μg/mL or less [6]. Successful use of azithromycin for the treatment of acne has been reported previously[1,13,14,15].

Clindamycin, a synthetic derivative of lincomycin namely 7-chloro-7-deoxylincomycin has been stated to be efficacious in the treatment of acne in several controlled studies[8,9,16,17]. Its efficacy in the reduction of free fatty acid content of sebum by suppressing the production of exracellular lipase and in reducing colony counts of Propionbacterium acnes has also been demonstrated[8].

In the current study the age of the patients was ranged from 16 to 35 years with the mean age of

22.14 ± 4.88 years. One study conducted in Sylhet MAG Osmani Medical college hospital [18] the age of the patients with acne ranged from 13 to 42 years with the mean age of 22.59 ± 6.02 years which was observed similar with the present study[19].

Current study showed that 46.2% of patients with acne vulgaris were male and 53.8% were female suggesting female preponderance. There were 54.5% male and 45.5% female in the clindamycin group; whereas 37.5% male and 65.2% female in the azithromycin group ($p=0.168$) suggesting a sex matched study. Similar female preponderance with observed in other studies.[20,21]

In this study, the duration of acne vulgaris in the clindamycin group ranged from 9 months to 9 years with the mean of 2.92 ± 1.84 years; whereas the duration of acne vulgaris in the azithromycin group ranged from 4 months to 7 years with the mean of 2.47 ± 1.62 years ($Z=1.054$; $p>0.05$) suggesting duration matched study.

In the current study, the mean lesion count was 29.5 ± 11.6 before the initiation of treatment which decreased steeply to 21.8 ±10.2 at 2nd week, 15.3 ±8.7 at 4th week; 9.4 ±7.6 at 6th week and 5.8 ± 5.5 at 8th week in the clindamycin group. Whereas in the azithromycin group, mean lesion count was 28.9 ± 11.3 before the initiation of treatment which decreased steeply to 22.8 ± 9.8 at 2nd week, 17.3 ± 8.8 at 4th week; 11.6 ± 8.1 at 6th week and 7.2 ± 6.6 at 8th week. Reduction of lesion count in both clindamycin and azithromycin treated group as estimated at the end of 2nd, 4th, 6th and 8th weeks as compared to baseline was significant ($p<0.001$). But when the lesion count of the two treatments were compared, there were no significant differences.

In the present study, the percentage reduction of lesion count was 29.9% at 2nd week; which decreased steeply to 48.3% at 4th week; 68.1% at 6th week and 79.1% at 8th week as compared to baseline in the clindamycin group.

In the azithromycin group, the percentage reduction of lesion count was 21.2% at 2nd week; which decreased steeply to 42.6% at 4th week; 56.3% at 6th week and 74.8% at 8th week as compared to baseline. Percentage reduction of lesion count in both clindamycin and azithromycin treated group as estimated at the end of 2nd, 4th, 6th and 8th weeks as compared to baseline was significant. But when the effectiveness of the two treatment groups were compared, there were no significant differences.

The current study showed that at the end of 8th week of treatment the response was good in 66.7%, moderate in 18.2%, poor in 12.1% and no response in 3.0% of patients in clindamycin group; whereas the response was good in 56.2%, moderate in 25.0%, poor in 15.6% and no response in 3.1% in azithromycin group. The difference between groups was not significant. These findings were similar with[13,14,22].

In this study, the clindamycin group adverse effects were nausea (12.1%), epigastric pain (9.1%), photosensitivity (3.0%), itching (3.0%) and diarrhoea (3.0%); while in the azithromycin group, nausea (9.4%), epigastric pain 3(9.4%), diarrhoea (3.1%), constipation (6.2%) and anorexia (6.2%). No difference in adverse effects of treatment between the groups.

In conclusion, with this observation, both clindamycin and azithromycin were equally effective drugs in treatment of chronic acne vulgaris with similar safety profile.

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ORIGINAL ARTICLE

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Hyperinsulinemia in non-obse and non-diabetic patients with essential hypertension

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Abstract

Essential hypertension depends on interaction between multiple genetic and environmental factors. This comparative study was designed to investigate the serum insulin levels among hypertensive patients and to study the possible relation with blood pressure, body mass index (BMI) and cholesterol. Total 60 subjects of 20-60 years of age were studied and grouped into two groups (Gr-I-Cases, n=30 with essential hypertension , Gr-II- controls age and sex matched healthy subjects, n=30). Secondary causes of hypertension (HTN), persons taking lipid lowering drugs, pregnancy, Diabetes mellitus (DM), Dyslipidemia, were excluded. Fasting serum Insulin, Fasting blood glucose (FBG) and serum lipid profile were estimated. Study showed significantly high (P<0.001) levels of insulin (37.823±7.272μU/ml) among the Hypertensives compared to controls(10.383±1.29μU/ml). A significant positive correlation was found (r=0.271 & sig 0.05level) between serum Insulin and serum Triglyceride. A significan correlation was obsertved with Systolic BP & diastolic BP(level of significance 0.01). Correlation of serum Insulin with BMI and blood sugar level was weekly negative and insignificant. In conclusion, serum insulin levels are significantly higher among hypertensive and significantly correlated with serum cholesterol levels compared to controls.

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Introduction

Epidemiological studies have shown that Insulin is a risk factor for coronary heart disease. Nearly 40 years ago, Welborn and colleagues observed that nondiabetic patients with essential hypertension had significantly higher plasma insulin concentrations than did normotensive individuals. This positive relationship has been confirmed in several longitudinal studies, but the results are not entirely consistent. In some studies, the association between hyperinsulinemia and incident hypertension disappeared after adjustment for body mass index, suggesting that the association is confounded or mediated through obesity. Therefore, the causal role of insulin resis ance/ compensatory hyperinsulinemia in the develop nent of hypertension continued to be debated.

In order to understand the relationship between insulin resistance and clinical syndrome associated with the defect in insulin action, it is necessary to discuss the relative roles of insulin resistance versus compensatory hyperinsulinemia in bringing about these changes. Insulin-mediated glucose disposal varies widely in apparently healthy, nondiabetic individuals. However, not all tissues share the defect in insulin action. Our demand for fuel varies from moment to moment, but for normal functioning of brain blood sugar level needs to remain stable. The body monitors blood sugar levels and release insulin in just the right amounts. That's why a healthy body is described as 'insulin sensitive'. But in certain conditions- the cells quit responding to this signal. at this point the body is "insulin resistant". One immediate consequence is that the body is forced to release even more insulin.

Letting blood sugar get too high is simply not acceptable. The resulting excess of insulin in the bloodstream is called hyperinsulinemia. But the body wasn't designed for these prolonged high levels of insulin, which disrupt cellular metabolism and spread inflammation. There are many negative health effects before full-blown diabetes. Several mechanisms whereby insulin resistance could cause an alteration in

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lipid metabolism have been described. Hyperinsulinemia is known to enhance hepatic very-low-density lipoprotein synthesis and thus may directly contribute to the increased plasma triglyceride and LDL cholesterol levels. Resistance to the action of insulin on lipoprotein lipase in peripheral tissues may also contribute to elevated triglyceride and LDL cholesterol levels. Excess amount of insulin needed to overcome insulin resistance (loca... muscle and adipose tissue) has adv... ...ct on tissues that remain normally insulin sensitive. Muscle tissue and adipose tissue differ in the nature of their dose response to insulin. Adipose tissue is much more insulin sensitive. This difference in the insulin dose-responce curve of the two tissues are essential for normal energy metabolism.

When insulin levels are low after an overnight fast, the anti-lipolytic effect of insulin is minimal, Free fatty acid (FFA) release from adipose tissue stores is accentuated, and relatively little glucose is taken up by muscle. Once food is consumed, plasma insulin concentrations increase, muscle glucose uptake is maximized, and the effect of insulin on adipose tissue is to enhance glucose disposal and inhibit further breakdown of stored Triglyceride (TG) to FFA.
Fasting insulin levels correlate with systolic blood pressure, and the drop in blood pressure following weight loss is related to the improvement in insulin sensitivity.This work was aimed to study the serum insulin levels in our own hypertensive groups & compare the results with normotensive controls as well as to study the correlation with lipid profile.

Materials and Methods

Thirty, non obese, nondiabetic patients with untreated essential hypertension and 30 normotensive normoglycemic controls were studied. All those subjects with history, clinical or electrocardiographic evidence of coronary artery disease were excluded. A detailed history & physical examination was carried out in each patient including measurement of blood pressure, height & weight. Body mass index was calculated by using formula-

BMI= Weiht in Kg/(Ht in Cm)2

BMI between 20-25 was taken as normal weight, 25-29 overweight and >30 obese,Blood was drawn using aseptic measure after an overnight fast for the determination of serum insulin, blood sugar, serum cholesterol, triglyceride & HDL. Correlation coefficient between serum Insulin level, blood pressure & lipid levels calculated. Permission was taken from the ethical committee of Sylhet MAG Osmani Medical College (SOMC). Informed written consent was taken from each participant under study.

Results were expressed as mean ± SD or median where applicable. Analyses were done by SPSS using the relevant tests of significance. (Students unpaired 't' test, Spearman's correlation test, Mann-Whitney test).

There is a growing body of evidence indicating that adipocytes produce several cytokines, the so-called adipokines, such as leptin, TNF-α, NEFAs, adiponectin, resistin and angiotensinogen, which can influence insulin sensitivity. according to the contribution of visceral fat to insulin resistance, a recent study revealed that mice fed with a high-fat diet showed up-regulation of the angiotensinogen gene expression in the visceral fat but not subcutaneous fat. In obese humans, the levels of the circulating components of the RA system are elevated, however, weight loss is associated with a decrease in the levels of these components of the RA system. A-II, is well known to be a key substance influencing endothelial function and involved in the development of cardiovascular disease, through the activation of NADPH oxidase. Moreover, A-II is also involved in the development of insulin resistance, possibly by oxidative stress.

Results

Results were presented in tabulated form.

Table-I: Clinical characteristics of study subjects

Characteristic		Hypertensive (30)	Normotensive (30)
Age		41.20±9.02	43.21±7.40
Sex	Female	12	16
	Male	18	14
Body Mass Index		25.80±3.43	24.00±3.92
Systolic Blood Pressure		143.50±5.28	121.67±9.13
Diastolic Blood Pressure		92.50±5.53	86.55±7.00

Table II: Comparison of Biochemical parameters between hypertensive & Normotensive study subject

Parameters	Hypertensive (30)	Normotensive (30)	P value
serum Insulin (μU/L)	37.823±7.272	10.383±1.29	<0.001
Blood sugar fasting(mg%)	89.93±8.878	92.70±8.018	Not significant
serum cholesterol (mg%)	191.80±33.918	173.90±26.838	Not significant
serum triglyceride	201.43±41.834	174.10±50.513	Not significant
Serum LDL	114.00±33.363	99.73±30.524	Not significant
Serum HDL	38.47±6.021	39.63±5.822	Not significant

Table III: Correlation of fasting serum Insulin to lipid profile Parameters of Hypertension

Parameters	correlation coefficient	significance of Correlation
Systolic Blood Pressure	.366	.004*
Diastolic Blood Pressure	.410	.001*
Serum Cholesterol	.129	.324
Serum Triglyceride	.271	.037*
Serum LDL	.038	.774
Serum HDL	.129	.326
Blood sugar fasting	-1.267	.210

*Spearman correlation test done and $P < 0.05$ was the level of significance

Discussion

A comparative study was carried out to see the association of hyperinsulinemia with essential HTN. There was no significant difference of age and BMI but difference of blood pressure (BP) parameters between cases and controls. Serum insulin did not follow normal distribution and thus median value was considered for statistical analysis. We found significant difference of S. insulin between cases and controls ($p<0.05$). Our result was consistent with findings of Lissner et al (1992), who evaluated the role of hyperinsulinemia in the development of essential hypertension in a prospective study in Sweden. It was found that high fasting insulin (at base line) subsequently developed hypertension over 12 years follow up period.

In our study there was significant difference of Total cholesterol (TC), TG between hypertensive cases and normotensive controls. Zavaroni et al (1992) found high TG in patients with hypertension and hyperinsulinemia. Serum Insulin showed significant positive correlation with TG when correlated in total study subjects (n=60). Our result was consistent with Zavaroni et al (1989) who found significantly raised TG in subjects with hyperinsulinemia with raised systolic and diastolic BP. In an animal study Insulin and TG were significantly raised in spontaneously hypertensive rats.

...relation of Insulin with only TG but not w... ...ractions of lipid profile- might be the degree of IR- with increasing severity there might be increasing dyslipidaemia. In our study-serum Insulin showed no correlation with any BP parameters in study cases with sample size 30. But when total study subjects with sample size 60- were correlated, there were significant correlation with all BP parameters (SBP, DBP). This finding was consistent with Lucas et al (1985), who found that both SBP and DBP were related to el evated fasting Serum Insulin. Probably larger sampl size in total study subjects showed the trend of hypertension development in hyperinsulinemic persons.

In conclusion, it may be concluded that hyperinsulinemia and insulin resistance are associated with essential hypertension. Further more, this is a small study, the results of which are needed to be varified on larger scale. Our observation corresponds to the results obtained by many studies conducted in the west which have demonstrated hyperinsulinemia to be a feature of hypertension. study with larger sample size with longitudinal follow up for insulin status and IR of risk groups having familial predisposition to essential HTN –may be recommended. This may warn risk people to modify life style and dietary habits so that development of essential hypertension may be delayed.

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RESEARCH ARTICLE

The Osmani Medical Teachers Association Journal Volume 12 Number 1

Usg-Guided Fine Needle Aspiration Cytology (FNAC) In The Diagnosis Of Intestinal Mass

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Abstract

The present study was carried out with the aims to diagnose intestinal masses by FNAC with the help of ultrasonography guidance and to determine the diagnostic accuracy of FNAC. Fifty six consecutive patients were studied during the period from January 2005 to December 2005. Histopathological examination was done to correlate with the cytologic diagnosis. The results of comparative study of USG-guided FNAC and histopathology were significant (P value was < 0.001). In USG-guided FNAC, it was found that 28 were malignant tumors, 25 were inflammatory and 3 were inadequate materials. As a whole test results of USG-guided FNAC were sensitivity 90.32%, specificity 100%, positive predictive value 100%, negative predictive value 89.29% and accuracy 94.64%. USG-guided FNAC has been proved to be a rapid, reliable and cost-effective diagnostic method and may also obviate the need for any type of surgery at all in many cases.

[OMTAJ 2013; 12(1)]

Introduction

An accurate preoperative diagnosis is invaluable in the management of patients with intestinal masses. Diagnosis of the exact nature and cause of the intestinal mass at the tissue level are necessary before specific treatment is given. Fine needle aspiration (FNA) biopsy has proved its usefulness in the diagnosis of a wide variety of benign and malignant neoplasms[1].

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Diagnostic cytology helps to establish the presence or absence of malignant neoplasm as well as benign lesions. The method has much to offer by saving patients from inappropriate operations and investigations and allowing surgeons to plan quickly and more rationally. FNAC is quicker to report and easily repeatable.

Modern imaging ...
extended to vir...
USG guida...
safely sampled ... of the body are now routinely biopsied under guidance. In case of very small mass or non palpable deep mass, FNAC can be done with the help of imaging modalities like ultrasound to increase the probability of obtaining a representative sample[3]. The aspiration of large, deep-seated intestinal masses requires radiologic guidance to ensure the sampling of viable solid areas of the tumor. FNAC is increasingly being applied to paediatric tumours since it permits a rapid diagnosis with minimal intervention and carries low complication rates. Large paediatric abdominal mass that requires preoperative chemotherapy to shrink the tumor to an operable size, emphasize the need for such diagnostic procedure which would be of great value if accuracy and correct cell typing could be achieved.[4]

Ultrasonically guided fine needle aspiration biopsy can sample intra-abdominal masses.[5]

Materials and Methods

This study was perfomed in the Department of Pathology, Sylhet MAG Osmani Medical College, Sylhet, during the period from January 2005 to December 2005. Among the patients with intestinal

masses attending outpatient and inpatient departments of Sylhet MAG Osmani Medical College Hospital, 56 patients were selected consecutively. FNAC were done in these patients. In this method the representative cellular aspirates is collected with fine bore needle, stained by Papanicolaou's stain and examined under microscope. Out of 56 patients, biopsy was available in all the cases for histopathological examination to correlate with the cytologic diagnosis.

A detail clinical history was taken and relevant examinations were done. Findings of all investigations were recorded in a register book. Informed consents were obtained from all patients. FNAC was done prior to biopsy in different settings. The cytopathological examination of the slides was histopathological were examined to for malignant

Specimens were co surgical excision and needle biopsy. For microscopic examination routine paraffin sections were stained with Haematoxylin and Eosins staining method.

The number of false-positives and false-negatives were obtained using the criteria as[6]. All data were analyzed by standard statistical methods[7,8] and various indices such as sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated. The Chi-square test and Pearson correlation test were done by using SPSS version 12.

Result

Cytological diagnosis of 56 intestinal masses:
Satisfactory smears were obtained in 53 cases and 3 were inadequate materials. Cytopathological diagnosis was made in 53 cases. 28 were adenocarcinoma, 25 were tuberculosis and 3 were inadequate materials. Results of USG-guided FNAC is shown in table no-I.

Histopathological findings of 56 abdominal masses:
Of the 56 abdominal masses 28 showed adenocarcinoma, 25 tuberculosis,1 adenoma, 2 leiomyoma. Results of histopathological findings is shown in table no-II.

Comparison between histopathological & cytopathological diagnosis:
This is shown in table no- III.

Sensitivity, specificity, ppv, npv and accuracy of USG-guided FNAC:
They are as below respectively
90.32%, 100%, 100%, 89.29% and 94.64%.
True positive were 28%, True negative were 25%, False negative were 3% and False positive were 0%.

As a whole result of USG-guided FNAC:
As a whole test results of usg-guided FNAC were sensitivity 90.32%, specificity 100%, positive predictive value 100%, negative predictive value 89.29% and accuracy 94.64%. True positive were 28%, true negative were 25%, false negative were 3% and false positive were 0%. This has been shown in table no- IV.

Table-I: USG-guided FNA diagnosis of 56 intestinal masses:

USG-guided FNA diagnosis	No of cases
Adenocarcinoma	28
Tuberculosis	25
Inadequate materials	3
Total	**56**

Table-II: Histopathological diagnosis of 56 intestinal masses:

Histopathological diagnosis	No of cases
Adenocarcinoma	28
Tuberculosis	25
Adenoma	1
Leiomyoma	2
Total	**56**

Table-III: Comparison between histopathological & cytopathological diagnosis:

Histopathological diagnosis	No	USG-Guided FNAC diagnosis	No
Adenocarcinoma	28	Adenocarcinoma	28
Tuberculosis	25	Tuberculosis	25
Adenoma	1	Inadequate material	1
Leiomyoma	2	Inadequate materials	2
Total	**56**		**56**

Table-IV: As a whole result of USG-guided FNAC.

USG-guided FNAC	Test values (%)
Sensitivity	90.32
Specificity	100
PPV	100
NPV	89.29
Accuracy	94.64
True positive	28
True negative	25
False negative	3
False positive	0

PPV= Positive predictive value. NPV= Negative predictive value.

Discussion

USG-guided FNAC were done in fifty six patients with intestinal masses for pathological diagnosis. In FNAC, in the present series, sensitivity was found 90.32%, specificity was found 100%, predictive value of positive diagnosis was 100%, predictive value of negative diagnosis was 89.29% and accuracy was 94.64%. Sundaram et al and Lees et al[9] found Sensitivity 77% and 96.3%, specificity 100% and 100%, predictive value of positive diagnosis 100% and 100%, predictive value of negative diagnosis 76.9% and 85.7%. They found accuracy 96.02% and 95% respectively.

In the present study 3 inadequate smears were found. Later on these 3 cases were found as false negative when histopathological findings were obtained. Reviewing the literature, it was found that false negative results were less in USG-guided aspiration. Frable (1983)[10] found 7%, Zajicek et al (1980) found 7.9% and Frable and Frable (1979) found 2.1% (cited by Innes et al [11] (1982). In the present study the rate of inadequate smear was less than that of above investigators.

The results of comparative study of USG-guided FNAC and histopathology were significant (P value was < 0.001).The accuracy of FNAC depends on clinical history, physical examination, better preparation and careful evaluation of smear. It was evident that FNAC is a simple, reliable and acceptable procedure for the diagnosis of abdominal mass. It can be repeated if necessary. It also helps in confirmation of clinical information without surgical biopsy.

All the findings of the present study were not always consistent with the findings of the other workers because this study was done in a small sample, the study period was short and the samples were collected only from Sylhet MAG Osmani Medical College Hospital. But in some cases the findings were more accurate than the findings of the other workers.

In conclusion,. the result of the present study is encouraging though it was done on a small sample, locality based and in a short period. It should be done in a large scale to obtain more accurate results with the close cooperation among the clinicians and cytopathologists, which will reduce the cost effectiveness of the patients and sometimes un-necessary surgery. So doing USG-FNAC we can provide better service to the patients and thus decrease the mortality and morbidity of the patients.

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ORIGINAL ARTICLE

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Comparisons of Semisolid Agar Antifungal susceptibility test with the CLSI M-38 broth Microdilution test for susceptibility testing of dermatophytes.

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Abstract

Although CLSI recommended antifungal susceptibility test is developed but it is not routinely practice for many difficulties to perform. A simple Semisolid Agar Antifungal susceptibility (SAAS) test emerged for screening drug susceptibility for both yeast and moulds. The results of SAAS screening test was assessed by comparing MICs of three commonly prescribed antifungal drugs namely-fluconazole(FCZ), itraconazole(ITZ) and terbinafine (TER) with the results of the Clinical Laboratory Standard Institute (CLSI) reference broth microdilution method for 29 *t.rubrum* clinical isolates. In SAAS test 0.5% agar with BHI broth media used and MICs were read visually after incubation at 35° c for 72 hours. CLSI reference method was performed in according to M-38 A. Comparison of test – concordance of MIC results betweens tests was defined as the percentage of MIC results by both methods that fell within three drug dilutions (1 dilution) for each isolate. In SAAS test twenty five (86.1%) were within MIC range of 0.5-64μg/ml and four (13.7%) had MIC value ≥ 64μg/ml for FCZ. In CLSI test twenty four (89.5%) were within MIC range of 0.5-64μg/ml and five (10.3%) had MIC value ≥ 64μg/ml for FCZ. In both tests all isolates (100%) were within MIC range of 0.03-16μg/ml in case of both ITZ and TER. In consideration of MIC range the results of SAAS test were comparable with the results of CLSI reference broth microdilution method. Among the three antifungal drugs terbinafine was most effective drug against *T.rubrum* than ITZ and FCZ. SAAS test is simple, widely applicable and may be effective method for screening of drug susceptibility of antifungal agents against dermatophytes.

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Introduction

Dermatophytosis is a worldwide fungal infection and more common in tropical and sustropical countries like Bangladesh [1 2 3]. In spite of available antifungal drugs in the market dermatophytosis associated with relapse after cessation of therapy may be due to development of drug resistance [1 3]. Antifungal drug susceptibility test of available antifungal drugs against dermatophytes will help to clinician for the proper drug selection and effective treatment of patient. But there is no suitable, standardized and widely applicable method for drug susceptibility testing of dermatophytes [4].

The Clinical Laboratory Standards Institute (CLSI) recommended a reproducible standarad methodology M-38 A for antifungal drug susceptibility testing of moulds [5]. Although broth micro dilutions method is a standard method but without reference laboratory this method is difficult to perform because requirement of special equipment, media, spectrophotometric inoculum preparation based on conidial size and expertisement [5 1]. However for the result of drug susceptibility test leads to unnecessary delay and dependence to the reference laboratory in CLSI method [6].

Many investigators have focused on Semisolid Agar Antifungal Susceptibility testing method for screening drug susceptibility of both yeast and mould which can possible to perform with minimum requirement in any microbiological laboratory [6 7 8]. In this method 0.5% agar with BHI media were used and inoculum prepared from original culture growth without special equipment and expertise. Growth in the test tube is visualized and scored as 0(100% inhibition), 1+ (≥75% inhibition), 2+ (≥50% inhibition), 3+ (≥25% inhibition), 4+ (growth as control) [6 7]. Though it is a screening method because of its simplicity it may be useful for susceptibility testing of antifungal agents against dermatophytes.

The purpose of the study was to compare results of drug susceptibility testing in Semisolid Agar

Antifungal Susceptibility (SAAS) method with broth micro diilution method for three commonly prescribed antifungal agents namely- fluconazole(FCZ), itraconazole(ITZ) and terbinafine(TER) against 29 clinical isolates of *T.rubrum*.

Materials and Methods

Ethical aspects: Ethical clearance was taken from Institutional Review Board of BSMMU and was approved on 17/10/11.

Test isolates

A total of twenty nine *T.rubrum* strains obtained from clinical specimen like skin and nail were studied. These were isolated by culture in Sabouraud dextrose agar (SDA) and Dermatophyte test medium (DTM). The cultures were maintained in sterile distilled water at room temperature. For antifungal susceptibility test, the strains were sub cultured on potato dextrose agar (PDA) at 28° C for 7 days to ensure the viability and purity of the isolates

Antifungal agents:

Three antifungal agents including - fluconazole (FCZ), itraconazole (ITZ) and terbinafine (TER) were studied. These obtained (Square pharmaceuticals, Bangladesh) in the form of dry powder with known potencies (100%). FCZ was dissolved in sterile distilled water and ITZ & TER were dissolved in dimethylsulfoxide (DMSO). Each drug was prepared according to the manufacturer's direction and as described for the CLSI method [5].

Antifungal susceptibility testing

Test procedure of SAAS method:

Preparation of stock solutions, working solutions and antifungal drug supplemented media:

Stock solutions of drugs were made as follows. FCZ was dissoloved in sterile distilled water at concentration of 1280μg/ml; ITZ and TER were dissoloved in 100% dimethyl sulfoxide at concentration of 1600μg/ml. The same diluents were used to make two fold dilutions (working solution). The drug concentration ranges as follows FCZ: (0.125 to 64 μg/mL), ITZ: (0.03 to16 μg/mL), and TER: (0.03 to16 μg/mL).

Five milliliter aliquots of semisolid agar (BHI broth contains 0.5% agar base) at a ph of 7.4 were prepared in glass tubes under sterile condition. Specific concentration of antifungal working solution of each drug was added to the media and kept at 45 to 50°c in water bath to achieved the final concentration of drugs e g FCZ (0.125 to 64 μg/mL), ITZ: (0.03 to16 μg/mL), and TER: (0.03 to16 μg/mL). Drug free media were prepared to use for growth control (positive control). After cooling, both the drug- supplemented and drug free media containing tubes were stored in sealed plastic bags at 4-8°C.

Inoculum preparation and incubation:

T. rubrum were grown in PDA media at 25°c for 4 days and were covered with 4 to 5 ml sterile normal saline and gently rubbed by sterile cotton swab stick soaked with Tween 80, and suspension were transferred to a sterile tube. The suspensions were vortexed if heavy particles persisted they were allowed to settle and the homogeneous suspension was adjusted to achieve a turbidity of 0.5 McFarland standard. The semisolid agar media containing specific concentration of antifungal agents (FCZ, ITZ and TER) as well as drug-free controls were prepared in duplicate. Both the media were inoculated with one loopful (Himedia Flexiloop 4) of inoculum suspension by inserting the loop deep within the semisolid agar. A loopful of the inoculum suspension was streaked on to SDA to check for purity and viability of isolated dermatophytes.

Test procdure of CLSI method:

In CLSI recommended (clinical and laboratory standard institute) reference method RPMI-1640 buffered with MOPS were used as media. Microtiter plate preparation with three drug dilutions, inoculum preparation, inoculation, and incubation were performed in accordance with CLSI- M-38 document [5].

Determination in vitro susceptibility:

MICs of the antifungal agents (FCZ, ITZ and TER) were determined by visual inspection for both SAAS and CLSI broth micro dilution test by comparing all tubes or wells with drug free control growth and scored as 4+ (Growth comparable to that of drug free control), 3+ (growth approximately 75% of that of control), 2+ (growth approximately 50% of that of control), 1+ (growth approximately 25% or less than that of control), 0 (No visible growth). MIC was defined as the lowest concentration of drug that produced significant inhibition of growth and it also depends on types drug (approximately 80% in azole and 100% in Terbinafine) [1].

Comparison of test – concordance of MIC results betweens tests was defined as the percentage of MIC results by both methods that fell within three drug dilutions (1 dilution) for each isolate.

Results

TableI: MIC of antifungal agents (FCZ, ITZ and TER) in both SAAS and broth microdilution method against *T. rubrum* (n=29).

Name of antifungal agents	MIC range μg/ml	SAAS method N (%)	Broth microdilution method N (%)
FCZ	0.5-16	16 (55.1)	22(75.8)
	32-64	9(31.0)	4(13.7)
	>64	4(13.7)	3(10.3)
ITZ	0.03-0.5	15(51.7)	25(86.2)
	1-4	8(27.5)	3(10.3)
	8-16	6(20.6)	1(3.4)
TER	0.03-0.5	16(55.1)	24(82.7)
	1-4	8(27.5)	5(17.2)
	8-16	5(17.2)	00

Table- II: MIC of FCZ, ITZ and TER against *t. rubrum (n=29).*

Antifungal agent	MIC range (μg/ml)	SAAS Method		Broth Microdilution Method	
		MIC-50 (μg/ml)	MIC-90 (μg/ml)	MIC-50 (μg/ml)	MIC-90(μg/ml)
FCZ	0.5-64	16	>64	2	>64
ITZ	0.03-16	0.5	8	0.06	1
TER	0.03-16	0.5	8	0.06	2

Table 1 shows MIC value of antifungal agents (FCZ, ITZ and TER) in both SAAS and CLSI broth microdilution method against twenty nine *T.rubrum*. In SAAS test *twenty five* (86.1%) isolates and in broth microdilution twenty six (89.5%) were within recommended MIC range of (0.5- 64 μg/ml) for FCZ. In SAAS four (13.7%) and in CLSI method three (10.1%) were not within recommended MIC range (≥ 64 μg/ml) for FCZ. In SAAS twenty three (79.2%) and in CLSI method twenty eight (96.5%) were within MIC range of 0.03- 4 μg/ml for ITZ. Six (20.6%) in SAAS and one (3.4%) were in CLSI method within MIC range of 8-16μg/ml for ITZ. In case of TER twenty four(82.6%) in SAAS test and twenty nine (99.9%) were in CLSI method within MIC range of 0.03-4μg/ml. Five (17.2%) isolates were within MIC range of 8-16 μg/ml In SAAS method only and none was in MIC range in CLSI method for TER.

Table 2 also showed MIC_{50} and MIC_{90} of three antifungal agents (FCZ, ITZ and TER) in both SAAS and CLSI broth microdilution methods where 50% and 90% isolates were inhibited by each drug. For FCZ in comparison of both methods MIC^{90} was same but MIC^{50} was higher than CLSI method. In case of both ITZ and TER MIC50 and MIC90 were almost two or three dilution higher in SAAS test than broth microdilution method. The order of antifungal activity of three drugs against *T.rubrum* were as follows terbinafine ≥ itraconazole ≥ fluconazole.

Discussion

Although antifungal drugs are available for the treatment of dermatophytosis but now a day's fluconazole showing less effectiveness against dermatophytes [3 9 10]. The lake of simple, widely applicable and reproducible antifungal susceptibility test leads to inappropriate drug selection and treatment. Not available study regarding antifungal susceptibility test in Bangladesh. The semisolid Agar antifungal susceptibility test was developed for rapidly screening of antifungal agents against both yeast and moulds in any microbiological laboratory [6 7]. SAAS test differs from CLSI reference broth microdilution method in different ways. Special synthetic RPMI-1640 is used as media and spectrophotometric inoculumn preparation based on conidial size is needed in CLSI test method. As in SAAS method no need to prepare calibrated inoculumn, special media and equipment so it can be easily applicable in any laboratory. However SAAS test was rapid for screening of antifungal agents because organism identification and antifungal susceptibility test can possible to perform simultaneously.

As the interpretative break point has not yet been established for moulds so sensitive or resistance interpretation is difficult [11]. Our study showed among twenty nine T.*rubrum* in consideration of MIC range one isolate differ between two methods in both within and out of MIC range for FCZ. In case of both ITZ and TER all isolates were within the recommended MIC range in both methods. Although MIC range for each drug is almost same in both methods but their particular MIC value is not same in both methods. The particular MIC value of each isolate of each drug in SAAS method is two or three dilutions higher than CLSI recommended broth microdilution method. The MIC_{50} and MIC_{90} of each drug also higher in SAAS than CLSI reference method except MIC_{90} of FCZ which was same in both method. As the SAAS test was developed for screening of antifungal drug susceptibility or resistance so MICs in SAAS test not replace the MICs of CLSI recommended method. However for test validity, results of SAAS test were compare with result of CLSI test. In consideration of MIC range the concordance of

results between two methods was high for three antifungal agents. Our study showed in both methods TER was most effective drug against *T. rubrum* which correlate many previous study12, 13. The limitation of our study was not use ATCC strains for reproducibility and accuracy of the test results.

Statistical analysis showed 100% correlation with respect to sensitivity, susceptibility positive and negative predictive value of SAAS method with CLSI test [6]. Kuzucu et all (2004) also showed excellent concordance of results between SAAS and CLSI broth microdilution test for antifungal drugs aginst moulds.

Though CLSI reference method is suitable as a standared and interlaboratory aggrement is high but it is expensive, time consuming and cumbersome to perform. This method not possible to perform for any microbiological laboratory because of its special equipment and expertisement. SAAS method is simple, cheap, rapid and easy to perform for any microbiological laboratory.

As the dermatophytosis is endemic in Bbangadesh SAAS test may be useful for choosing proper antifungal drug and optimization of therapy. Because of its simplicity it will be more familial and acceptable for screening of antifungal drugs in comparison to the CLSI test for any microbiological laboratory in our country.

To establish SAAS test for screening drug susceptibility of antifungal agents further study should be done on large number of antifungal drugs and different species of dermatophytes including ATCC strains and compare results with the CLSI standard method.

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REVIEW ARTICLE

The Osmani Medical Teachers Association Journal Volume 12 Number 1

Role of Albumin: in Health & Disease

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Abstract

Albumin is a major protein, comprises about 70% of totalplasma proteins. It is large enough to be excluded from filtration by glomerular membrane, but smaller of large MW molecules, so that it is filtered earlier by glomerular membrane, whenever there is increased glomerular permeability. So albuminuria is a renal(glomerular) function test. Albumin has diverse functions including transport function, plasma colloid osmotic pressure(COP), nutritive function, etc. It has therapeutic application as plasma expander. Reduced plasma albumin is related to hemodynamic alteration of microcirculation. Albuminlevel as a negative acute phase protein, falls in acute inflammation in presence of inflammatory cytokines, such as IL-6. Reduced albumin is a predictor of clinical outcome of some acute life threatening illnesses like stroke. The aim of this review article is to recognize the importance of maintenance of normal albumin concentration for health and application of knowledge of albumin in assessment and management of diseases.

[OMTAJ 2013; 12(1)]

Introduction

Plasma contains hundreds of different proteins. Total plasma protein conc. is 6-8 g/dL.Total plasma proteins may be considered under 3 groups: Albumin(3.5-5.0 g/dL), Globulins(2.5-3.5 g/dL), Fibrinogen(0.2-0.4 g/dL). Albumin : Globulin ratio is (1.2-1.5: 1).Quantitatively major plasma protein is albumin[1]The name 'Albumin' is derived from *albus*(Latin albus=white), appearance of white portion of boiled eggs, which is albumin.It is a large protein with 585 amino acids and 17 disulfide bonds. Molecular weight 69,000 which is smallest of high MW molecules to escape glomerular filtration and absent in urine. So, in diseases that increase glomerular permeability, albumin appears in urine earlier than other high MW molecules, as it accounts for 70% of plasma proteins.[1,2]

It is a simple protein, having only amino acids in composition, soluble in water, coagulated by heat. Lactalbumin in milk and egg albumin are similar proteins. Dietary albumin, like all proteins, is digested to and absorbed as individual amino acids. So there is no direct dietary source of serum albumin, rather it is synthesized in liver.[1].

Role of Albumin in Health[1,3]

1. Contributes plasma COP(25 mmHg).
   Total osmolality of plasma is about 300 mOsm/kg.1 Osmole = 22.4 atmosphere,
   1 atm=760 mm Hg. Total osmotic pressure exerted by osmotically active solutes in plasma is about (300 x 22.4 x 760) / 1000= 5100 mmHg. Whereas Plasma protein, mainly albumin contributes about 0.5 % of total plasma osmotic pressure (about 1.5 mOsm/L). So, COP exerted by albumin is : (1.5 x 22.4 x 760) / 1000=25 mmHg.
   This small but very important contribution is largely responsible for maintenance of blood volume and for distribution of nutrients and drugs to tissue and removal of wastes of metabolism. According to Starling's hypothesis, fluid exchange at capillary is regulated by difference between hydrostatic pressure and COP. Edema is seen when plasma albumin level is <2 gm/dL.

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2. Transport of various hydrophobic substances(Bilirubin, fatty acids, many drugs, some hormones, copper and heavy metals, etc). Only unbound drugs or hormones are biologically active. Blood levels of these substances are affected by change of plasma albumin levels.
3. Buffering action. Albumin has 16 histidine residues which contribute this buffer effect.
4. May be considered as circulating reservoir and transport form of essential amino acids from liver to extrahepatic cells.
5. Protein nutritional values of different foods(particular essential amino acid content) can be obtained by comparing with Egg protein(white portion/ albumin) as a reference protein due to presence of easily available all essential amino acids.[1]

Role of Albumin in diseases: causal, indicators and therapeutic role

1. Albumin transports unconjugated bilirubin from site of production in RES to liver, and thus prevents unconjugated lipophilic bilirubin to enter brain. In infants, if serum bilirubin, >20 mg/dL, albumin can't bind unconjugated bilirubin,consequently this free bilirubin crosses easily through immature BBB, deposited in basal ganglia (Kernicterus), leading to mental retardation, fits, toxic encephalitis & spasticity.[1]
2. Proteinuria is excretion of excess protein in urine,> 300 mg/d, gives positive heat coagulation test or dipstick test for protein. There are many causes of proteinuria, renal glomerular impaired function is clinically the most important one. Whenever glomerular function is impaired, progressively increasing amount of protein is passed in urine, predominantly albumin. So, the terms proteinuria and albuminuria are used interchangeably, though albumin is slightly less than total protein in urine. Proteinuria is usually asymptomatic, large amounts may make urine froth easily.[2]
3. Small amount of albumin in urine <30 mg/d, is usually of no consequence. Albumin in urine 30-300 mg/dl (microalbuminuria), is an early sign of reversible nephropathy, particularly in prolonged uncontrolled or poorly controlled diabetes mellitus.[2]
4. Albumin is solely synthesized in liver, about 12 gm/d, which is about 25% of hepatic protein synthesis and half of its secreted protein[4]. Serum albumin reflects the extent of functioning liver cell mass.As its half life in blood is about 20 days, it is not a good indicator of acute liver diseases, but decreased albumin is a good indicator of all chronic diseases of liver. A reversal of A/G ratio in cirrhosis of liver is due to hypoalbuminemia and associated hyperglobulinemia[1]
5. Human Albumin is therapeutically useful to treat burns, hemorrhage and shock.[1]
6. Calcium in blood is of three forms: (a) about 50% ionized(free, metabolically active form), (b) about 10 % is complexed with some anions,(c) the rest 40% is albumin bound. In hypoalbuminemia, total blood calcium is lowerd, due to reduction of this protein bound fraction, but ionized calcium may be normal and so, tetany does not occur. This fact should be kept in mind before treating markedly low hypocalcemia without tetany. Calcium is lowered by 0.8 mg/dL for a fall of 1 gm/dL of serum albumin.[1]
7. Clinically significant drug interaction may occur due to competitive displacement of one drug from protein bound form by another(e.g. phenytoin- dicoumarol interaction)[1].

Albumin is a negative acute phase protein, falls mildly in presence of inflammatory cytokines, such as IL-6[1].

Discussion

In addition to its role in health and diseases, albumin level may have predictive role in clinical outcome of

life threatening cardiovascular and cerebrovascular diseases.

CV risk increases markedly with increasing amount of albumin in the urine (even within the now considered normal range). The predictive power of urinary albumin levels for CV risk is independent of other CV risk factors and not only is present in individual with diabetes and/or hypertension but also in healthy individuals.

Microalbuminuria seems to reflect a state of (patho)physiologic vascular dysfunction that makes an individual susceptible to organ damage. High levels of albuminuria may be found in young children and reflect a normal physiologic variation in endothelial function associated with CV and renal risk at later age. Intervention strategies aimed at repairing this vascular function could be very useful not only in secondary but also in primary prevention. Albumin excretion levels may represent the primary marker for success of such therapies.[5]

In a prospective observational study, patients were followed up for 30 days postoperatively in the setting of 44 tertiary care Veterans Affairs (VA) medical centers. A total of 54,215 major noncardiac surgery cases were evaluated from the National VA Surgical Risk Study.Main Outcome Measures were 30- days operative mortality and morbidity.A decrease in serum albumin from concentrations greater than 46 g/L to less than 21 g/L was associated with an exponential increase in mortality rates from less than 1% to 29% and in morbidity rates from 10% to 65%. In the regressionmodels, albumin level was the strongest predictor of mortality and morbidity for surgery as a whole and within several subspecialties selected for further analysis. Albumin level was a better predictor of some types of morbidity, particularly sepsis and major infections, than other types.Conclusions from the study was that serum albumin concentration is a better predictor of surgical outcomes than many other preoperative patient characteristics. It is a relatively low-cost test that should be used more frequently as a prognostic tool to detect malnutrition and risk of adverse surgical outcomes, particularly in populations in whom comorbid conditions are relatively frequent.[6]

Based on the data from large single and multi-center clinical trials, including the Heart Outcomes Prevention Evaluation (HOPE) study, it is clear that the presence of microalbuminuria is a signal from the kidney that cardiovascular risk is increased and that vascular responses are altered. This is exemplified by the studies that have demonstrated that the compensatory vaso-dilation seen following relief from prolonged ischemia or infusion of vasodilators such as nitroglycerin is blunted in people with microalbuminuria. Agents known to reduce the rise in microalbuminuria or actually reduce the level of microalbuminuria, such as ACE inhibitors, angiotensin receptor blockers, HMG-CoA reductase inhibitors, beta blockers, non-dihydropyridine calcium channel blockers and diuretics, have all been shown to reduce cardiovascular mortality and in some cases preserve renal function. A reduction in the rise of microalbuminuria is a significant consideration in the selection of agents to treat a given risk factor (cholesterol or blood pressure) to a recommended target goal. Achieving such a goal with agents that also impact microalbuminuria will provide for a more complete cardiovascular risk reduction[7].

In a study it was observed that, serum albumin level had a predictive role on ischemic stroke outcome. Seven hundred fifty-nine(759) consecutive patients with acute ischemic stroke were included. Functional outcome was measured 3 months after stroke using modified Rankin Scale (mRS). Poor outcome was defined as mRS > 3 or death. Serum albumin level was measured within 36 hours after stroke onset.Patients with poor outcome had significantly lower serum albumin level than patients with non poor outcome (34.1 ± 7.4 versus 36.8 ± 6.7 g/L). On logistic regression analysis, serum albumin level remained independent predictor of poor outcome (odds ratio [OR]: 0.43; 95% confidence interval [CI]: 0.26 to 0.70).Relatively high serum albumin level in acute stroke patients decreases the risk of poor outcome. Experimental Studies showed that human albumin therapy substantially improves neurological function, markedly reduces the volume of infraction and eliminates brain swelling inanimals with acute stroke[8].

Suma et al(2011)studied the effect of hypoalbuminemia on clinical outcome of stroke. Twenty (20) hypoalbuminemic patients (S.albumin < 3.5 g/dl) showed poor clinical outcome in comparison with 28 normoalbuminimic (S.albumin > 3.5 g/dl) ischemic stroke pts, evaluated 3 weeks after ischemic stroke, assessed by mRS scale(modified Rankin Scale):

Grade 0,no symptoms, Grade 1, minor symptoms not interfering lifestyles, Grade 2, some restriction, not interfering capacity to self look after, Grade 3, restriction preventing total independent existence, Grade 4, Clearly prevent independent existence but no constant attention required, Grade 5, Totally dependent, requiring constant attention. Poor outcome defined as mRS > 3 or death. Reduced albumin level during acute life threatening cerebrovascular event might be reflection of poor nutrition and has a predictive role of poor clinical outcome. This emphasizes the need for maintenance of normal S. albumin level, that may minimize acute hemodynamic complications to some extent. Studies on beneficial role of therapeutic infusion of human albumin may be carried out for early recovery from stroke or MI[9].

Reports of major controlled and uncontrolled therapeutic trials, reviews, and summary articles published in English between 1972 and 1991 were identified through library and MEDLINE searches. Case series, prospective studies, and blinded therapeutic trials were identified from the bibliographies of these sources. All sources were critically evaluated for information about the comparative physiologic results and patient outcomes of the therapeutic use of albumin solutions, crystalloid solutions, and volume expanders other than albumin. The therapeutic use of albumin is of marginal benefit for many conditions for which it has been administered, apparently because of the body's capacity to quickly compensate for rapid colloid osmotic shifts. Human studies showed little or no demonstrable value for albumin when it was administered for nutritional supplementation, wound healing, perioperative fluid replacement, treatment of early thermal injury, or therapy during extensive retroperitoneal surgery (including aortic aneurysm resection). Therapeutic albumin had well-defined value in several special circumstances: large-volume paracentesis in cirrhotic patients, acute nephrotic syndromes with diuretic resistance, organ transplantation, and plasmapheresis.[10]

Supplementation of human serum albumin showed contradictory results about its beneficial role.With the possible exception of kwashiorkor, a rare nutritional state, serum albumin is an unreliable marker of nutritional status. Furthermore, nutritional supplementation has not been clearly shown to raise levels of serum albumin. Many studies offered a rationale for considering albumin as a marker of illness rather than nutrition. Viewed in this manner, hypoalbuminemia may offer an opportunity to improve patient well-being by identifying and treating the underlying disorder.Albumin levels fall in patients with inflammatory disorders and other illnesses. Possible contributory mechanisms include downregulated production of albumin mRNA by the liver, leading to reduced synthesis, increased albumin catabolismand vascular permeability.

The effect of nutritional supplementation on serum albumin and mortality has been tested only in the French Intradialytic Nutrition Evaluation study (FineS). Patients were randomly assigned for 1 yr to intradialytic parenteral nutrition*versus* no treatment, although both arms were prescribed oral supplements for 2 yr. Two-year mortality was the primary end point, and serum albumin was a secondary one.The intervention did not affect mortality rates, but serum albumin rose early in both groups (3.15 to 3.35 g/dl) and remained stable thereafter. Although the early rise in serum albumin may be construed as resulting from the nutritional intervention, a plausible alternative explanation involves the introduction of bias through the study's unblinded design that led to extranutritional interventions that reduced inflammation. In fact, study subjects' baseline characteristics more strongly suggest the presence of systemic inflammation rather than malnutrition, and early albumin changes were negatively correlated with changes in C-reactive protein ($r = -0.47$; $P < 0.001$). Therefore, on the basis of the available literature, there is insufficient evidence to conclude that nutritional

supplementation raises serum albumin in CKD patients with hypoalbuminemia

Although it was demonstrated that serum albumin was not a good nutritional index in the great majority of cases, it is a powerful way to detect underlying illness; that is, the higher the serum albumin, the more intact is overall health.

Frequently,in presence of hypoalbuminemia, physicians consider nutrition supplementation. This may delay identification of an underlying treatable disorder. The clinicians may try to establish a differential diagnosis. Mitch *et al* described a common pathway—the ubiquitin proteasome system—through which a number of CKD-related complications, including metabolic acidosis, reduced insulin action, higher angiotensin II levels, and inflammation, induce protein breakdown and muscle loss. The model of a common pathway is useful to consider when investigating hypoalbuminemia, especially in light of the established association between inflammation and albumin synthesis.An illness or inflammatory state can reduce serum albumin levels by suppressing synthesis, increasing catabolism and/or vascular permeability to albumin, or a combination of these.

Because the cause of hypoalbuminemia cannot always be reversed or even identified, the use of serum albumin as a quality performance measure should focus only on whether it triggers a search for underlying causes rather than on the albumin level itself.[11]

Conclusion

Concept of albumin in health and disease may be helpful to monitor critically ill patients. Proper attention may be given to improve nutritional status. Serum albumin level is useful to assess hepatic impairment and along with urinary protein can diagnose impaired renal function. Serum albumin level should be considered for drug action and interactions, predicting outcome of critical illness. Further studies are required for its prognostic &therapeutic use.

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Importance of Sputum Microscopic Examination for AFB in the Diagnosis of Tuberculosis (Pulmonary).

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Abstract

Lung cancer cases are often wrongly diagnosed as pulmonary tuberculosis and similarly pulmonary tuberculosis cases are also misdiagnosed as lung cancer. Adequate history, careful physical examination, proper/related investigation is very important to come to a conclusive/accurate diagnosis. In this article ultrasono guided FNAC of lung (rt upper zone lesion) and no sputum for AFB microscopy/culture initially has misdiagnosed as carcinoma lung. But later only positive sputum AFB report and negative bronchoscopy has concluded the diagnosis as pulmonary tuberculosis. But it was late (having no improvement after getting five settings of radio-chemo therapy.)

[OMTAJ 2013; 12(1)]

Introduction

About 9 million new cases and 1.7 million deaths occur every year in the world due to tuberculosis[1], In Bangladesh about 3 lac new cases of TB occur every year and about 60 thousand people die[8]. One person gets infected every two minutes and one person dies every ten minutes from TB. Pulmonary TB is most common, responsible for spread of disease and is 85% of total TB cases[4]. One third of world population and half of the Bangladeshi people have been infected that is they are carrying TB germs in their body[10]. 10% of them become case in lifetime.

In 1882 Robert Koch, a German scientist first discovered Mycobacterium Tuberculosis as the causative agent for TB both pulmonary and extra-pulmonary[9]. Till today it is the major tool for the diagnosis of TB in National Tuberculosis Control Program (NTP). Identification of the bacilli either by microscopic examination or culture of specimen gives definite diagnosis of TB infection[10].

Sputum microscopy for AFB is a major diagnostic tool for TB in DOTS (Directly Observed Treatment Short Course) strategy. Three samples of sputum for AFB microscopy are considered for diagnosis. a) Spot sample b) morning sample c) again spot sample. If two samples become positive he or she is declared as a case of pulmonary TB, open case, infectious, and dangerous for spread. According to NTP report 10-15 cases become sputum positive out of 100 suspected cases examined. These 10-15% positive cases are about 100% confirmed to have active pulmonary TB. Sensitivity of the test is less but if positive it is much more specific for TB.

Case report:

Mr Jashim Uddin- 62 years, known diabetic attended my chamber on 26-9-05 with the history of radiotheraphy and chemotheraphy 5 times/fractions having no improvement regarding his chest complaints. At first he attended medicine specialist on 30-6-05 for the complaints of cough, haemoptysis, fever for long time.

Investigations were done. Chest X ray report showed right upper zone lesion. Radiologist's

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comment was pulmonary tuberculosis/growth with breakdown. RBS 371mg/dl, Urine R/E pus cell 3-5 /HPF. Sugar (++++). Blood -ESR raised. FNAC (ultrasound ، guided)-Squamous Cell carcinoma grade-1. But no sputum sample was examined for AFB (culture or routine microscopy). Diagnosis on the above investigations was confirmed histopathologically as Squamous cell carcinoma grade1.

Accordingly he was advised for hospitalization for oncology consultation and was admitted in a clinic. Board composed of medicine specialist and two oncologists confirmed the diagnosis as carcinoma lung and suggested for radio-chemotherapy. Board referred the case to Professor of oncology at Dhaka for anticancer treatment.

The patient attended the professor at Dhaka as per decision of the board. At Dhaka he was advised for radio-chemotherapy after getting hospitalization in a clinic and was done accordingly. No further investigations were done at the clinic. After getting five settings /dose of radio-chemotherapy at the clinic the patient was not improving rather deterioration of his chest problems.

No revisional diagnostic attempt was done during his deterioration. Differential diagnosis about pulmonary TB also not considered. No sputum for AFB was done before, during chemotherapy and even after deterioration. Bronchoscopy was also not done. The patient decided to leave the clinic for review of his treatment and diagnosis.

He attended my chamber and gave his detailed history of illness and treatment. As he is a diabetic (Prone person for TB), complaining of low-grade fever, evening rise, cough and haemoptysis for a long time, chest X-ray opacity right upper zone involvement (suggestive of TB) and no improvement after 5 settings of radiochemotherapy. I decided to review the diagnosis in the line of TB. Have examined the patient physically. Three samples of sputum for AFB were done and gave positive result. X-ray chest was also done which suggested to be TB. Bronchoscopy gave no significant lesion in favour of malignancy. FNAC was not repeated as sputum report was positive for TB and bronchoscopy negative for malignancy.

Diagnosis was confirmed as pulmonary TB. Anti-TB started along with anti-diabetic insulin. Patient responded very well to treatment. After six months 2RHEZ+4RH he was declared as cured having X-ray improvement and negative sputum report with physical improvement of his health having no chest complaints.

Discussion

Sputum microscopy is a very specific, non-invasive and non-expensive test for the diagnosis of TB (Pulmonary). Diabetic patients are much prone to TB due to their immune suppressive condition. They are also prone to any other infection. In this case patient symptom of cough, low grade fever evening rise for long time, hemoptysis, pain chest strongly suggested in favour of TB. But here in this case sputum was not examined and for this reason the diagnosis of tubercular co-infection was missed. Ultrasono guided FNAC sometimes misses to locate the exact site of lesion and also unable to define the exact nature of the lesion. CT guided FNAC can definitely locate and define the nature of the lesion. But it was not done here. Bronchoscopy can also help to locate the lesion and if required biopsy can be taken for more confirmation. But it was not done here.

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