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Pakistan – Double burden of diseases

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Keywords: Double burden of diseases, Non-communicable diseases, Life style factors

Globally deaths from non-communicable diseases (NCDs) are expected to reach 47.9 million by the year 2020 which is 77% increase from the statistics of 1990 (28.1 million). Among these 70-80% deaths occur in low and middle-income countries.¹

South Asian countries face a double burden of disease (DBD) due to communicable and non-communicable diseases, Pakistan being one of them. On one end of the spectrum is the challenge of controlling the spread of communicable diseases (CD's) while on the other end is the increase in the prevalence of NCDs which will place an unavoidable burden on health services; their availability and affordability.² Unfortunately Pakistan has yet to control the communicable diseases like tuberculosis, malaria, dengue fever, typhoid, viral hepatitis, cholera, vaccine preventable diseases and other infectious diseases. Moreover, there is a rising trend of non-communicable diseases like cardiovascular diseases, diabetes mellitus, hypertension, cancers, stroke, mental health problems and accidents and injuries.³ despite number of vertical and horizontal national health programs, Pakistan is having high maternal and neonatal mortality rates, due to the causes like sepsis and hemorrhage which are mostly preventable. Furthermore, in young children, diarrhea and respiratory illnesses are considered as the major killers. The estimated prevalence for various forms of malnutrition in children under 5 years of age is: 31.6% underweight, 10.5% wasting, 45.0% stunting and 4.8% overweight. While half of the women of reproductive age are anemic i.e. 50.4%.³

According to the WHO country profile of Pakistan, about 80 million individuals suffer from one or more of these NCDs. Among these, 25.3% individuals had hypertension, while 19% had CVD diseases. Moreover,

17% of adult population had diabetes mellitus, while 6% had chronic respiratory diseases, and 8% had cancers.⁴

The factors responsible for the emergence of NCDs are the combination of urbanization, global trade and consumer markets, besides lifestyle factors as lack of physical activity, smoking and drug abuse. However, the number of aging populations is also increasing due to the increasing life expectancy. Non-communicable diseases can largely be prevented by adopting healthy life style. So, proper laws and regulations should be made for making people understand the importance of opting for healthy choice as the easy choice.⁵

Furthermore, if we talk about the communicable diseases, Pakistan ranks 5th highest among the burden of tuberculosis globally. While, malaria is endemic and unfortunately poliomyelitis is yet to be eradicated – for which more than 10 cases have been reported in the first four months of 2019. Presently NCD's along with Injuries and mental health diseases constitute the other half of the burden of diseases. Injuries account for more than 11% of the total burden of disease and is likely to rise with increasing road traffic, urbanization and social conflicts.⁵

One of the factors affecting the health systems strengthening includes low GDP being allocated for health sector, poor spending on social indicators along with slow economic growth, lack of public and private sector partnership for health. However, due to high-cost for curative care it is becoming difficult for the individuals belonging to low socio-economic groups to access and utilize those health services.

Disease prevention and health promotion are the most effective interventions for solving this issue. So, Government needs to give priority to health sector and increase its budgetary allocation for healthcare.⁶

Pakistan needs to chalk out an extraordinary strategy for the existing and the upcoming challenges related to the burden of diseases. Cost effective interventions include early screening, life style modifications; cessation of tobacco use, control of blood pressure by low salt intake, increased consumption of fruits and vegetables along with adopting physical activity in daily routine.⁷

The cost incurred on chronic NCD's include both the direct cost (attributable to illness) and indirect cost (attributable to productivity losses) is very high; in order to decrease this burden of disease (BOD) following recommendations are made.⁸

1. Health education and awareness campaigns using social media should be conducted to highlight the deleterious effects of tobacco use, unhealthy diet, sedentary life style, obesity, drug abuse and alcohol use. Community based activities should be carried out.
2. Provision of recreational and sports facilities including sports ground, parks and walking tracks at community level should be ensured.
3. High risk groups across country should be identified and subjected to screening for early detection.
4. Emphasis should be laid on adopting preventive measures. This may be carried out through the use of health care brochures, through print and electronic media.
5. At the national level increasing taxation and strict legislation on tobacco smoking and manufacture of unhealthy processed food.

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Healthcare associated infections in a tertiary care cardiac hospital: A point prevalence survey

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A B S T R A C T

Objective: Hospitalized patients can pick infections from healthcare facilities which may lead to extended hospital stay, increased morbidity and mortality of hospitalized patients and economic burden on health care. Active surveillance of HAIs that is continuous and prospective in nature has been accepted as a gold standard approach in preventing and controlling healthcare associated infections. To estimate the prevalence HAIs and their types in a tertiary care cardiac center and to identify associated risk factors.

Methodology: Nine prospective point prevalence surveys were conducted on three separate days in three consecutive weeks for three months. A data collectors team comprising of two research officers and an infection control nurse, visited the enrolled patients and patient's history, demographics, physical examination, laboratory findings and other details were reviewed from patient files and recorded on study questionnaire.

Results: A total of 559 patients were enrolled in the study. The prevalence of HAIs was 6.4%, which means 36 HAIs were identified in 559 patients. Univariate analysis showed a significant association between HAI and being in ICU/CCU ward (OR 3.4, 95% CI 1.5-7.4) longer duration of hospital stay (OR 3.0, 95% CI 1.5-6.0, P=0.001), exposure to urinary catheter, use of antimicrobials (OR 2.8, 95% CI 1.3-6.1, P=0.006), and diabetes (OR 2.5, 95% CI 1.2-5.2, P=0.008).

Conclusion: Healthcare associated infection is a major public health problem and rate of HAIs in the selected centers was found to be 6.4%. Present survey provided baseline evidence for further surveillance and multifaceted infection.

Keywords: Hospital acquired infection, healthcare associated infections, surgical site infection, catheter associated urinary tract infection, point prevalence survey.

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Introduction

Healthcare associated infections (HAIs) also known as nosocomial infections are defined by World Health Organization (WHO) as "An infection acquired in hospital by a patient who was admitted for a reason other than that infection; an infection occurring in a patient in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission; this includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility".¹ Center for Disease Control and Prevention

(CDC) classifies HAIs in four main types: central line-associated bloodstream infections (CLABSI), catheter-associated urinary tract infections (CAUTI), ventilator-associated pneumonia (VAP) and surgical site infection (SSI).² Hospitalized patients can pick infections from healthcare facilities which may lead to extended hospital stay, increased morbidity and mortality of hospitalized patients and economic burden on health care.³ Therefore, HAIs are one of the major, yet preventable, threats to patient's safety and wellbeing. There are some factors

which may predispose a patient to HAIs for example decreased immunity of the patient, complex medical procedures, invasive techniques providing potential routes for infection, poor hygiene and over-crowding leading to transmission of drug-resistant microorganisms.⁴

A prevalence survey conducted worldwide, by World Health Organization (WHO) reports that on average 8.7% of all hospitalized patients suffer from nosocomial infections and these rates are higher for Eastern Mediterranean and South-East Asia Regions (11.8% and 10.0% respectively) as compared to European and Western Pacific Regions (7.7% and 9.0% respectively). Moreover, around 1.4 million people in the world suffer from HAIs at any point in time.⁵ The most commonly reported HAIs include surgical site infections, urinary tract infections and respiratory tract infections. Highest prevalence of such infections has reported to occur in critical care units, intensive care units and surgical wards. The patients with old age, complex underlying illness and/or on chemotherapy are more likely to develop HAIs.^{6,7}

Despite of putting earnest efforts in preventing occurrence of HAIs, they continue to occur at a prevailing rate.⁸ Majority of the HAIs can be prevented by applying appropriate preventive measures.⁷ Active surveillance of HAIs that is continuous and prospective in nature has been accepted as a gold standard approach in preventing and controlling HAIs. But continuous prospective surveillance of HAIs is a lengthy process and requires quite a lot of resources. Therefore, point prevalence surveys are recommended for resource limited countries to determine the magnitude of HAIs in their local settings. Point prevalence surveys are relatively cheaper and do not require extensive resources.^{9, 10}

Hence, the aim of this point prevalence study was to estimate the burden of various HAIs and associated risk factors in our tertiary care hospital. This study helped us to discover target areas for quality improvement and formulating a preventive strategy for HAIs.

Methodology

This study was designed to conduct the prospective point prevalence survey on three separate days in three consecutive weeks of each month for three times at 3 months intervals.

Therefore, nine point-prevalence surveys were conducted in the months of May 2016, September 2016 and January 2017. Surveys were conducted at Armed Forces Institute of Cardiology / National Institute of Heart Diseases (AFIC/NIHD), which is a 400 bedded hospital consisting of 2 critical care units (CCUs), 2 intensive care units both for adult and pediatric patients, a high dependency unit for cardiac surgical patients and 12 post-catheterization/general medical wards. AFIC/NIHD is a tertiary care hospital located in Rawalpindi and it acts as a referral hospital for a large population of upper Punjab, federal capital Islamabad, Khyber Pakhtunkhwa province, Azad Kashmir and referred cardiac cases from all the Armed Forces hospitals of the country.

All the patients admitted for more than 48 hours on the days of survey were enrolled in the study, patients admitted or retained in the emergency department were excluded. The study questionnaire was specifically designed for the survey, comprising of patient's demographics, ward name, date of admission, clinical history, comorbidities, diagnosis, medical procedures / interventions received, laboratory findings, prescribed antimicrobial drugs along with doses, use of any urinary catheter, central or peripheral intravascular line, endotracheal tube or mechanical ventilator support and presence of any HAIs. CDC/NHSN surveillance definition for HAIs and criteria for specific type of infection was used to identify infected patients.¹¹ Patients identified with blood stream infection, ventilator associated pneumonia, surgical site infection or any other HAI were investigated in further detail for presence of fever, raised TLC, blood / pus cultures etc. Patient's history, demographics, physical examination, laboratory findings and other details were reviewed from patient files and recorded on study questionnaire. A data team of collector comprising of two research officers and an infection control nurse, visited all the enrolled patients at least once a day and more visits were made in order to complete any missing data or information.

All the data were entered in computer software IBM SPSS (version 23.0). For descriptive statistics of continuous variables, means and standard deviations were calculated, while frequencies and percentages were calculated for categorical data. For calculating prevalence of HAIs, all types of HAIs were included for all infected patients with one or multiple infections divided by total

number of admitted patients. Associations among comparable groups were calculated by using student's t test and chi square test for continuous and categorical variables respectively. Association of various risk factors with occurrence of HAIs was calculated and reported as odds ratios (OR) with 95% confidence intervals. Multiple logistic regression model was used for variables with p-value less than or equal to 0.05 in univariate analysis. A p-value of less than or equal to 0.05 was considered to show statistically significant differences. The study was approved by Institutional Ethical and Review Board (IERB) of AFIC/NIHD prior to data collection.

Results

A total of 559 patients were enrolled in the study. There were 374 (66.9%) males and 185 (33.09%) females in the study sample group. The ages of patients ranged from 1 to 90 years (median = 53 years) with a mean of 55.25 ± 19.46 years among males and 45.57 ± 25.24 years among females. 271 (48.5%) patients were from Intensive care unit and/or critical care unit, while 288 (51.5%) were admitted in post-catheterization and/or general cardiology wards.

The prevalence of HAIs was 6.4%. Out of 36 patients, the most frequently reported HAIs included surgical site infections (55.55%), catheter-associated urinary tract infections (22.22%) central line-associated bloodstream infections (16.66%), and ventilator-associated pneumonia (5.55%). Microbial cultures were performed for all patients with HAIs, out of which 19.4% (7/36) culture growths were obtained. Isolated microorganisms included *Staphylococcus aureus* [42.8% (3/7)], *Acinetobacter* [28.5% (2/7)], *Pseudomonas aeruginosa* [14.2% (1/7)] and *Escherichia coli* [14.2% (1/7)].

Majority of the HAIs occurred in patients admitted to intensive care units and/or critical care units as compared to post-catheterization and medical wards (75.0%) vs (25.0%) p value 0.009]. A total of 296 (52.9%) patients were receiving antibiotics on the days on survey, out of which 96 (32.4%) patients were on antibiotics for curative purpose while remaining 200 (67.6%) received antibiotics for pre-operative or post-operative prophylactic reason. The most frequently used class of antimicrobial drugs was Ceftriaxone [144 (48.6%)] a broad-spectrum third generation cephalosporin, followed by levofloxacin [84

(28.4%)] belonging to fluoroquinolone antimicrobial drug class; while other antibiotics included broad and narrow spectrum β -lactam antibiotics/ beta-lactamase inhibitors i.e. Amoxicillin/clavulanic acid and Piperacillin/tazobactam [46 (15.5%) and 22 (7.4%) respectively].

Table 1: Comparison of demographics and clinical characteristics of patients with or without hospital acquired infection

Characteristics	Hospital acquired infection		p-value
	Yes (n=36)	No (n=523)	
Age	52.2 \pm 25.3	50.1 \pm 21.4	0.78 ^a
Gender			
Males	26 (72.2%)	348 (66.5%)	0.48 ^b
Females	10 (27.8%)	175 (33.5%)	
Type of ward			
ICU/CCU	27 (75.0%)	244 (46.7%)	0.001* ^b
Post-cath ward	9 (25.0%)	279 (53.3%)	
Co-morbidities			
Hypertension	12 (33.3%)	199 (38.0%)	0.57 ^b
Diabetes	13 (36.1%)	95 (18.2%)	
Duration of stay			
>1 week	22 (61.1%)	178 (34.0%)	0.001* ^b
<1 week	14 (38.9%)	345 (66.0%)	
Antimicrobial use			
Yes	27 (75.0%)	269 (51.4%)	0.006* ^b
No	9 (25.0%)	254 (48.6%)	
Exposure to urinary catheter			
Yes	5 (13.9%)	21 (4.0%)	0.007* ^b
No	31 (86.1)	502 (96.0%)	
Exposure to IV-line			
Yes	6 (16.7%)	157 (30.0%)	0.08* ^b
No	30 (83.3%)	366 (70.0%)	

*Significant p-values

^a Independent t-test

^b Pearson's Chi-square test

A total of 259 (46.3%) patients were suffering from chronic illness, out of which 108 (19.3%) patients were diabetic, 211 (37.7%) were hypertensive. Out of these 259 suffering patients with chronic illness, 46 (8.2%) were both hypertensive and diabetic. No significant association has been found between presence of chronic illnesses (both hypertension and diabetes) and developing HAIs, but while considering only diabetes, it was found that diabetic

patients tend to develop HAI significantly more as compared to non-diabetic patients [13/95 (12.0%) vs 23/428 (5.1%) p value 0.008].

Univariate analysis showed a significant association between HAI and being in ICU/CCU ward (OR 3.4, 95% CI 1.5-7.4, p 0.001) longer duration of hospital stay (OR 3.0 95% CI 1.5-6.0, p 0.001), exposure to urinary catheter, use of antimicrobials (OR 2.8, 95% CI 1.3-6.1, p 0.006), and diabetes (OR 2.5, 95% CI 1.2-5.2, p 0.008). Multiple logistic regression found only one significant association i.e. between developing HAIs and long hospital stay (OR 2.1, 95% CI 1.1-6.5, p 0.01).

Discussion

The prevalence of HAIs reported in this study (6.4%) is comparable to the published results from other HAI surveys conducted worldwide, where HAI prevalence lie between 4 to 7%.¹²⁻¹⁴ Some studies have also reported quite a higher prevalence of HAIs occurring among ICU patients, which ranges from 15 to 29%.¹⁵ Similarly, high prevalence of HAIs has been reported in most of the studies conducted in low and middle income countries where prevalence ranges up to 15%.^{16, 17} High variability in HAI rates might be caused by high occupancy rate, seasonal variations, epidemics, and variability in duration and conditions under which prevalence surveys are conducted.^{17, 18}

A significantly higher number of HAIs were encountered in ICUs/CCUs (21/271, 10%), because more invasive procedures and surgeries were being done on ICU/CCU patients, the patients are usually seriously ill, have compromised immunity, and are being administered with multiple therapeutic agents. The most common type of HAI in our study is reported to be the surgical site infections i.e. (20/36), followed by catheter-associated urinary tract infections (8/36). Surgical site infections are most prevalent in our study because our hospital acts as a main referral hospital in the region where most complicated and serious surgical cases are referred and catered for and appears to match the rates reported in other studies conducted at cardiac hospitals.¹² In a study conducted by Andrioli et al, the most frequently encountered HAIs were surgical site infections (24/60), followed by urinary tract infections (14/60), bloodstream infections (11/60) and pneumonia (11/60).¹² Other studies reports urinary tract infection to be the most commonly encountered HAI and significant

association between developing urinary tract infection and indwelled urinary catheter has also been established by various authors.^{11, 13, 19, 20} Ventilator-associated pneumonia and intravascular line-associated blood stream infections were least commonly reported HAIs in literature, results of whom are in line with findings of our study.^{11-13, 20}

Microbiological cultures were performed for all cases of HAIs, out of which 7 positive cultures were obtained, where isolated microorganisms included *Staphylococcus aureus* (3/7), *Acinetobacter* (2/7), *Pseudomonas aeruginosa* (1/7) and *Escherichia coli* (1/7). The number of positive cultures is quite low, because empirical broad spectrum antibiotic therapy is usually started immediately which results in negative culture growths. A study conducted by Stichi et al, the most commonly isolated micro-organism was methicillin-resistant *Staphylococcus aureus*, followed by *Enterobacteriaceae*.²¹ Results of a study conducted by Xie et al, reports *Pseudomonas aeruginosa* to be the most commonly isolated organism, followed by followed by *Escherichia coli*.¹³ Other studies conducted by Afle et al and Phu et al, reports gram negative *Acinetobacter baumannii* to be the most common isolates in HAIs.^{22,23}

The most significant predictors of developing HAIs were found to be long hospital stay and indwelling catheter/intravascular line/ventilator. Literature also reports similar sort of predictor variables to be significantly associated with developing HAIs.^{9, 15, 20, 23} A study conducted by Kolpa et al reports long hospital stay and intubation to be the most significant predictors of HAIs, while another study conducted by Jroundi et al reports critical illness, immune status, surgery and catheterization to be the most significant predictors.^{20, 24}

In the end it is to be summarized that HAIs do occur, and there is dire need to continuously conduct active surveillance and point prevalence surveys, in order to understand current trends of HAIs occurring at health care facilities and to prevent them by adopting various infection control programs and other multifaceted interventions.

Conclusion

Healthcare associated infection is a major public health problem and rate of HAIs in our centre is reported to be 6.4%. Present survey provided baseline evidence for further surveillance and multifaceted infection.

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Effect of deep breathing exercises and incentive spirometry on respiratory distress scoring in second degree inhalational burn patients

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A B S T R A C T

Objective: Study was conducted for 6 months in PIMS Hospital Islamabad. Data was collected on self-structured Questionnaire, Respiratory distress scoring, Objective tools of Arterial blood gases and vital signs with signed consent.

Methodology: The subjects were randomly allocated in experimental and control groups. Baseline data was collected and re-collected on Day 0 and Day 7 respectively and assessed using non-probability convenient sampling technique. Both groups were given standard medical and nursing care.

Results: The experimental group was given single treatment regimen i.e. Deep breathing exercises (with 5-10 repetitions of each DBE being possible onto patient for 15-30 minutes twice daily). The control group was given 10-15 cycles of ISM with prior steam inhalation and nebulization with salbutamol for a period of 15-20 minutes for 35-45 minutes twice daily for a period of 07 days.

Conclusion: The experimental group results show that deep breathing exercises are significantly effective in improving post burn complications like pneumonia in patients suffering from second degree inhalation burns.

Keywords: Deep breathing exercise, incentive spirometry, burn patients.

Introduction

Injury to the pulmonary system through direct mode can result from both heat injury and chemical irritation produced as a result of the combustion end products. The metabolism of mitochondria is disturbed due to inhalation of gases like carbon dioxide and hydrogen cyanide which leads to systemic insult. The death rate and incidence of illness can further be complicated and increased from 3-10% to 20-30% due to injury caused by inhalation of smoke, therefore it is important to recognize the presence of inhalation injury.^{1,2} The factors responsible for indicating the factors responsible for increasing death rate due to the burn injury caused by inhalation involve increase in TBSA scoring and increase in age.³⁻⁶ Further an increase in requirements of fluid and onset of Acute respiratory distress syndrome is also responsible for increasing the incidence of death rate.⁶ The mortality rate also

significantly increases if inhalation injury is being complicated by some specific diseases like pneumonia.^{7,8} The circumstances of the burn injury are also quite important in indicating inhalation injury, like if a burn occurring in an area that is completely bounded like an automobile then there is very high chance of inhalation burn injury because the temperature in such an environment may increase up to 1000°F (538°C).^{9,10} A lot of researches have been done to address the post-burn respiratory complications but the most important and major gaps being still found in this regard include how to prevent these post burn complications irrespective of the good hygiene. Pakistan is deprived in Burn care as only a few setups are available and there is not much work done in cardiopulmonary physical therapy. This study was done to aware people about better cardiopulmonary rehabilitation.

The current research was based on finding out the most effective treatment regimen in preventing complications in post inhalation burn patients suffering from second degree inhalation burn. This study is going to add evidence-based treatment in the practice of chest physical therapy and an effective treatment of pneumonia in second degree inhalation burn patients.

Methodology

A total of 30 patients from both genders between the age of 20-50 years, suffering from second degree inhalation burns after first surgical intervention using nasal cannulas and face mask were included in the study. Unconscious patients and those suffering from other types of burns were excluded. Non-probability convenient sampling technique was used.

After taking informed consent, the participants were randomly allocated to control group and experimental group containing 15 patients each. Patients in control group were given 5-6 cycles of incentive spirometry ISM twice a day for seven days, with each session lasting 20-30 minutes. The patients were also given steam inhalation and nebulization prior to ISM. Patients in the experimental group were given 4-6 repetitions of deep breathing exercises DBE, twice a day for seven days. The DBE involved belly breathing, pursed lip breathing, diaphragmatic breathing and active cycle of breathing techniques. Baseline data was collected by physical therapist on Day 0 and then patients in both groups were given two sessions of allocated regimens each day and then data was re-collected on day 07. Respiratory distress was measured using Silverman-Andersen retraction scoring with 0 score indicating lag, score 1 as normal and score 2 as lead.

The study was conducted according to the ethical guidelines of Pakistan Medical Research Council (PMRC) and the Declaration of Helsinki. Anonymity and confidentiality of participants was maintained throughout the research. This data was analyzed by using statistical package for social science SPSS version 21. Categorical variables were presented as frequency and percentages whereas continuous variables were presented as mean and standard deviation. Statistical significance between groups was assessed using independent samples t-test and for within the group comparison paired samples t-test

was used. Statistical significance was assumed at p-value <0.05.

Results

A total of 30 participants were enrolled in the study with 15 males and 15 females. The demographic variables are shown in Table 1. There were 7 males and 8 females in the Control group, and 8 males and 7 females in the experimental group. The mean age of participants was 29.6 years and 38.4 years, mean GCS 13.6 and 14.2, and duration of exposure 10.2 seconds and 9.7 seconds in the control and experimental group respectively.

Table 2 describes the comparison of Silverman-Anderson respiratory distress score after the delivery of physiotherapy sessions in control and experimental group. Significant difference was noted for post-session chest movement between the two groups. The experimental group had a significantly lower score than control group, 1.66 ± 0.48 compared with 1.93 ± 0.25 , $p=0.021$. There was no significant difference in the other variables.

Table 3 shows the effect of intervention on respiratory distress before and after administration of session. There was a significant improvement in chest movement, the score improved from 2.06 ± 0.26 to 1.66 ± 0.48 post session, $p=0.009$. Similarly, a significant improvement in the Silverman-Anderson score for intercostal retractions was observed, 2.0 ± 0.37 pre-session compared with 1.40 ± 0.50 post-session, $p<0.001$. Reduction of respiratory distress score was noted in the remaining variables, like xiphoid retractions, nasal flaring and expiratory grunt as well but it was not statistically significant.

Table 1: Demographic Variables

Variable	Control	Experimental
Age (mean \pm SD)	29.6 \pm 6.66 yrs	38.4 \pm 4.91 yrs
Gender Male, n (%) Female, n (%)	7 (46.7) 8 (53.3)	8 (53.3) 7 (46.7)
GCS (mean \pm SD)	13.6 \pm 1.11	14.2 \pm 1.08
Duration of exposure (mean \pm SD)	10.2 \pm 5.2 sec	9.7 \pm 3.8 sec

Table 2: Post session scores of Control and Experimental group

Feature	Group	Silverman-Anderson Score		p-value
		Mean	S.D.	
Chest movement assessment post-session	Control	1.93	0.25	0.021*
	Exp.	1.66	0.48	
Intercostal retraction assessment post-session	Control	1.06	0.25	0.207
	Exp.	1.40	0.50	
Xiphoid retraction assessment post-session	Control	1.06	0.25	0.200
	Exp.	1.40	0.50	
Nasal flaring assessment post-session	Control	1.06	0.26	0.200
	Exp.	1.40	0.51	
Expiratory grunt assessment post-session	Control	1.06	0.26	0.200
	Exp.	1.40	0.51	

* Significant difference ($p < 0.05$)

Table 3: Pre and post session scores of experimental groups

Feature	Group	Silverman-Anderson Score		p-value
		Mean	S.D.	
Chest movement	Pre-session	2.06	0.26	0.009*
	Post-session	1.66	0.48	
Intercostal retractions	Pre-session	2.00	0.37	<0.001*
	Post-session	1.40	0.50	
Xiphoid Retractions	Pre-session	1.60	0.63	0.082
	Post-session	1.40	0.50	
Nasal flaring	Pre-session	1.53	0.63	0.164
	Post-session	1.40	0.50	
Expiratory grunt	Pre-session	1.53	0.63	0.164
	Post-session	1.40	0.50	

* Significant difference ($p < 0.05$)

Discussion

The results of between group comparisons with the help of student's t-test are given in table 2. The mean, standard deviation and p-values for variables of both experimental and control group variables are mentioned above. The significant value is $p < 0.05$. The results show that both techniques were giving significant results for certain variables including Nasal flaring and Expiratory grunt with $p < 0.05$. The rest of the variables studied in the treatment were also giving better results but the results are not that much significant that is in those $p > 0.05$ and hence were not considered significant. Hence favoring acceptance of Null hypothesis and Alternate hypothesis is not accepted. The table 2 shows the results for experimental group patients showing significant effect of Deep breathing Exercises on variables including Chest movement and Inter-costal retractions by giving p-value that is $p < 0.05$. The rest of variables were being improved but the $p > 0.05$ and hence were not considered significant.

In June 2007 a study was conducted on comparison between two burn rehabilitation protocols, F. Okhovation with co-workers conducted a research on patients of General hospital Tehran in year 2005. The aim of the study was to compare the aim of burn rehabilitation treatment with routine burn rehabilitation treatment to find out rehab related problems. The results of this study indicate significant difference ($p < 0.01$) in burn contractures between two groups, that intensive burn rehabilitation decreases burn complications. BRT could consider BRT protocols.⁸ The journal BURNS witnessed a research conducted by Oscar E. Suman and his coworkers on Respiratory management of pulmonary injury. Chest physiotherapy has come to mean gravity-assisted bronchial drainage with chest percussion and vibrations.

Conclusion

The experimental group results show that deep breathing exercises are significantly effective in improving post burn complications like pneumonia in patients suffering from second degree inhalation burns. The current research results of some variables are not significant due to small sample size. A large sample multicenter study with appropriate design is necessary to conclude more significant results.

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Comparison of auditory steady state response (ASSR) & auditory brainstem response (ABR) hearing thresholds in young children

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A B S T R A C T

Objective: Hearing loss (HL) with a local prevalence of 5.7%, is the commonest childhood disability, requiring Early Hearing Detection and Intervention (EHDI) programs to reduce the disability burden. Knowing the degree, type and configuration of HL is prerequisite for appropriate amplification, with Automated Auditory Brainstem Responses (ABR) being commonly used for this purpose, however Auditory Steady State Response (ASSR) has been recently introduced in the region. This study was conducted to compare ABR to ASSR, as an early diagnostic tool in children under five years of age.

Methodology: This cross-sectional comparative study was performed at the Auditory Verbal Institute of Audiology and Speech (AVIAS) clinics in Rawalpindi and Islamabad, from December 2016 to September 2017. It included thirty-two cases (n=32) who visited AVIAS clinics for hearing assessment and conformed to the investigative protocol using non probability convenient sampling technique, and subjected to both ABR and ASSR for comparative purposes. Correlations were calculated between the thresholds obtained by ABR and ASSR.

Results: N=32 children (64 ears) with male female ratio of 2.2:1 and mean age of 33.50±17.73 months were tested with ABR and ASSR for hearing thresholds and correlation coefficient between 2KHz, 4KHz ASSR and average of both with ABR was calculated to be 0.92 and 0.90 and 0.94 respectively.

Conclusion: ASSR provides additional frequency specific hearing threshold estimation compared to C-ABR, essentially required for proper setting of amplification devices.

Keywords: Brainstem evoked response audiometry, auditory brainstem response, Hearing loss.

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Introduction

Hearing loss with a local prevalence of 5.7%¹ and 13.6% in 5-15 years old school children,² being the commonest childhood disability, results in a high burden on economies like Pakistan.³ Importance of Early Hearing Detection and Intervention (EHDI) programs cannot be over emphasized, since even a delay in intervention up to first year of life results in detrimental effects on communication and psychosocial development of the child.⁴ Oto-acoustic emissions (OAE) and Automated Auditory Brainstem Responses (ABR) are being used for objective hearing screening of new-born, and those failing

hearing screening are referred for further diagnostic evaluations.⁵ Rehabilitation of hearing impaired demands timely detection & intervention through appropriate amplification, for which pre requisites like the degree, type and configuration of HL before 6 months of age are absolutely essential.

ABR and Auditory Steady State Responses (ASSR) are objective electrophysiological tests to detect hearing sensitivity. Click evoked ABR (C-ABR) is recorded as a far field transient response with the help of electrodes

mounted on the scalp. It has been in use since long for objective hearing evaluation. Neural synchrony is needed to record ABR by the use of abrupt onset stimulus such as click. However, this abruptness of the onset of the stimulus implies broadness of the stimulus spectrum.⁶ Thus C-ABR lack the ability to provide useful frequency specific knowledge about hearing thresholds and due to transducer limitations for producing high intensity abrupt onset stimulus, it is poor in differentiating between severe and profound hearing losses,⁷ indicating a clear need for better techniques to manage the technical limitations of C-ABR. Therefore the focus shifted to the use of slowly rising frequency specific stimulus to evoke auditory potentials such as Tone Burst to produce reliable threshold estimates within 15dB of behavioral thresholds.⁸ However, low frequency tone burst evoked response waveforms are less distinct and difficult to identify through visual inspection,⁹ as low frequencies have to travel to the apical end of the cochlea to evoke the response thus loss of neural synchrony is observed and thus poorer wave morphology was observed and also transient nature of the response limits the assessment of multiple frequencies. ASSR seems to cater to these issues. These are rhythmic brain potentials noted in response to ongoing periodic stimulus. In ASSR, multiple frequency tones called carrier frequency, are amplitude/frequency/mixed modulated with respect to distinct tones called modulating tone, and simultaneously presented. Detection is automatic through statistical methods resulting in robustness of the technique. ASSR might have more important usage compared to C-ABR assessment of state of arousal and supra-threshold hearing in anesthetized state, in addition to auditory threshold measurements.¹⁰

ASSR is a new technique rarely being used in the country while C-ABR is a widely used technique. The widespread clinical application of ASSR demands a thorough comparative study of the two techniques. Therefore, the current study was designed to compare Auditory Brainstem Response (ABR) to Auditory Steady State Response (ASSR) as an early diagnostic tool in children under five years of age. This study is important because no such study has come up from this part of the world.

Methodology

This cross-sectional study was conducted at Auditory Verbal Institute of Audiology and Speech (AVIAS) clinics, located in Islamabad and Rawalpindi. Data collection was conducted in a span of 10 months from Dec 2016 to Sept 2017. The Study population consists of n=32 patients selected by convenience sampling, and from both the genders, under the age of 5 years who visited AVIAS clinics for hearing assessment. Patients having any other disability and/or those in whom ABR and/or ASSR could not be performed were excluded from the study. Both ABR and ASSR were performed on the same visit in a quiet room with patient in deep sleep with syrup chloral hydrate given per orally in a dose of 50 mg/kg body weight. Electrode placement included high forehead (Fpz) for recording, left mastoid (M1) for reference and right mastoid (M2) for ground after skin sites prepared by rubbing with Nu prep skin preparation gel to keep impedance under 5kohm, followed by electrode placements. Additionally, it was ensured that impedance difference between reference and recording electrode was under 1kohm so that effective common mode rejection ratio was achieved.

PATH Medical's Sentiero Advanced Instrument was used to perform all ABR and ASSR tests and data was transferred to a laptop for reporting purpose using PATH medical's software Mira. The ABR reporting and wave marking was done by the researcher himself and reviewed by colleague audiologists. For ABR, click stimulus at a rate of 10 clicks per second was used with a time window of 12ms and click stimulus presented 3000 times with response averaging, while for ASSR, frequency modulated tones at 80Hz was used to evoke ASSR test and recording done at four stimulus frequencies including 500 Hz, 1 KHz, 2 KHz and 4 KHz. However, where needed responses on 250 Hz, 6 KHz and 8 KHz were also recorded.

Test results having no response on 2 KHz or 4 KHz ASSR or C-ABR were excluded from the sample for this study, because correlation coefficient cannot be calculated between them without making assumptions. The data was organized and SPSS 20 (Statistical Package for Social Studies) was used for statistical analysis. Correlation coefficients between 2 KHz and 4

KHz ASSR and the average of both with click evoked ABR (C-ABR) hearing thresholds were calculated. The results obtained were then compared with local and international literature.

Results

With a view to compare C-ABR to Auditory Steady State Response (ASSR) as an early diagnostic tool in children under five years (60 months) of age, hearing threshold estimation with ABR and ASSR was done followed by statistical analysis of the test results. Total sample population included 32 children (64 ears) with a male female ratio of 2.2:1. Their age range was 4 to 60 months with a mean age of 33.50 ± 17.73 months (table 1) with maximum population $n=10$ (31.25%) in the age group of 12-24 and 48-60 months each (table 1 and 2).

Table 1: Demographic Data of Study Population (n=32)

Gender	Male	22 (56%)
	Female	10 (44%)
Age (Months)	Minimum	4
	Maximum	60
	Mean	33.50
	Median	37.00
	Standard Deviation	17.73

Note: Multiple modes exist. Only the smallest value is shown.

Table 2: Distribution of Age & Gender: Age Group *Gender Cross Tabulation (n=32)

Age Group (Months)	Female		Male		Total		Cum %age
	No	%	No	%	No	%	
0-12	1	33.33	2	66.67	3	9.37	9.37
12-24	3	30.00	7	70.00	10	31.25	40.62
24-36	1	50.00	1	50.00	2	6.25	46.87
36-48	2	28.57	5	71.43	7	21.88	68.75
48-60	3	30.00	7	70.00	10	31.25	100
Total	10		22		32		

No: Absolute frequencies

?: Relative frequencies

A total of 64 ears were tested and out of these 64 ears 18 were excluded from data analysis since no response to C-ABR was observed up till the limits of the equipment and thus no comparison could be made with ASSR thresholds, thus leaving behind a total of $n=46$ cases on which data analysis was performed. Figure 1, shows the ABR and ASSR thresholds of the study population.

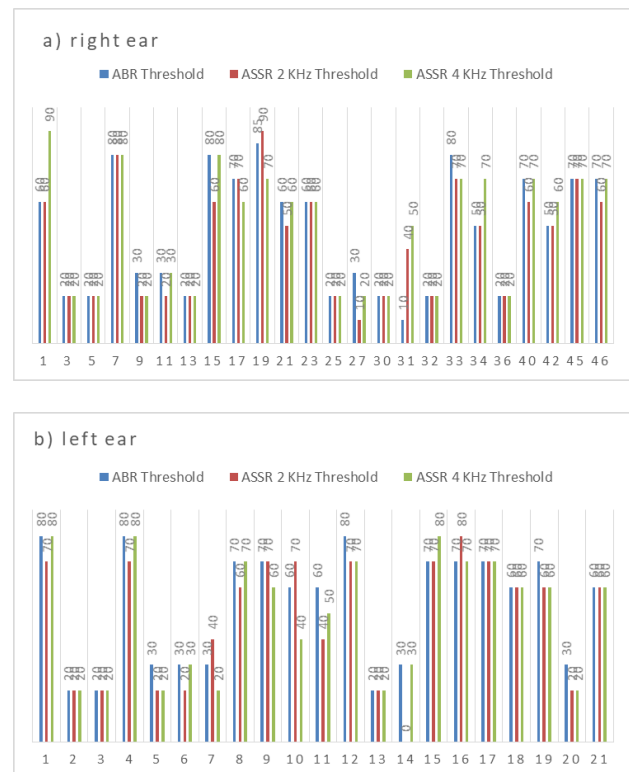


Figure 1: Auditory Thresholds of study population of a) right ear (n= 25 ears) b) left ear (n=21 ears)

Pearson correlation calculated for C-ABR thresholds with 2kHz ASSR, 4kHz ASSR and the average of both was found to be 0.92 and 0.90 and 0.94 respectively (Table 3).

Table 3: Pearson Correlation coefficients between ABR and 2 KHz and 4 KHz ASSR (n=46 ears)

		ASSR (2 KHz)	ASSR (4 KHz)	ASSR avg.
ABR threshold	Pearson Correlation	.918*	.904*	.938*
	Sig. (2-tailed)	.000	.000	.000
	N	46	46	46

* Correlation is significant at 0.01 level (2 tailed).

Discussion

In infants and children frequency specific thresholds of hearing are important for better amplification and ASSR with its multiple frequency testing facility provides an opportunity for estimation of frequency specific thresholds of hearing in babies.¹¹ ASSR has shown comparable results to pure tone audiometry in adults.¹² Since hearing thresholds obtained by C-ABR is closely related behavioral thresholds in 2 KHz – 4KHz frequency region, this study calculated how well the 2 KHz and 4 KHz ASSR hearing thresholds correlate to those obtained by C-ABR. N=46 ears were tested with ABR and ASSR for hearing thresholds and correlation coefficient between 2 KHz, 4 KHz ASSR and average of both with C-ABR was calculated to be 0.92 and 0.90 and 0.94 respectively. These results are consistent with previous studies. In a similar study by Vander Werff KR et al, conducted on infants and young children with significant correlation of 0.97 was found for C-ABR with 2 KHz and 4 KHz ABR.¹³ In contrast in a study Luts H et al, found correlation of 0.77, between ABR and ASSR thresholds at 2 KHz frequency.¹¹ Also Celik O et al, found strong correlation between ABR and ASSR thresholds at 4 KHz, however the correlation at other frequencies were not strong.¹⁴

It is important to point out that out of total of n=64 ears, n=18 ears were excluded from data analysis, since no response to C-ABR was present till the limit of the equipment and these were cases in which ASSR showed responses at least at the low frequencies (250 Hz, 500 Hz, 1 KHz). This is an important result and have also been reported by other studies.¹⁵ This information about residual hearing is not only beneficial in selection of a particular intervention such as hearing aids or cochlear implants but also help fitting process of hearing aids. The stimulus used to evoke ASSR have narrower frequency spectrum thus gives more frequency specific information about hearing thresholds than the tone burst or click evoked ABR.

ASSR can be recorded binaurally at multiple stimulus frequencies simultaneously thus it takes less time to complete than tone burst ABR,¹⁶ and completes procedure before the child wakes up or the sedation wears off. Also, statistical measures are applied to generate results in ASSR, eliminating the possibility of

error made in ABR that depends on marking of waves by audiologist. Another benefit of ASSR over ABR reported by many studies is that due to the nature of stimulus used in ASSR it can be used as a tool to demonstrate benefit of amplification.¹⁷ Previously many studies focused to evaluate role of click evoked ABR for this purpose, but since abrupt onset of click stimulus cause distortion when presented with free field speakers. A digital hearing aids process such stimulus differently, C-ABR is not used for aided response evaluation except in cases with bone conduction hearing implants (BAHA).¹⁸

However, Click evoke ABR has its own diagnostic importance. ABR evoked thorough clicks of alternate polarity may help in identifying retro-cochlear pathologies and also the morphology of ABR waveform can lead to the site of lesion. Thus, ABR should be performed as part of complete audiological test battery for infants and young children. In difficult to test children where behavioral observation audiometry is not conclusive, ABR is the investigation which can detect the sensitivity of the ear, being useful for early detection.¹⁹ Song et al, in their study to screen newborns with ASSR and DPOAE, concluded that ABR can be substituted with ASSR for screening,²⁰ while Celik O et al, concluded that ASSR is not a reliable for screening purposes, but as a complementary diagnostic investigation.¹⁴

Conclusion

ASSR provides additional frequency specific hearing threshold estimation compared to C-ABR, which is essential in infants and children with hearing loss for provision of amplification devices.

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To compare the postprandial glucose response of dates and white bread in diabetics and non-diabetics

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A B S T R A C T

Objective: To evaluate the postprandial glucose response of dates and white bread (25g) in diabetics and non-diabetics.

Methodology: It was cross-over/cross observational study done at Shifa International Hospital in May-October 2016. The study subjects were adults with Type 2 diabetes mellitus (DM) of age more than 30 years and the healthy controls. Each group was administered equally weighed (25 g) dates and white bread for two days with one week apart. Post prandial blood glucose measurements for dates and white bread was done in both groups and compared by applying student's t-test.

Results: Each group had twelve participants. The mean blood glucose response for both food groups was significantly higher in diabetics than controls. The peak response for dates in both groups was at 30 minutes and the peak response for bread was 60 and 30 minutes in diabetics and controls respectively. Response of dates and bread in diabetics was not statistically significant. The mean fasting glucose in diabetics and non-diabetics was 131.04 mg/dl and 90.12 mg/dl respectively.

Conclusion: Dates are suitable for diabetics and their consumption bears no added risk or danger over white bread.

Keywords: Dates, post prandial glucose, diabetes

Introduction

Diabetes mellitus type II has recently become endemic in Pakistan which is probably related, in part, to the rapid social and lifestyle changes experienced by our people particularly in the past two to three decades. Studies reported the high prevalence of diabetes in urban than rural areas.^{1, 2} Reports of the Pakistan National Diabetes Survey have shown considerable increase in prevalence rates of diabetes mellitus. As the life expectancy increases in Pakistan, projected prevalence rates of DM will also increase significantly.³ We frequently encounter diabetic patients in clinics who ask about intake of different varieties of fruits available in our region. Carbohydrate has the most nutritive caloric value in fruits which is in the form of sugars. Equal amounts of dietary carbohydrates have variable blood glucose response

considerably as a function of specific food ingested.⁴ The rate of entry of glucose in blood and the duration for which its levels are elevated, affect the magnitude of a number of metabolic and hormonal changes that can modulate many disease- and health-related parameters.⁵ There is an agreement that diet low in glycemic index is pertinent to the prevention and management of diabetes and coronary heart disease along with obesity.⁶ The glycemic response of many fruits has been characterized;^{7, 8} however, there are certain fruits in our region consumed in a particular month which are less studied.

Dates (*Phoenix dactylifera*) have great importance in Islam. It is one of the few foods directly referred to in the Muslim's Holy book, Quran and Hadith (sayings of Holy

Prophet) describing the health benefits and nutritional significance. It is taken to break the day long fast during Ramadan.⁶ Dates are very sweet in taste and difficult to be refrained by diabetics especially in the month of Ramadan.⁹ Miller et al., reported the glycemic response to dates in the normal subjects.¹⁰ However, in diabetics it has not been completely studied. However, in diabetic patients it has not been completely studied, except one study in which Alkaabi M et.al reported oral glucose tolerance comparison which revealed that the glycemic index for dates was not significantly different from the value in control subjects.⁶

Date producing countries cultivate various varieties of date. They are consumed in various stages of ripening and are used to produce range of commercial products. Dates, are available in three forms mostly: soft (about 80% of the dry matter is invert sugars); semi-dry (about 40% of the dry matter is invert sugars and 40% sucrose); and dry (20-40% of the dry matter is invert sugars and 40-60% is sucrose). A 100 g portion of fresh dates is a good source of vitamin C and supplies 230 Kcal (960 KJ); 100 g of dried dates (three weighed with seeds) provides 3 g of dietary fiber.¹¹

The suitability of dates as a source of carbohydrate for patients with type II diabetes mellitus is unclear as there have been very few studies regarding glycemic response to date consumption. People generally and some health professionals believe that dates cannot be used by the diabetic patients because they can lead to a postprandial hyperglycemia and worsening of diabetic control.

Our study aimed to evaluate the postprandial glucose response to dates (*Phoenix dactylifera*) in comparison to 25 g white bread in diabetics and compared postprandial response to dates and white bread in diabetics and non-diabetics.

Methodology

It was a cross over case-control study conducted in the Endocrinology Clinic of Shifa International Hospital Islamabad from May-October 2016. Study population comprised of adult patients with type two diabetes mellitus presenting at the Endocrine Clinic of the hospital within the study duration. 26 patients were included in the study and were split into diabetics and non-diabetic groups (controls).

The study was carried out in two days' time (day one and day two). Eligible participants were instructed not to consume food or beverages (other than water) after 2200hrs the night before the tests. In the morning they were asked to refrain from physical exercise and report to the clinic in a fasting state at 0900hrs for the test. Patients were asked to take their usual anti-diabetic medications before the start of the test. Capillary blood samples were taken using a lancet and measured on a Glucometer (Accutrend, Roche). Every 10th sample was re-validated from the laboratory glucose oxidase method for accuracy of the result. A fasting blood glucose level was used as a baseline measure and was recorded as "start time" of the test. Participants were given a test food (dates and white bread) in accordance with the randomization sequence. The food was consumed in 5-10 minutes along with 150ml of water. Capillary blood samples were taken at 30, 60, 90, 120 minutes for analysis after the start time. Participants were asked to remain seated during the tests. The patients and controls were randomized to have either dates or white bread on day one. This was followed after one week (wash out period) by the second day test. On the 2nd (use same format everywhere "second") day, patients and controls were given different foods from the one they consumed on day one.

The mean glucose blood response of dates and white bread at 30, 60, 90 and 120 minutes was noted after the start time, mean values were calculated. Comparisons between patients and controls were made using t-tests. All data was analyzed and computed on SPSS version 23. Informed consent was obtained from all patients and the study was approved by the Institutional Review Board.

Inclusion Criteria for Patients: Adult patients of age more than 30 years with Type II diabetes mellitus for more than 5 years duration, having well controlled diabetes with HbA1c between 6% - 7% and resident of Islamabad.

Inclusion Criteria for Controls: Adult healthy volunteers with no history of diabetes or impaired glucose intolerance and resident of Islamabad.

Intervention: Commercially available test foods, dates and white bread were taken. Semi dried, dark brown dates of same size and variety were purchased from the vendor. Their seeds were removed and measured on a digital scale to make each serving of 25 g. Control food

(white bread) was purchased from the same vendor and weighed on a digital scale to make each serving to 25 g (both foods equal in weight).

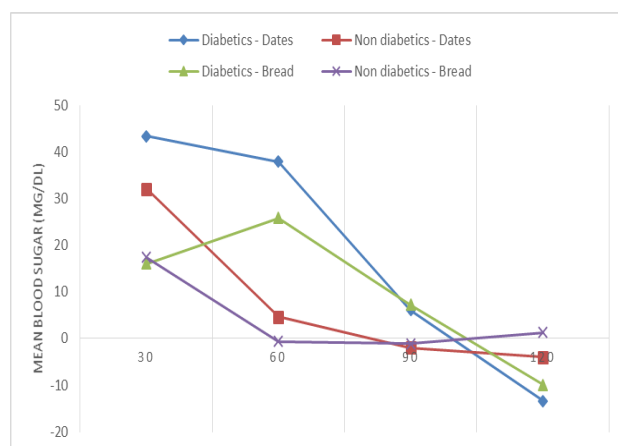
Results

In Type II Diabetics the mean blood glucose response to dates in contrast with bread was considerably higher in the first two time intervals and then lowered in last two intervals, though this difference was not significant at any point in time. Peak response to dates was achieved in 30 minutes while that to bread was achieved in 60 minutes. Beyond 90 minutes both values decreased to sub-basal levels. This decrease was more in case of dates than white bread. Values are illustrated in Table 1 and Figure 1.

Table 1: Response in diabetics (dates vs bread) expressed as mean \pm SD

Diet	30mins	60mins	90mins	120 mins
Dates	43.38 \pm 26.21	37.92 \pm 23.10	6.07 \pm 22.77	-13.38 \pm 20.03
Wheat	16.00 \pm 26.17	25.84 \pm 29.52	7.23 \pm 23.62	-9.92 \pm 21.61
p-value	0.015	0.257	0.900	0.676

Figure 1. Mean blood glucose response (mg/dl) curves of the case and controls to dates and bread



The mean blood glucose response to dates and bread was predominantly higher in diabetics with significantly higher values for both food groups. This difference was

especially marked for dates. At 60 minutes the p-value of 0.000 and 0.004 for dates and bread respectively was achieved which is statistically significant. The glucose response curve for diabetics fell to sub-basal level in three hours being lesser than non-diabetics concurrently. In both study groups peak glucose response levels for dates was 30 minutes while for bread it was 60 and 30 minutes in diabetics and non-diabetics respectively as shown in Tables 1 and 2.

Table 2. Mean blood glucose response to dates & bread (diabetics vs non-diabetics).

Response to Bread				
	30 mins	60 mins	90 mins	120 mins
Diabetics	16.00 \pm 26.17	25.84 \pm 29.52	7.23 \pm 23.62	-9.92 \pm 21.61
Non-Diabetics	17.38 \pm 7.17	-0.69 \pm 5.55	-1.15 \pm 8.60	1.23 \pm 9.61
p-value	0.918	0.004	0.241	0.102
Response to Dates				
	30 mins	60 mins	90 mins	120 mins
Diabetics	43.38 \pm 26.21	37.92 \pm 23.10	6.07 \pm 22.77	-13.38 \pm 20.03
Non-Diabetics	32.07 \pm 29.66	4.61 \pm 11.52	-2.07 \pm 12.17	-4.38 \pm 16.66
p-value	0.313	0.000	0.266	0.225

C max was higher in diabetics for both food groups at all time of points. The mean fasting glucose in diabetics and non-diabetics was 131.04 mg/dl, 90.12 mg/dl respectively.

Discussion

Our study results suggest that although the glucose response to dates and bread in diabetics is higher but is not statistically significant (Table 1). AlGeffari et al also reported no significant fluctuations in the glycemic response by consuming dates.⁵ According to the American Diabetic Association (2014) the primary goal in the management of diabetes is the regulation of blood glucose levels near normal concentrations. Whereas the difference between blood glucose responses in two food groups among diabetics and non-diabetics is statistically significant (p-values 0.000 and 0.004 for dates and bread respectively). Study has reported that the utility of

Glycemic Index (GI) is a significant determinant of the mean glycemic response elicited by a range of test meals of varying nutritional composition when tested in a group of subjects.⁴

Our study results depict the comparison made between response to dates and bread between the two study groups, a pattern is established whereby 1) blood glucose rise is consistently higher in diabetics in both food groups than the non-diabetics; 2) blood glucose rise to dates in contrast to bread is higher in both study groups. 3) In both study groups, blood glucose falls to sub basal level in three hours. The fall occurs earlier in non-diabetics, it is steeper and higher in diabetics than the former. In both groups the peak rise in blood glucose response for dates is attained at same time that is 30 minutes which is followed by a gradual fall while peak response for bread is achieved at a variable time being 60 minutes for diabetics and 30 minutes for non-diabetics. It is noteworthy that in non-diabetics sub basal fall in glucose levels is at 60 minutes for the bread while in diabetics the sub basal fall is relatively later at 120 minutes explained by the dysfunctional blood sugar regulation (Figure 1). However, the difference is insignificant at all points in time when the two food groups are compared in diabetics (Table 1).

The insignificant postprandial blood sugar fluctuations observed in our study for dates and bread in diabetics is contradictory to the popular notion that dates are better avoided in diabetics.¹¹ However direct comparison is not feasible with our study as the amount of test food used in our study was 25 g as opposed to the standard of 50 g.

Conclusion

Both dates and white bread carry an equal index of safety in diabetics. Dates are a suitable food group for diabetics and their consumption bears no added risk or danger over white bread.

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Association of depression, physical activity levels and general psychological health among physical therapy students of Rawalpindi and Islamabad

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A B S T R A C T

Objective: To determine the association of depression, physical activity (PA) levels and general psychological health among physical therapy students of Rawalpindi and Islamabad.

Methodology: This was a cross-sectional study conducted among students of physiotherapy department at Rawalpindi and Islamabad Institutions, from August 2015 to January 2016. Five hundred students were recruited using non-probability convenient sampling. The data was collected through a questionnaire that comprised of demographic information, Beck Depression Inventory-II (BDI-II), General Health Questionnaire-12 (GHQ-12) and Rapid Assessment of Physical Activity (RAPA). The data were analyzed using SPSS version 20 and correlation analysis was performed to see the relationship amongst depression, PA and general psychological health.

Results: Majority of the students (42.6%) had mild depression. However, 64.8% students had no psychological distress. Moreover, 33.4% of the students were involved in aerobic activities and majority of them (37.6%) were not doing any activities to improve flexibility and increase muscle strength. There was an inverse correlation between RAPA and BDI-II ($p < 0.001$) and a positive association between RAPA and GHQ-12 ($p < 0.001$).

Conclusion: The study concluded that majority of the students had mild depression but their general psychological health was not affected as they were involved in routine physical activity. The result of this study provides evidence that there is a negative relation between physical activity and depression and a positive relation between physical activity and general psychological health.

Keywords: Depression, general psychological health, physical activity, students.

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Introduction

Physical activity (PA) is an important consideration to lead a healthy life.¹ Physical inactivity (PI) is considered as modifiable risk factor for depression and other medical conditions e.g. cardiovascular disease, hypertension, diabetes mellitus and obesity. There are psychological benefits of PA among patients with depression and poor psychological health as it reduces stress, ward off anxiety and feelings of depression, boosts self-esteem, add and improves sleep.² PI is the fourth leading risk factor for

global mortality.³ The present test is to create projects and researches to advance physical exercise for all in our undeniably sedentary environment. Aerobic and resistance exercise improves mental states.⁴ Routine PA presumably eases a few manifestations connected with mild to moderate depression. Daily activity exhibits an improved physical as well as psychological health.⁵

Psychological issues might be the underlying cause of distress felt by a person. The clinical therapy can inhibit

distress but may not address the psychological diseases.⁶ Depression is one of the many primary factors that leads to psychological distress and thus interferes with the general psychological health/well-being of a person.⁷ An increase in physical fitness will reduce the risk of premature death and vice versa. Even a small improvement in physical fitness is associated with a significant reduction in risk. A study showed that the participants with the highest levels of physical fitness at baseline and who maintained or improved their physical fitness over a prolonged period had the lowest risk of premature death. Modest enhancements in physical fitness in previously sedentary people have been associated with large improvements in health status. For instance, in another study, people who went from unfit to fit over a 5-year period had a reduction of 44% in the relative risk of death compared with people who remained unfit.⁸

Students who are habitual of doing daily PA exhibit more noteworthy self-confidence, improved general psychological health and better classroom execution.⁹ Increased PA can manage sleep deprivation and depression and expand the capacity to concentrate on a specific assignment.¹⁰ Taliaferro LA et al, provided empirical evidence to establish association between physical exercise, particularly aerobic movement, and decreased depression, hopelessness and suicidal conduct among students.¹¹

Deepthi R et al. have shown that engagement in PA may be an essential contributing element in high-quality intellectual health of medical students and hence promotion of PA is essential for good mental wellbeing and treating mental health problems among medical students.¹² Robert A et al. concluded that PA is mandatory for prevention of mental illness among medical students, by introducing PA in medical student's curriculum to assist the students in improving their mental as well as physical health.⁵

Over ninety percent of mental health problems are anxiety and depression and co-morbidity which one make it clear and revise sentence is common. Five out of the ten leading disorders that generate the most disability-adjusted life year (DALYs) are psychiatric in nature including depressive disorders. Two-third of the affected people is living in the developing countries; and this ratio

is expected to rise. Pakistan is a developing country, where 25% to 30% of study population is suffering from anxiety and depression.¹³ An estimated 121 million people living in the world revise sentence writing world population rather living in world currently suffer from depression. Doctors face particular challenges and conditions such as high patients' attendance, long duty hours, limited resources to work, repetitive exposure to traumatic events, potentially violent situations, difficult patients, ethical dilemmas and critical decision making that place them at more risk of anxiety, depression and other stress related psychosocial problems.¹³ A study conducted in Azra Naheed Medical College, Lahore assessed the physical therapy students and recommended that engagement in physical movement can be a vital contributory component in the psychological wellness of college students.¹⁴

Rehabilitation is an emerging field in Pakistan and has a key role in patient care and treatment.¹³ Students of rehabilitation studies are under constant pressure of tough study schedule as the physical therapy practice is becoming increasingly complex.¹⁵ A study was conducted among rehabilitation students to assess level and causes of depression by Anum Hussain et al. to determine the level of depression among rehabilitation students which reported that depression prevails among physical therapy students.¹⁶ So attention should be given to improve academic outcomes of physical therapy students by exploring the factors that can boost up their general psychological health.

This study aimed to explore the association of depression, physical activity levels and general psychological health among physical therapy students in Rawalpindi and Islamabad.

Methodology

This was a cross-sectional study conducted among students of physiotherapy department at Rawalpindi and Islamabad Institutions, from August 2015 to January 2016. Five hundred students were recruited using non-probability convenient sampling. Physical therapy students of both genders with age ranging between 18 and 26 were included in the study. Students of other professions/disciplines, with underlying disease, disability, trauma, and students with diagnosed psychological

illnesses were excluded. A questionnaire used in the current study was pre-tested and consisted of questions regarding age, gender, domicile, accommodation, and semester of a student. Questions on Depression, Physical activity and General Psychological Health were taken from Beck Depression Inventory-II (BDI-II) with 21 questions, Rapid Assessment of Physical Activity (RAPA) with 9 questions, and General Health Questionnaire-12 (GHQ-12) with 12 questions respectively. These tools demonstrated high reliability (Cronbach's Alpha = 0.814). Students were approached in the universities and their consents were taken. Data were analyzed using SPSS software version 20. Descriptive statistical methods were used to determine mean and standard deviation in the assessment of the data and spearman's rank-order correlation test was performed to relate the three variables. The significance was defined as $p < 0.01$.

Results

There were 307 (61.40%) female and 193 (38.60%) male students registered in the study. The mean age of the students was 20.73 ± 1.626 (range 18-26). Demographic characteristics of participants are presented in table 1.

Table 1: Demographic characteristics

Variable		n (%)
Age	18	21 (4.2%)
	19	113 (22.6%)
	20	126 (25.2%)
	21	75 (15.0%)
	22	83 (16.6%)
	23	54 (10.8%)
	24	24 (4.8%)
	25	3 (0.6%)
	26	1 (0.2%)
Gender	Male	193 (38.6%)
	Female	307 (61.4%)
Domicile	Rural	133 (26.6%)
	Urban	367 (73.4%)
Accommodation	Day scholar	320 (64%)
	Living in dormitory	180 (36%)
Semester	1st	55 (11.0%)
	2nd	76 (15.2%)
	3rd	65 (13.0%)
	4th	56 (11.2%)

	5th	50 (10.0%)
	6th	88 (17.6%)
	7th	14 (2.8%)
	8th	43 (8.6%)
	9th	16 (3.2%)
	10th	37 (7.4%)

More students (42.6%) had mild depression on BDI-II scale (2.13 ± 0.876) while 64.8% students had minimal psychological distress on GHQ-12 scale (1.41 ± 0.606). A significant proportion (33.4%) of students were involved in aerobic activities on RAPA - aerobic exercise scale (3.76 ± 1.126) while 37.6% students were not doing any physical activity to improve flexibility and increase muscle strength on RAPA-anaerobic exercise scale (Table-2).

Table 2: Descriptive statistics of BDI-II, GHQ-12, RAPA

Variable		n (%)
BDI-II	minimal depression	128 (25.6%)
	mild depression	213 (42.6%)
	moderate depression	124 (24.8%)
	severe depression	35 (7.0%)
GHQ-12	minimal distress	324 (64.8%)
	mild distress	147 (29.4%)
	moderate distress	28 (5.6%)
	severe distress	1 (0.2%)
RAPA 1: Aerobic Exercise	1-sedentary	23 (4.6%)
	2-underactive	48 (9.6%)
	3-under active regular light activities	108 (21.6%)
	4-5 under active regular	167 (33.4%)
	6-7 active	154 (30.8%)
RAPA 2: Anaerobic Exercise	0-none	188 (37.6%)
	1-Strengthening exercises	44 (8.8%)
	2-Flexibility exercises	161 (32.2%)
	3-both strengthening and flexibility exercises	107 (21.4%)
	minimal depression	128 (25.6%)
	mild depression	213 (42.6%)
	moderate depression	124 (24.8%)
	severe depression	35 (7.0%)
	minimal distress	324 (64.8%)

Spearman's rank-order correlation test was performed to correlate depression, physical activity and general health (table 3).

Table 3: Inferential Statistics of the Study

Spearman's rank-order correlation	r	p-value
BDI-II* RAPA-Aerobic exercise	-0.459	<0.001
BDI-II* RAPA-Anaerobic exercise	-0.554	<0.001
GHQ-12* RAPA-Aerobic exercise	-0.419	<0.001
GHQ-12* RAPA-Anaerobic exercise	-0.485	<0.001
BDI-II* GHQ-12	0.591	<0.001

(*) shows that correlation is run between 2 particular variables.

Discussion

The study found that physical therapy students suffered from mild depression, minimal psychological distress and were physically active. Furthermore, there was a significant negative correlation between physical activity and general psychological health measured on RAPA and GHQ-12; and physical activity and depression measured on RAPA and BDI-II respectively as the higher scores of RAPA are associated with low scores of GHQ-12 and BDI-II which suggests that higher levels of physical activity are associated with improved psychological health and a decrease in depression.

Our study showed that more physical therapy students (24.8%) had moderate depression. This finding differs from another cross-sectional survey done on medical college students in 2008 in Dubai that showed only 3.88% students had significant depression.¹⁷ The potential reason of this inconsistency could be the burden of academic syllabus.¹⁸ Overall, 74.4 % students were found to have mild, moderate or severe depression. This result is supported by another study performed on a public medical college in Karachi, which reported high prevalence (70%) of depression among the students.⁹ It was found that more than half of the students (64.2%) were physically active as compared to a study conducted on undergraduate students, which reported that more than half of the students were physically inactive. This

could be due to the lack of time and motivation of the medical students as reported in that study.¹⁹

We found that 64.8% students had minimal psychological distress, a few (5.6%) students had moderate psychological distress and only one (0.2%) student had severe psychological distress. Compared to our study, another study conducted on physical therapy students showed that 27% students had a significant psychological morbidity.²⁰ It could be due to higher level of physical activity among physical therapy students of Rawalpindi and Islamabad.¹⁶ We found a significant negative association of physical activity level and depression; this finding is similar to previous studies reporting a bidirectional relationship between physical activity level and depression i.e. higher physical activity levels can lesson depression and vice versa.²¹ Many studies favored the study outcome that higher intensity of physical activity can improve general psychological health of physical therapy students.²²

Strengths and limitations:

No study has been conducted on Doctor of Physical Therapy Students that addresses the association between physical activity, depression and general psychological health in Pakistan. The study is limited by the fact that majority of students in the study were females. The sample size was small and non-probability convenient sampling was used to collect the sample; which could be a source of potential bias and influence external validity of the study. However, an effort was made to collect data equally from different physical therapy colleges of Rawalpindi and Islamabad to improve the overall representation so that it can be generalized within the two cities. It is a challenge for all of the physical therapy colleges to enhance the well-being of students by organizing "coping course" skills sessions so that they can learn how to deal with the depression. Students should be encouraged to engage in physical activities. Both individual as well as population level approaches are required for this. Individual approach can be mediated by developing social influence from friends and families as a key tactic to enhance physical activity. For population-based approach, physical therapy college policymakers can take appropriate measures to highlight significance of student's involvement in regular physical activity programs as an active participant to overcome the

difficulties they face during their studies and/or personal life.

Conclusion

Our study showed that majority of the students had mild depression but their general psychological health was not affected as they were involved in routine physical activity.

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Histamine receptors as drug target: Current and future therapeutics

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A B S T R A C T

Histamine is a neurotransmitter responsible for central regulation of inflammatory reactions. Initial studies were done by Sir Henry Dale in 1993. Histamine acts on its four type of receptors. H1 and H2 are well-established with pharmacological status. H1 receptors are mainly linked with inflammatory responses and developed to mitigate the inflammatory symptoms. While H2 antagonists are established with their role in decreasing basal gastric secretions by decreasing the cyclic adenylyl mono phosphate (cAMP), thus used as therapy line for gastric ulcers. H3 being located centrally imparts its central effects in cognitive functions that are pain, sleep, and memory modulation of neurotransmitters release including, dopamine, acetylcholine, noradrenalin and serotonin. H4 is discovered recently during cloning of H3 and found on immune related cells as, mast cells, T cells and dendrites. Experimental studies are helping in development of more pharmacologically worth drugs that can increase the quality of life.

Keywords: Histamine antagonist, inflammatory reactions, neurotransmitter

Introduction

Histamine was first discovered as an autacoid, which acts as a local hormone which works near the synthesis site for a brief duration unlike endocrine glands.¹ The earlier studies published on histamine and regarding its neurotransmitter properties and inflammatory actions.² It is found in blood circulation all over the body but its higher concentrations are found in lungs, skin and gastrointestinal tract. Histamine is a basic amine formed by decarboxylation of histidine, an amino acid, in the presence of decarboxylase enzyme. It is found in mast cells, basophils and as histaminocytes. Histamine is stored in an inactive form in intracellular granules in association with acidic protein and heparin. It is released by exocytosis when allergic stimuli interact with cell surface receptors or antigen IgE interaction with antibody and results in type I inflammatory reaction.³ When released, it is metabolized either by action of di-amine oxidase DAO and histamine-N-methyl transferase (HNMT). DAO is stored in epithelial cells and released in blood circulation, when required, and is responsible for extracellular histamine metabolism and reducing its effect.

While, HNMT is responsible for the fate of intracellular histamine.⁴ Anti-histamine drugs are developed in order to mitigate the inflammatory response, by blocking any of the relevant histamine receptors. Locations and effects of histamine receptors are shown in table 01.

Histamine receptors as drug targets:

All four types of histamine receptors are specific in their immune responses. The H1 and H2 receptors and their therapeutic uses have been studied in detail, while, H3 and H4 are still under in-depth investigation.

H1 receptors as drug targets:

H1 receptor histamines were discovered in early 20th century by Swiss-Italian Pharmacologist Daniel Bovet for the relief of allergic symptoms. He won the Nobel Prize for this discovery in 1957. The discovery of H1 Antagonist led to the development of first, second and third generation of histamine antagonists.⁵ H1 receptors which are found on mast cells, basophil, eosinophil, when activated by antigen or stimuli binding with receptors lead to the bursting of these cells ultimately resulting in the release of

Inflammatory mediators interleukins, leukotriene, cytokines, and Histamine that then impart their inflammatory actions. H1 receptor antagonist are mainly involved in mitigating the symptoms of nasal congestion, itch, edema, rhinitis airways and skin inflammation.⁶

Table 1: Location and effects of histamine receptors

Histamine Receptor	Location by cells	Systemic location	Major effects
H1	Smooth muscles, Endothelial cells, Epithelial cells, Neutrophils Eosinophil Monocytes, Macrophage, T and B cells	Exocrine	Increase mucus secretions
		Respiratory	Bronchiolar constriction Decrease Lung capacity
		Intestinal	Intestinal Cramps Diarrhea
		Skin	Triple response
		Neuromuscular	Itch & pain
		Cardiovascular	Positive Chronotropic, Ionotropism
H2	Parietal cells	Stomach	Increased acid secretion
	Smooth cells	Cardiovascular	Positive chronotropic
H3	Histaminergic neurons	CNS	Cognitive effects Pain, sleep
H4	Mast cells, Eosinophil, T & Dendritic cells	Immune system	Immune response

Following are the different generations of H1 antihistamines:

First generation:

The first generation H1 antagonists are lipophilic and can cross the blood brain barrier (BBB) resulting in CNS effects of marked sedation, increased appetite and weight gain. They are still used because of their high receptor binding ability despite their binding to acetylcholine, serotonin and calcium channels. Decreased alertness and marked sedation are their major side effects.^{7, 8}

Second generation:

The histamine antagonists cannot cross Blood Brain Barrier (BBB), thus avoiding the CNS effects. Moreover, these are selective to the H1 receptors avoiding the muscarinic effects. They are potent and efficient than the first-generation drugs. Some of these even have longer duration of action, thus having a competitive advantage over the first generation.⁹ However, some of these like terfenadine and astemizole show marked cardiotoxicity leading to market withdrawal. Some of these second-generation histamine antagonists also show somnolence and sedation at high doses.¹⁰

Current and future findings of H1 antagonist:

Possible third generation:

Apart from the well-established first- and second-generation antihistamines, the second-generation histamine blocker used to relieve nasal congestion and other respiratory inflammation symptoms. Dr. Holgate first introduced, Ebastine, in 2003 which had significant competitive therapeutic profile over the already discovered antagonists. As shown in table 02, but being an inverse agonist is not good alone and need other H1 antagonists in combination for profound pharmacological effect.¹¹ However, its one metabolite, Carebastine has H1 antagonist property.¹² But according to Consensus group on new-generation antihistamines (CONGA) recommendations and its clinical effectiveness it has the potential to be added in the third generation of H1 antagonist.¹³

H2 receptor drug targets:

H2 receptor antagonists are mainly related to the treatment of gastric ulcer by decreasing the basal and food related acid secretion. H2 antagonist binds to histamine receptors leading to the decrease in cAMP and thus inhibiting the gastric secretion.¹⁴

Most well-known H2 antagonists include: Cimetidine, Famotidine, Nizatidine, and Ranitidine. Although all of the given H2 antagonists are effective in decreasing basal gastric acid secretions, studies have revealed that Famotidine is 9 and 32 times more potent than Ranitidine and Cimetidine respectively. It has long duration of action

and has been proven safe and effective in long term therapies as in Zollinger-Ellison syndrome.¹⁵

Table 2: First- and second-generation antihistamines and their potential advantages and disadvantages

Advantages	H1 Antagonists	Disadvantages
First Generation		
Use for motion sickness	Diphenhydramine Hydroxyzine	
Long duration of action	Promethazine Cyproheptadine	Appetite & weight gain
Second Generation		
Long duration of action Non-sedating	Fexofenadine	
Non-sedating	Loratidine	Appetite & weight gain
Non-sedating	Cetirizine	
Long duration of action	Astemazole	Slow onset of action Cardiotoxicity
Possible third generation		
Non-sedating No cardiotoxicity No muscarinic effects	Ebastine	H1 inverse agonist

Current findings and future for H2 antagonists:

Long term therapy with H2 antagonist results in development of tolerance against the drug. But in 2010 under the light of research it was suggested that the intermittent administration of H2 antagonist do not cause tolerance.¹⁶

H3 receptor drug targets:

H3 receptors are present in the histaminergic neurons in small part of the hypothalamus and its axons spread as fine paths throughout the brain,¹⁷ resulting in its effects on CNS. Although histamine in circulation cannot cross the BBB but here histamine acts on histaminergic neurons for its outcomes. Histamine executes its effect through G protein coupled receptors. H3 receptors being involved in negative feedback, self-neurotransmitter release produces histaminergic effects but also involve in modulating effects of other neurotransmitters.¹⁸ Presynaptic effects help in controlled release of Histamine

while postsynaptic modulate the release of other neurotransmitters like acetylcholine and dopamine.¹⁴ H3 plays important role in memory, cognitive functions, sleep, pain, and regulation of normal haemostasis of body and also in a tension deficit hyperactivity disorder (ADHD), Alzheimer's disease, sleep cycle and obesity.^{15, 16}

Acetylcholine modulation:

H3 antagonist enhances the release of acetylcholine while its agonist decreases its release. Thus, use of H3 antagonist has implications in short-term memory impairment.¹⁹

Dopaminergic modulation:

H3 antagonist also has effect in modulating Dopaminergic release. As observed in Schizophrenia, H3 antagonist modulates release of dopamine and helps treat dopamine imbalance. Hyperdopaminergic, positive schizophrenic symptoms (attention deficiency, apathy) can be targeted by using H3 antagonists.²⁰ Studies reveal that H3 agonist result in decrease dopamine release but H3 antagonist alone produce no direct effect.²¹ However administering H3 antagonist in the presence of Methamphetamine (Amphetamine derivative) can potentiate the dopaminergic effect. H3 antagonist here potentiates the methamphetamine effects centrally showing their effect in CNS.²²

Norepinephrine modulation:

Norepinephrine, present in cortical and hippocampus regions is responsible for attention and behavioural responses. Many psychotic ailments are modulated by noradrenergic release. H3 receptor antagonists are also here to serve their purpose especially GSK189254* (H3 antagonist in pre-clinical models), an H3 antagonist increased basal noradrenergic release resulting betterment in cognitive impairment.¹³

Serotonin modulation:

Serotonin is linked with treating unipolar depressions by using Serotonin re-uptake inhibitors. The role of H3 antagonist in Serotonin modulation is different. H3 antagonist increased the release of serotonin in-vitro however the effect was not corroborated by studies conducted in vivo. The action of H3 agonist is observed as the decreasing effect on the release of serotonin in vivo and its effect was successfully conversed by the use of H3 antagonist. Furthermore, alone it has no effect on serotonin release. However, this field can be of good

interest to carry on research for any combination of H3 antagonist and serotonin reuptake inhibitor for serotonin modulation.⁸⁻¹¹ H3 antagonist being a modulator of above, and also Histamine itself is involved in cognitive regulation. Some of the studies reported that its inhibition is effective for smooth cognitive functions. Thioperamide, an H3 antagonist has shown compelling results in improving cognitive functioning.¹³

Future for H3 antagonists:

GSK189254*, an H3 antagonist that modulates the release of acetylcholine, dopamine and noradrenergic neurotransmitters is under investigation for therapeutic intervention of cognitive impairments. Moreover, Pfizer has more than a dozen applications for patent rights for anti-inflammatory drugs for respiratory inflammation in combination and also CNS effecting drugs.¹⁴ Apart from H3's Central effects H3 receptors are also found peripherally in gastrointestinal system, Respiratory system and cardiovascular system. H3 receptors found in postganglionic region in bronchi are seemed to be effective in asthma therapy as these can prevent bronchoconstriction. Combination of H1 and H3 pharmacophores, thought to be effective in nasal congestion and cutaneous itch, are being designed. GlaxoSmithKline (GSK) developed a ketopiperazine compound, GW-784568X that has passed Phase I/II Clinical trials and applied for its patent right. It is meant for relieving the nasal congestions. Moreover, two other compounds; a combination of H1 and H2 antagonists are also in Phase II of clinical development for relieving allergic rhinitis.¹⁵

H4 receptor antagonist:

During the cloning of H3 receptor researchers have found that previously discovered G-protein coupled receptor is H4 receptor as responded to the Histamine by decreasing the cAMP production.²¹ H4 receptors are found abundantly on eosinophil, monocytes, basophils, dendritic cells, mast cells, and T cells, suggesting its implications in treatment of inflammatory disorders and pruritus.²²

Current H4 targets and future Aspects:

Studies are being carried out to understand H4 receptor. It is related to itch as H4 agonist clobenprop. It led to pruritus and itch so its antagonizing effect will possibly treat these conditions. One of the standard H4

antagonists JNJ7777120 is used in studies to find out more about H4 receptors. A study carried out to check the anti-inflammatory effects of JNJ7777120 in rat model with carrageenan induced inflammation and thermal hyperalgesia. A 10 to 30 mg/kg subcutaneous administration into the subjects lead to the evident relief of oedema in initial 2 hours along-with it temperature was also moving to normal thus having significant anti-inflammatory and analgesic effect.²³ It has shown experimentally that combination of H1 and H4 antagonist can be worth in developing therapy for murine asthma. Combination of Mepyramine (H1 antagonist) and JNJ7777120 (H4 selective antagonist) has shown synergic effect for treating murine asthma. Furthermore, this experimental study also gives a new sight for study and development either of developing combination drugs of H1 and H4 targets or by one ligand for both receptors or two ligands forming a synergic pharmacophore.²⁴

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From idiopathic thrombocytopenic purpura to systemic lupus erythematosus

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A B S T R A C T

Thrombocytopenia is one of the cardinal features of Systemic Lupus Erythematosus (SLE). It is recognized as the earliest and rarely the sole manifestation of SLE at the time of diagnosis. This report narrates the case of one such patient who had an abrupt onset of life-threatening thrombocytopenia and was subsequently diagnosed as having SLE.

Keywords: Idiopathic thrombocytopenic purpura, systemic lupus erythematosus, thrombocytopenia

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Introduction

SLE is an autoimmune disease in which a person's immune system mistakenly attacks its own tissues itself. It can affect any organ system of the body like skin, brain, cardiovascular system, gastrointestinal tract, kidney and locomotor system and hematological system. We will discuss a case report of severe thrombocytopenia which was due to SLE.

Case report

A 25-year-old single lady from Gujrat, with no previous pre-morbid illness, was admitted in Medical ward of a tertiary care hospital of Islamabad through emergency. Her chief complaints were gums and nasal bleeding for 3 days along with a petechial rash for 01 day. She was taken to a local doctor in Gujrat who gave her Proton Pump Inhibitors and Multivitamin tablets. Two days later she developed generalized petechial rash more prominent on limbs. At this point she was taken to District Head Quarter (DHQ) hospital Gujrat where her blood complete picture showed severe thrombocytopenia. She was

transfused with 06 units of Platelets and then referred to a tertiary care hospital.

When she was seen in our hospital, she had petechial rash all over her body while her nasal and gum bleed had temporarily stopped. However, next day she again developed nasal and gum bleed along with macroscopic hematuria. She did not have any history of fever or any other systemic upsets except history of arthralgia. Her past medical history was insignificant as was her personal and family history. On examination her vital signs were stable. General physical examination only revealed widespread petechial rash on her body most prominent on limbs with no palpable lymph nodes, pallor or jaundice. She had sub-conjunctival hemorrhage in her left eye with normal vision. Systemic examination was also unremarkable.



Figure 1: Petechial rash on legs.



Figure 2: Sub-conjunctival hemorrhage.



Figure 3: Petechial rash on upper limbs.

Keeping her symptoms in view our list of differential diagnosis for the patient included Idiopathic Thrombocytopenic Purpura (ITP), Dengue Fever, Malaria, Hematological malignancy and Systemic lupus erythematosus. Her investigations showed a normal white cell count, Hemoglobin of 10.7 with MCV 76 and markedly low platelets count of 9000. Her electrolytes, liver and kidney function tests were normal as was her urinalysis. Malarial parasite and Dengue fever screening were negative. Chest imaging by X-ray and ultrasound abdomen were also normal. Results of clotting profile and

D-Dimers also came out negative. To evaluate the cause of thrombocytopenia her bone marrow biopsy was performed and report showed a hyperplastic marrow with the impression of peripheral destruction of platelets. At this point a diagnosis of ITP was considered, however, before labeling patient as a case of ITP an autoimmune screen was run along with complement levels. Both ANA (performed by indirect immunofluorescence method) and Anti ds DNA antibodies were strongly positive and complement levels were markedly low – C3= 50 (Ref: 83-140), C4= 5 (Ref: 10-20). Hence, on the basis of these test results, the patient was diagnosed as having SLE.

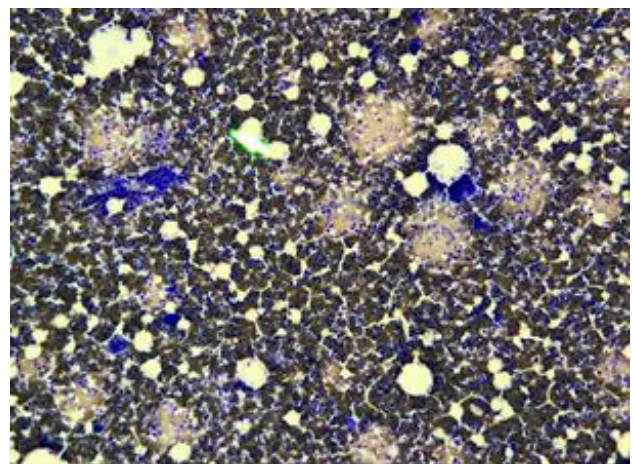


Figure 4: Bone Marrow biopsy – Megakaryocytes can be clearly seen

The patient was transfused with platelets to prevent active bleeding. She was given pulsed Methylprednisolone 1 gram for three consecutive days followed by oral Prednisolone at 1mg/kg body weight. Calcium and Vitamin D supplements were also prescribed to prevent Glucocorticoid induced osteoporosis. She was also given Hydroxychloroquine to prevent flares of her disease. Iron supplement was also started as she had a mild microcytic anemia. Her Platelets began to increase on day 3 and on discharge her blood CP showed a Platelet count of 1, 14,000. She has been advised a regular follow up in outpatient department.

Discussion

SLE is an autoimmune disease involving different organ systems of the body.¹ The spectrum of clinical features in patients of SLE is very wide and varies from a mild skin rash to severe organ or life threatening disease.²

Based on such variable presentation of symptoms it can be easily said that no two patients of SLE are alike. Hematological manifestations of SLE include anemia, thrombocytopenia and low white cell count or a combination of any of these. Thrombocytopenia is one of the criterions mentioned in the American College of Rheumatology (ACR) classification criteria for SLE.³ This case report highlights the importance of screening patients with thrombocytopenia for connective tissues diseases particularly SLE before labeling them as a case of ITP. Traditionally a diagnosis of SLE and other connective tissue diseases is thought of only when a patient presents with a particular set of symptoms. However, from literature review it is clear that sometimes low platelet count may be the only manifestation for some time before development of overt SLE.

The prevalence of thrombocytopenia in patients of SLE has been shown to be 7% to 30% according to studies conducted in the past.⁴ Also it has been seen that thrombocytopenia is associated with increased risk of lupus nephritis, neuropsychiatric manifestations of SLE, hematological involvement and over all a high prevalence of thrombocytopenia in patients of SLE has been shown to be 7% to 30% according to studies conducted in the past.⁴ Also it has been seen that thrombocytopenia is associated with increased risk of lupus nephritis, neuropsychiatric manifestations of SLE, hematological involvement and over all a high disease activity and more chances of end organ damage compared with SLE patients who had normal platelet count.⁵ However, on the other hand these patients are seen to have low prevalence of skin involvement.

Thrombocytopenia is sometimes the sole manifestation of SLE. Such cases are often erroneously labeled as ITP till the time they develop other symptoms of SLE. Studies conducted in early nineties^{6, 7} demonstrated that low platelet count can be one of the earliest manifestations of SLE. Such patients also often have history of arthralgia or arthritis and sometimes presents with skin rash too. It can take between 4 and 14 years for the patients to fully develop manifestations of SLE.⁵ Our patient too gave history of arthralgia involving both knee joints and sometimes small joints of hands. Other than the musculoskeletal system rest of the systems were found to be uninvolved in our patient both

in past and also during her admission in hospital. Literature review also shows that presence of Anti Ro antibodies in patients of thrombocytopenia can be used as a predictor of development of SLE at a later stage.⁷ None of the true ITP patients are positive for this antibody.⁶ Because of affordability issue ENA profile could not be done in our patient to look for Anti Ro antibody positivity but we plan to get it done in future when she comes for follow up visits.

Conclusion

Thrombocytopenia in a young female should not be ignored. SLE should be included in the list of differential diagnosis in all patients presenting with thrombocytopenia. By timely diagnosing SLE effective measures can be taken to prevent life threatening complications of this disease.

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Assessment of research methodology concepts through critical appraisal among undergraduate medical students and their perception: A single center study.

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A B S T R A C T

Introduction: Evidence based medicine is an interplay of individual clinical acumen and best available evidence through scientific systematic research. With the advent of modern medicine in the last two centuries, medical education has seen and continues to experience its revolutionary effects. An important aspect in this regard is the integration of biomedical research.

Objectives: To assess the research skills among undergraduate medical students exposed to the teaching of research longitudinally through all the five academic years.

Methodology: A mixed method study was conducted in which third year MBBS students were assessed in a group through power point presentation regarding different concepts of research while critically appraising a research article. Quantitative and qualitative data were collected. Descriptive statistics were calculated, as well as thematic analysis was done.

Results: From a total of 102 participants, 58 were male and 42 were female. Majority of the participants (81.4%) achieved an average or a good score and only 18.6% achieved a poor score. Six themes were generated. General enthusiasm about the activity was noted among participants who considered it beneficial. However, only a few were in the favor of incorporating this activity as a mandatory component in undergraduate studies.

Conclusion: Incorporating research in a mandatory longitudinal theme component as part of undergraduate medical studies seems a potential method of laying the foundation for future physician scientists.

Keywords: Research, critical appraisal, undergraduate medical curriculum

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Introduction

Evidence based medicine is an interplay of individual clinical acumen and best available evidence through scientific systematic research.¹ While there has been a lot of focus on developing this clinical acumen throughout the history of medical education, interest in nurturing research skills has only surfaced in the last few decades. The issue of 'endangerment' of physicians pursuing clinical research was highlighted as early as the 1980s. However, 40 years down the line, the problem continues to persist. Multiple

reasons have been attributed to this, with the core lying at the level of colleges and universities.¹

In an attempt to curtail this extinction, medical schools throughout the world are incorporating research in undergraduate curriculum.²⁻³

These incorporations have been in the form of research driven curricula,⁴ research electives,⁵ compulsory research projects for graduation,⁶

programme for volunteers, and facilitation of research training by charitable non-governmental organizations.⁷ These have amalgamated in the form of student-led national collaborative research training initiative and student selected components of learning among others.⁸⁻¹⁰

In developing countries, however, the situation is much grimmer. The lack of four 'Is' have been implicated in the lagging behind of these countries; impulse, initiative, incentive and idols.¹¹ The 'brain drain' of qualified personnel, idols, produces a lack of research environment which fails to generate an impulse to initiate the potential learner; the 'lacking' environment offering little to no incentive whatsoever to curb the situation.

In Pakistan, where only seven medical journals are listed by the journal of citation reports with the highest impact factor still less than one,¹² priority of quality research among medical students remain low. As of a few years back, only two medical schools in the country dominated student publications in Journal of the Pakistan Medical Association, a PubMed indexed journal; a staggering 87.5% of the 96 articles were published by students of these two schools over 90 issues of that particular journal.¹³

A recent study done in a leading medical school in the country demonstrated that while most of the participating medical students considered research to be useful, only a third of them considered it a good career choice. However, a disturbing finding was that senior students not only considered it more difficult and stressful when compared with junior students, they were also less likely to be in favor of incorporation of research in professional education.¹⁴

In this study, based on the training of students in medical research in a longitudinal theme spread over five years of medical school education, assessment of the critical appraisal skills was carried out followed by documenting their perceptions.

Methodology

A mixed method study was conducted in July 2018; a quantitative cross-sectional study and a qualitative study in the form of focused group discussion. This study was conducted after taking ethical committee approval. Participants were ensured regarding confidentiality of data

collected. The study included students from a private medical school with integrated modular curriculum in Islamabad. Students are taught four different components of longitudinal theme over a period of 5 years; ethics, evidence-based medicine, research methodology and behavioral sciences. The first three years focus on developing the understanding while the last two years focus on instigating the students to practically implement the understanding of these concepts. All 3rd year MBBS students were included. Students who were in different years of MBBS at the time of study were excluded. Programme learning objective of research for year 3 MBBS students are given in box 1. Course topics, methods of teaching and learning, assessment for year 3 MBBS students are presented in box 2.

Box1: Programme Learning Objective: Year 3 MBBS

1. Develop a research question and write synopsis under supervision of assigned preceptor.
2. Submission of research proposal to ethical committee (IRB), Shifa Tamer-e-Millat University (STMU) and subsequent approval.
3. Critically appraised a given research article
4. Prepare and present an e-poster based on review of literature.

Box 2: Course Topics, Methods of Teaching and Learning, Assessment.

Course contents

Introduction to Evidence Based Medicine
Introduction to research
Steps of research
Literature search
Literature review
Selection of research topic
Developing research question
Epidemiological study designs
How to critique an article?
Writing a research proposal

Method of teaching and learning

Large group interactive session
Small group discussion
Team based learning

Method of assessment

Multiple choice questions
Short answer questions
Integrated practical exam

All participants were randomly assigned to 7 groups of 14 to 16 individuals. Randomization was done in Microsoft Excel using RAND function. Each of the 7 groups was given one published article related to Endocrinology and Reproduction as shown in Table 1.

Table 1: Topics assigned to each of the 7 groups

Groups	Topic Assigned
Group 1	Sexually transmitted infections
Group 2	Contraceptives
Group 3	Breast Cancer
Group 4	Goiter
Group 5	Rickets
Group 6	Complications of Diabetes Mellitus
Group 7	Diabetes Mellitus

We conducted an interactive lecture, which included all the participants, to refresh the knowledge of research protocol and critical appraisal. Participants were then given a week to prepare a presentation on the assigned article. The proposed criteria for assessment were shared with the participants. Each group was allotted a total of 20 minutes for their presentation. This was followed by 10 minutes of questions by assessors. A panel of five Professors assessed the presentations. Participants were marked with 0 being the lowest score and 10 being the highest. Those who did not play an active role in the presentation were cross questioned by the panel and assigned a score. The power point presentation included: abstract, introduction, materials and methods, results, discussion and conclusion. A good score refers to a score of 7 or more, an average score 4 to 6 and any score below 4 was considered poor. These were recorded on student logbook. Descriptive statistics were used to detail the gender and score of the participants.

Volunteers were invited from each of the 7 groups to reflect on the entire activity, a total of 3 groups were made. We conducted a focus group to gather the perceptions of students regarding this activity which was audio recorded that was later transcribed for generating different themes. Thematic analysis was done for the qualitative data by reviewing the audios recorded to streamline themes discussed.

Results

A total of 102 participants were included in the study; there were 58 (56.9%) male and 44 (43.1%) female. Figure 1 describes the distribution of scores while table 2 compares score with regards to gender.

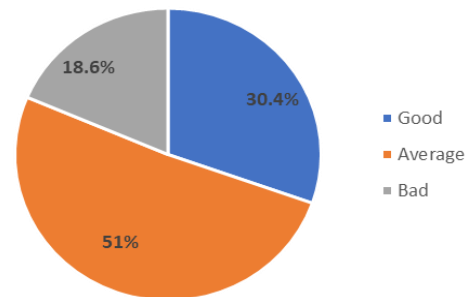


Figure 1: Frequency distribution of scores of participants.

Table 2: Comparison of scores on the basis of gender.

Score	Gender		p value
	Male	Female	
Good	16	15	p > 0.05
Average	33	19	
Poor	9	10	

Thematic Analysis

A total of 31 participants volunteered for this part of the study. Table 3 relates the volunteers with their scores. Six themes emerged from the discussions; usefulness and relevance, inspiration for research, longitudinal mode of content delivery, individual learning, peer assessment, and continuing the activity in future years.

Table 3: Distribution of volunteers for focus group according to score.

Detail of volunteers	Good	Average	Poor	Total
Number of volunteers	13	15	3	31
Percentage of volunteers from the specific category	41.9	28.8	15.8	30.4

Usefulness and relevance: All three groups of participants held the view that it improved their understanding of research and research methodology in practically implementing what they had been previously taught. Furthermore, it helped them realize the way an article is actually structured, what to look for in the articles and note flaws and weaknesses in articles; '... from all this activity, we found out how to go through an article, how to get out of it what we need out of it ...' Some participants, however, did consider this activity to be more than their capacity and attributed it to the difficulty level of articles as one put it '... you can't expect us to comprehend that fully ...'.

Inspiration for research: One group of participants was unequivocal in that they were inspired by this activity realizing that it doesn't have to be a completely flawless article or study in every aspect for it to be considered a reasonable study, '... you don't have to write a perfect article for it to be published ...'. Moreover, it helped them appreciate the importance of local research related to prevalence, risk factors and demographic details further encouraging them, in the words of a participant '... to understand Pakistan's pathologic demography, we'll need to promote local research more, since internationally they already know everything ...'.

Longitudinal mode of content delivery: Regarding the way the content had been delivered in interactive lectures in the longitudinal theme, one group did agree that it made sure that they weren't completely new to the subject. However, most believed that delivery of the content needed considerable improvements citing logistic factors; such as dissemination of information among small group discussions in contrast to large groups, or clearer instructions or a suggested procedure for critical appraisal given, or sample critiqued articles provided as references; '... if the instructions were a little clear on the exact procedure as to how stepwise we should proceed ...'.

Individual learning: Two of the groups were unsatisfied with the number of participants in a group since that ends up in only a third of the group doing the actual work with the rest not showing any interest whatsoever. '... You don't need so many people, it's useless to have so many people ...'. They extrapolated from it the suggestion that a single group should have a maximum of 3 to 5 participants with the participants deciding who they would

be willing to collaborate with rather than a randomized group; some even suggested a completely individualized activity. However, one group said '... the group must have learnt something for which reason they were able to answer it'.

Peer assessment: On floating the idea of peer assessment, none of the participants favored the idea and thought they were not trained to do peer assessment. '... it won't be fair ...'.

Continuing the activity in future years: While all three groups came up with suggestions on the frequency of the activity in a year from as less as annually to as much as nine times a year, when asked if they were given a choice to have the activity in future years, only one group was enthusiastic about it, as one participant confidently suggested '... I think it would be smart to implement it ...'.

Discussion

We observed that a staggering majority, a little more than 80%, of participants grasped the content in a longitudinal theme sufficiently. Most of the students agreed that the activity was useful in developing an understanding of research basics but differed with regards to the specifics of the incorporation.

The importance of clinical research as a field opted by physicians and its existence is lagging behind.¹ This was followed up by a subsequent report in 2002, which applauded the efforts undertaken but at the same time, emphasized further required leaps to successfully curb the problem.⁴

Medical schools throughout the world have employed and continue to employ different methods of following these recommendations; in preclinical years or clinical years or both.¹⁴

In developed countries, the situation has largely started improving with respect to incorporating it in the curricula, while in developing countries it still requires tackling skillfully.

Some schools include making a research elective mandatory in their curricula. This may be in the clinical or preclinical years as is the case with the Queen's University Faculty of Health Sciences, Canada, where students are required to undertake a minimum eight weeks course in their second year.¹⁵ Similar is the

University of KwaZulu-Natal, South Africa, where three 4 weeks courses are divided over three academic years; second, third and fourth years.¹⁶ Results from both these programs show improvements in research skills and understanding, on the basis of self-reported outcomes.

Another approach used is making a research project or thesis mandatory for graduation. This has been reported in the Albert Einstein College of Medicine, United States, 8 University Kebangsaan Malaysia¹⁷ and Aga Khan University Hospital, Pakistan.¹⁹ Our medical school originally adopts a similar approach as well. These have again showed improvements in research skills and understanding.¹⁷⁻¹⁸

Yet, a third strategy implemented is to have students involved in underserved community projects as conducted by University of Texas Southwestern Medical Center, United States.⁶ While this has also benefitted, the program itself was restricted to a selected number of students depending on applications and curriculum vitae making it difficult to generalize assessments for the entire student population, especially the academically weak students.

Two well established programs, having survived rigorous trials and challenges over several decades, are those of the Duke University and Stanford University. Duke University started with the introduction of an additional year in their curriculum which eventually evolved into multiple study tracks planned around electives.¹⁹ Stanford University, on the other hand, set out an 'all-elective curriculum' which encouraged research among students right from the beginning of their studies with indirect support from National Institute of Health (NIH) funded programs.²⁰

In contrast, Cleveland Clinic Lerner College of Medicine (CCLCM) combines multiple approaches by formal training of research foundations in the first two years followed by biweekly half day research seminars and a compulsory research project. Thus, by the end of the undergraduate program, the medical student graduates with special qualification in biomedical research.²¹ Our study describes a longitudinal research theme similar to the programs described for Stanford University and CCLCM, even if on a smaller scale.

While participants did not seem very enthusiastic about having a similar program incorporated in the form of a mandatory component, evidence suggests that mandatory undergraduate research involvement is positively associated with postgraduate research.¹⁸

There is also concern that such incorporations of research into the curriculum mainly focus on and benefits the already academically better students.⁴ Our approach managed to involve the majority of students with less than a fifth not benefiting at all. This lack of benefit also reflected among the focus group participants which revealed only 16% response from the bad score category.

Needless to say, a small sample size and lack of controls marred our study making it difficult to compare with other methods of incorporating research. Added to this was the fact that most available data report qualitative results rather than quantitative ones.

An important issue with previous studies remains the lack of well-defined objective criteria to assess research skills among medical students beyond submission or publications. Such was the case with our assessments as well in that we had a set of uniform yet untested criteria. Qualitative data from previous studies made the job no less difficult.

Conclusion

Incorporating research in a mandatory longitudinal theme component as part of undergraduate medical studies seems a potential method of laying the foundations for future physician scientists.

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It is policy of the Journal of Shifa Tameer-e-Millat University (JTMU) to publish articles pertaining to different fields of medical sciences (Medicine, Dentistry, Pharmacy, Applied Health Sciences and Nursing, etc.) providing sufficient contribution to medical knowledge. The articles may include new experimental methods of medical importance; new results obtained experimentally; new interpretation of existing results or data pertaining to clinical problems; or epidemiological work giving substantial scientific information pertaining to medical sciences.

All such articles should aim for development of medical concepts rather than mere recording of facts. Incomplete studies will be discouraged.

Objectives

1. To publish original, well documented, peer reviewed clinical, allied and basic health/medical sciences manuscripts.
2. To inculcate the habit of medical writing.
3. To enable medical professionals to remain informed in multiple areas of medical and health sciences, including developments in fields other than their own.
4. To share the experience and knowledge for benefit of patients in particular and humanity in general.
5. To document medical problems and challenges pertinent to community.
6. To achieve the highest level of ethical medical journalism and to produce a publication that is timely, credible, and authentic to read.

Editorial Freedom

The Editor-in-Chief has full authority over the editorial content of the journal and the timing of publication of its content. The Editor-in-Chief is supported by the editorial board which consists of highly competent individuals who have expertise in research including associate editors and international advisors. The editorial team makes decisions on the authenticity and validity of the submitted manuscripts in light of the journal's aims and scope. The publisher is not involved in any step of the manuscript review and decision-making process.

Editorial Independence

We believe that the editorial decision making process should be independent of all commercial concerns. We achieve this by ensuring that editors are unaware of authors preferences regarding business models, and by having a clear code of conduct that defines their responsibilities as respective members of the editorial board.

Authorship Policy

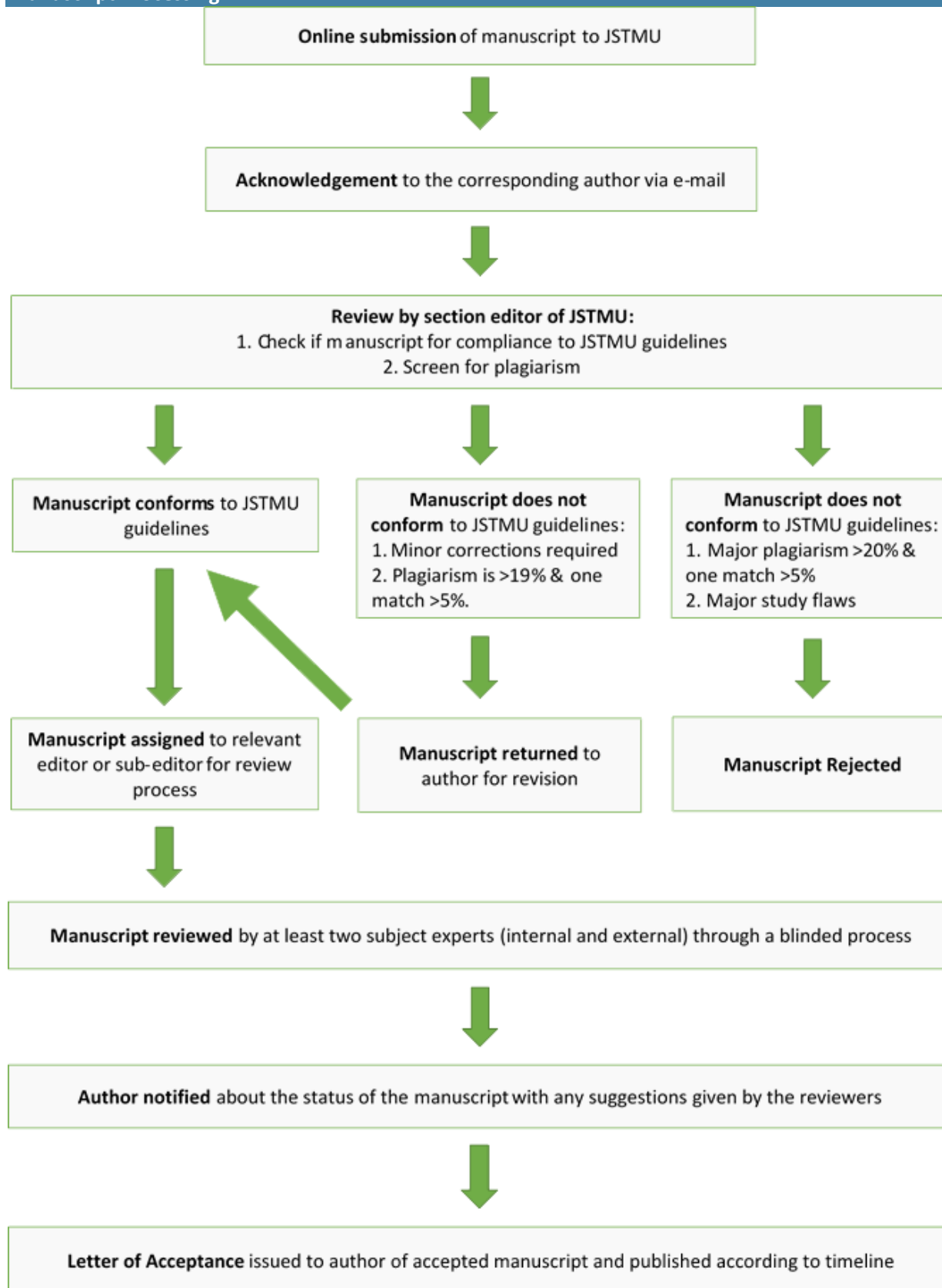
Authorship is based on the following four criteria:

1. Substantial contributions to concept and design of study, or acquisition of data or analysis and interpretation of data
2. Drafting the article or revising it critically for important intellectual content.
3. Final approval of the version to be published.
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Acquisition of funding, collection of data, typing the manuscript or general supervision of the research alone, does not justify authorship. JSTMU strongly discourages gift authorship.

Manuscript Processing



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Unethical withdrawal or no response from the authors to editorial board communication will be subjected to sanction a ban of 4 years to all authors, and their institute will also be notified.

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Peer review is the unbiased critical assessment of manuscripts submitted to JSTMU by experts who are not part of the editorial staff. Each article submitted to JSTMU for publication is reviewed by at least two specialists of the concerned specialty as a double-blinded process. Reviewers are therefore required to respect confidentiality of the peer review process and not reveal any detail of the manuscript or its review, during or after the peer review process, beyond the information released by the journal. If reviewers wish to involve a colleague in the peer review process, they should first obtain permission from the journal. The editor(s) should be informed of the names of any individuals who assisted in the review process when the report is returned. JSTMU shall not share manuscripts with third parties except in cases of suspected misconduct.

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We believe that the research we publish should adhere to high standards of transparency and robustness in their methods and results. This, in turn, supports the principle of reproducibility, which is a foundation of good research, especially in natural sciences. We achieve this by developing editorial processes and checklists to provide clarity for authors and supporting authors in the reporting of their work. We support the Transparency and Openness Promotion guidelines.

Conflict of Interest

Conflict of interest statement for Authors:

All manuscripts for articles, original research reports, editorials, comments, reviews, book reviews, and letters that are submitted to the journal must be accompanied by a conflict of interest disclosure statement or a declaration by the authors that they do not have any conflicts of interest to declare. All articles that are published in the journal must be accompanied by this conflict of interest disclosure statement or a statement that the authors have replied that they have no conflicts of interest to declare. To facilitate this policy, all authors must disclose 'ALL their potential conflicts of interest' to the editors of the journal at the time of submission. These include all financial and non-financial interests and relationships (see definitions provided a little later in the text), direct employment with a private sector entity (whether full or part-time), and service on private sector and non-profit Boards and advisory panels, whether paid or unpaid. Authors should also disclose any conflict of interest that may have influenced either the conduct or the presentation of the research to the editors, including but not limited to close relationships with those who might be helped or hurt by the publication, academic interests and rivalries, and any personal, religious or political convictions relevant to the topic at hand. In the article, the authors must include a draft statement that discloses all relevant conflicts of interest and affiliations. The relevance of financial conflicts of interest with private firms is defined as a relationship of any value with a firm that has a stake in the subject of the manuscript or its competitors. Relevance for patents is defined as any invention or pending invention connected in any way to the subject.

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The manuscript(s) submitted to JSTMU should not be more than allowable words limit (mentioned in relevant sections below) and NOT more than 5 Tables and/or figures excluding abstract (250 words), acknowledgments and references. The text of the manuscript should be doubled spaced with one-inch margin on all sides. The font should be in size 12 Times New Roman and all pages should be numbered. A certificate, signed by the author and co-authors should be accompanied along with the manuscript stating that the article has been read and seen by all authors and have not been submitted or published in another journal or elsewhere in a report or textbook. Any copyright material, if used, should be accompanied with a permission letter from the copyright owner by the corresponding author. The manuscript should be checked for spelling and grammatical errors before submission. Authors should write the Keywords in the manuscript below the abstract. *

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Title page *

Title page should contain the following information:

1. Complete title of the article
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3. Department(s)
4. Institution(s) at which work was performed
5. Official phone/fax number, mobile phone number, personal e-mail address of the corresponding author, and institutions address.

Abstract

The abstract should be structured and NOT more than 250 words. The abstract must be written under the following subheadings:

1. Introduction
2. Objectives
3. Methodology
4. Results
5. Conclusion

Text

Text must be arranged under the following headings:

1. Introduction
2. Methods
3. Results
4. Discussion
5. Conclusion(s)
6. Acknowledgements (if any)

Introduction: Should provide brief review of relevant literature in such a way that it highlights the importance of the study and that the purpose of the study should be clearly stated. The articles used in the review of literature should be properly referenced by Vancouver Style.

Methods: Should include the setting(s), the subjects (participants), sampling methods and sample size, if used, type of study design used, and other procedures that were conducted. The Methods section should be brief, crisp and detailed enough to enable the reader to replicate the study in another setting. Commonly used procedures and methods need not be described but require a reference to the original source.

Results: Should include the factual findings of the research study done and, presented in the form tables or figures. Each table and figures should be properly labelled with headings and numbers (e.g. Table

No. 1, Figure No. 1) on separate pages. The write-up of results in the text should highlight the important findings without duplication of presentations displayed in the tables or figures. *Explanation of the findings should be reserved for the Discussion section.*

Discussion: Should highlight the important findings comparing and contrasting the study's results with that of other similar researches published and it should be appropriately referenced. Discussion should be concise and supported by the presented data.

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Citation Example:

Equal amounts of dietary carbohydrates have variable blood glucose response considerably as a function of specific food ingested.¹

Bibliography/References Example:

1. Wolever TMS, Yang M, Zeng XY, Atkinson F, Brand-Miller JC. Food glycemic index, as given in Glycemic Index tables, is a significant determinant of glycemic responses elicited by composite breakfast meals. *Am J Clin Nutr* 2006; 83(6):1306–12.
DOI: <https://doi.org/10.1093/ajcn/83.6.1306>

B. Meta -Analysis/ Systematic Reviews

Meta-analysis are systematic, critical assessments of literature and data sources pertaining to clinical topics, emphasizing factors such as cause, diagnosis, prognosis, therapy, or prevention, and that includes a statistical technique for quantitatively combining the results of multiple studies that measure the same outcome into a single pooled or summary estimate. All articles or data sources should be searched for and selected systematically for inclusion and critically evaluated, and the search and selection process should be described in the manuscript. Inclusion and exclusion criteria must be mentioned. Details of searching articles and search engines used should be clearly stated. The specific type of study or analysis, population, intervention, exposure, and tests or outcomes should be described for each article or data source. These should be described in the Method section. The data sources should be as current as possible, ideally with the search having been conducted within several months of manuscript submission. Authors of reports of meta-analyses of clinical trials should submit the PRISMA flow diagram and checklist. Authors of meta-analyses of observational studies should submit the MOOSE checklist. Follow EQUATOR Reporting Guidelines. The text **should NOT exceed 6000 words** excluding abstract, references, tables and figures.

Each of the sections of these articles should include specific sub-sections as follows:

Structured Abstract: (Not exceeding 250 words):

1. Objectives
2. Methodology
3. Results
4. Conclusion

Text should be organized under the following headings:

Introduction:

1. Rationale
2. Objectives
3. Research question

Methods:

1. Study design
2. Participants, interventions, comparators
3. Systematic review protocol
4. Search strategy
5. Data sources, studies sections and data extraction
6. Data analysis

Results:

1. Provide a flow diagram of the studies retrieved for the review
2. Study selection and characteristics
3. Synthesized findings

Discussion:

1. Summary of main findings
2. Risk of bias
3. Limitations
4. Conclusions

** For all other information including title page, typing and reference style, please follow the original articles instructions.*

C. Systematic Review (without meta-analysis): Review articles

Systematic Reviews/ review article are critical evaluation and assessments of scientific literature and other sources of data relating to health sciences topics, emphasizing factors such as cause, diagnosis, prognosis, therapy, or prevention. Systematic Reviews without meta-analysis are published as Review articles; those with meta-analysis are published as Original Investigations.

Systematic Reviews should include the following:

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2. Introduction (150-250 words)
3. Methods (150-250 words)
4. Results (1000-1250 words)
5. Discussion (1000 words)
6. Conclusions (2-3 sentences)

Maximum length: **Should NOT exceed 3500 words of text** (not including abstract, tables, figures, acknowledgments, references), with no more than a total of 5 tables and/or figures and no more than 50-75 references.

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D. Case Reports/Case Series

The journal will consider only those case report/series that represent very rare case(s), or epidemic diseases that are new or emerging, or first observation(s) of some emerging phenomenon or disease. They should have clinical significance and may also include observation of new adverse effect(s) of a drug, vaccine, or procedure or other unique observations, etc. Informed written consent of the patient or next of kin (if patient is not alive or comatose/disabled) should be obtained before submission of the manuscript. A covering letter from the authors that convincingly describe the merits of the case in the light of the mentioned criteria and it's educational or scientific merits should be sent along with the manuscript.

Case Report /case series should contain a single paragraph abstract and text **should NOT exceed 1000 words** (excluding abstract, references, tables and figures) with maximum 10 bibliographic references and either three figures or three tables. Each case report must contain:

1. Abstract (unstructured - should not exceed 120 words)
2. Introduction
3. Case Presentation
4. Discussion
5. Conclusion
6. Competing interest
7. Patient consent

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E. Rapid/Special /Short Communications

Rapid/Special/Short communication should be complete work, such as COMPLETE results of a short RESEARCH study, NOT a preliminary report and **should NOT exceed 1500 words** with one figure and/or one table. An editorial decision will be provided rapidly without reviews.

F. Letters to Editor

Letters should only be written on a specific article in the most recent publication of journal. The letter should be objective and provide constructive opinions offer some academic or clinical interest to the readers.

Letters **should NOT exceed 400 words** of text and 5 references, 1 of which should be to the recent article. It should not have more than 3 authors. The text should include the full name, academic degrees, and institutional affiliation for author and the email address for the corresponding author. Letters considered for publication shall be forwarded to the author of the cited article for possible response. The editor reserves the right to shorten these letters, delete objectionable comments, make other changes, or take any other suitable decision to comply with the style and policies of the journal. For writing and references style, follow the same instructions listed above.

Letter in Reply

Replies by authors should not exceed 500 words of text and 6 references. They should have no more than 3 authors.

G. Editorial

The topics of the editorial are decided by editorial board and/or Editor-in-Chief. Editorial is written either by one member of the editorial board or some expert on that topic invited by the Editor-in-Chief. As a convention, the editorial addresses relevant areas of interest that may pertain to a range of areas influencing health and health care sciences.

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