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RFP Indian Journal of

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Contents

Original Article

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Bacteriological Profile of Uropathogens and their Susceptibility Pattern : A Study From a Tertiary Care Centre of Eastern India

Sarkar K[1], Pal S[2], Gonjhu D[3], Pramanik N[4]

Abstract

Introduction: Urinary tract infection (UTI) is one of the most common bacterial infections in developing countries. We face difficulties in choosing antibiotics during treatment of UTI due to emerging antimicrobial resistance among the predominant uropathogens.

Aims: This study was undertaken to know the prevalence and antibiogram of uropathogens in our hospital and to determine the type and antibiotic resistance pattern of the urinary pathogens.

Materials and Methods: The study was carried out on 103 consecutive patients suffered from UTI admitted at in-patient department of School of Tropical Medicine, Kolkata during one year.

Results: In the present study we isolated 103 bacteria in suspected cases of UTI. Among the bacterial profile of UTI, Escherichia coli was the predominant isolate (36.89%) followed by *Klebsiella* species, *Enterococcus* species, Staphylococcus species, *Pseudomonas aeruginosa and* Citrobacter species. We found only one each case of *Acinetobacter* species, Serratia and Stenotrophomonas maltophilia.

Conclusion: Emerging bacterial drug resistance has both clinical and financial implications for therapeutic purpose. Spectrum of bacterial drug resistance in an institution is important for epidemiological as well as clinical purposes.

Keywords: Uropathogens; Emerging antimicrobial resistance; Antibiotic susceptibility

Introduction

One of the most common bacterial infections in humans is urinary tract infections (UTIs). As they are not reportable diseases accurate assessment of the incidence of UTIs is difficult. It is the most common nosocomial infection. It is more common in catheterised patients (3.2%), even with adequate aseptic precautions during instrumentation [1]. 50% of the patients with in dwelling catheters have UTI with multidrug resistant bacteria (Ananthanarayan and Paniker, 2009). Females are more prone to acquire UTI and recurrent UTI especially between 1 to 50 years of age. Antimicrobial resistance (AMR) is a threatened problem worldwide in both hospital and community acquired infections [2]. Developing countries face the major brunt of the problem of AMR due to high prevalence of infections, irrational and indiscriminate use of antimicrobials with easy over the counter availability of drugs and lack of clinical microbiology laboratories for antimicrobial susceptibility testing.

Treatment outcomes depends on infections caused by resistant bacteria resulting in gradual narrowing of scope for effective molecules to combat even common community acquired bacterial infections including UTIs [3,4]. Treatment of UTI is often empiric and the extensive and inappropriate use of antibiotics which causes emergence of multi drug resistant bacteria that is a major problem worldwide. So, there is a need for hospital based studies in different areas to provide the pattern of sensitivity of the microorganisms to help formulate local empirical treatment guidelines for UTI. This study was undertaken to know the microbiological etiology and to study the antimicrobial susceptibility pattern of the uropathogens in a teaching hospital in Kolkata, Eastern India.

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Materials and Methods

It was a single centre, prospective, observational study. The study was done on 103 consecutive patients suffered from UTI admitted at in-patient department of Carmichael Hospital for Tropical Diseases, School of Tropical Medicine, Kolkata for one year period. A total of 103 clean catch midstream urine samples collected from suspected case of UTI and send for routine testing and culture sensitivity. All the selected patients were subjected to detailed assessment including focussed interview and history elicitation. Urine samples were tested for the presence of pus cells and the probable bacteria by performing a wet mount and a Gram stain smear. Then urine samples were inoculated on Blood agar and Mac Conkey agar media and incubated aerobically overnight at 37^0C. The bacterial isolates were identified and antimicrobial sensitivity test (AST) was done in VITEK. The antibiotic discs used for the AST included: ampicillin, amoxicillin/clavulanic acid, piperacillin/ Tazobactam, Cefuroxime, Cefuroxim Axetil, Ceftriaxone, Cefoperazone/Salbactam, Cefepime, Imipenem, Meropenem, Amikacin, Gentamicin, Nalidixic Acid, Ciprofloxacin, Levofloxacin, Nitrofurantoin, linezolid, vancomycin, Colistin and Trimethoprime/Sulfamethoxazole.

Results

In the present study 50.48% were males and 49.51% were females with male: female (1.01:1) (Fig. 1).

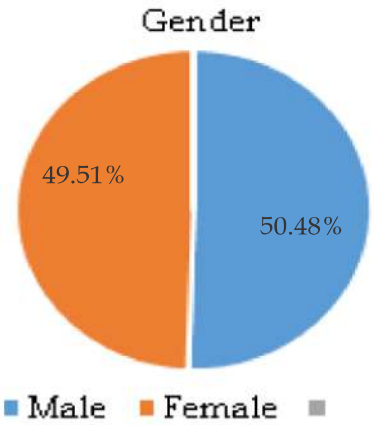

Fig. 1:

Out of 103 patients, age of the patient range from 16–82 years. Most patients are between 31–60 years of age. Most of the patient presented with fever and dysuria but a good number of patient (11.65%) was asymptomatic and they were diagnosed during evaluation of other disease (Table 1).

Table 1: Presenting symptoms

Symptoms	Number of Patients	Percentage
Fever	55	53.39
Dysurea	34	33
Increased frequency of micturition	20	19.41
Pain abdomen	13	12.62
Sepsis	12	11.65
Asymptomatic	12	11.65

In the present study we isolated 103 bacteria in suspected cases of UTI. Among the bacterial profile of UTI, Escherichia coli was the predominant isolate accounting for 36.89% followed by *Klebsiella* species, *Enterococcus* species, *Staphylococcus* species, *Pseudomonas aeruginosa* and *Citrobacter* species. We found only one each case of Acinetobacter species, Serratia and *Stenotrophomonas* maltophilia. Among 38 *Escherichia coli* isolates ESBL found in 3 cases, among 22 *Klebsiella* species isolates 3 cases were Klebsiellaoxitoca and others were *Klebsiella pneumoniae,* among 13 *Staphylococcal* species isolated 8 were *S.aureus* and 5 were *S.coagulase* negative (Table 2).

Table 2: Bacterial Profile of UTI

Bacteria isolated	Number	Percentage
Escherichia coli	38	36.89
Klebsiella species	22	21.35
Enterococcus species	17	16.5
Staphylococcus species	13	12.62
Pseudomonas aeruginosa	7	6.79
Acinetobacter species	1	0.97
Citrobacter species	3	2.91
Serratia	1	0.97
Stenotrophomonas maltophilia	1	0.97

Among gram negative organisms, maximum resistance was observed for ampicillin and amoxicillin/clavulanic acid (70–80%), cotrimoxazole (50–63%), cephalosporins (upto 60%), fluoroquinolones (42–68%) and amynoglycosides (28–54%) (Table 3).

In case of common Gram positive cocci, maximum resistance was observed against Ampicillin (92.3%) among *S.aureus* isolates and MRSA was 23.07%. *Enterococcus spp* had fluroquinolone (80–90%) and high level aminoglycoside resistance as 58.82%. (Table 4).

Table 3: Resistance pattern of Common Gram negative uropathogens

Antibiotics	*E. coli* (n=38)	*Klebsiella* (n=22)	*Pseudomonas* (n=7)
ampicillin	15 (39.47%)	18 (81.81%)	-
amoxicillin/clavulanic acid	27 (71.05%)	16 (72.72%)	-
piperacillin/Tazobactam	10 (26.31%)	13 (59.09%)	2 (28.57%)
Cefuroxime	10 (26.31%)	-	-
Cefoperazone/Salbactam	2 (5.26%)	-	2 (28.57%)
Ceftriaxone	23 (60.52%)	14 (63.63%)	3 (42.85%)
Trimethoprime/ Sulfamethoxazole	24 (63.15%)	11 (50%)	1 (14.28%)
Nitrofurantoin	7 (18.42%)	5 (22.72%)	2 (28.57%)
Ciprofloxacin	23 (60.52%)	15 (68.18%)	3 (42.85%)
Nalidixic Acid	1 (2.63%)	-	-
Gentamicin	14 (36.84%)	12 (54.54%)	2 (28.57%)
Amikacin	15 (39.47%)	11 (50%)	2 (28.57%)
Meropenem	11 (28.94%)	9 (40.90%)	1 (14.28%)
Imipenem	10 (26.31%)	-	-
Colistin	2 (5.26%)	3 (13.63%)	Nil (all sensitive)

Table 4: Resistance pattern of Common Gram positive uropathogens

Antibiotics	*Staphylococcus aureus* (n=13)	*Enterococcus spp* (n=17)
ampicillin	12 (92.3%)	10 (58.82%)
Amoxicillin/clavulanic acid	9 (69.23%)	9 (52.94%)
MRSA	3 (23.07%)	-
Levofloxacin	6 (46.15%)	14 (82.35%)
Ciprofloxacin	9 (69.23%)	16 (94.11%)
Gentamicin (120)	4 (30.76%)	10 (58.82%)
Vancomycin	Nil (all sensitive)	3 (17.64%)
Linezolid	Nil (all sensitive)	Nil (all sensitive)
Erythromycin	-	2 (11.76%)
Nitrofurantoin	Nil (all sensitive)	3 (17.64%)
Meropenem	-	1 (5.88%)
Fosfomycin	-	2 (11.76%)
Trimethoprime/Sulfamethoxazole	6 (46.15%)	3 (17.64%)

Discussion

Urinary tract infection remains one of the most common infections. The study was carried over 103 confirmed cases of UTI. It is well documented that UTI is more common in females than inmales due to certain anatomical and physiological factors [5]. But in our study male and female patient number was almost same. It may be due to it is a tertiary care centre and here among admission patient number of female patient is less than the male patient. Here all patients with confirmed UTI in this study were from admitted and hence, infection was mixed community acquired and nosocomial. *E.coli* was the most common isolate constituting 36.89% of all uropathogens in this study which correlates with most of the studies conducted in India. Community Studies have reported isolation rates of *E.coli* between 55–83% [6,7]. While, studies on inpatients with hospital acquired UTI have reported lesser *E.coli* isolation rates varying between 40–50% [8,9]. But studies from some other parts of the country have shown higher isolation rates (65%

to more than 90%) [8]. This difference probably due to ours is a tertiary care center as compared with the primary and secondary care levels of these centers.

Klebsiella species, the second most common isolate in the present study, accounted for 21.35%, which is quite high incidence than other studies of different parts of India [5,8]. We found gram positive bacteria *Enterococcus* species and *Staphylococcus* species in 16.5 % and 12.65% cases respectively which is little high in incidence than other studies. This is because we studied at a tertiary care centre and all patient were from inpatient department. *E.coli* had very high resistance against cephalosporins -Ceftriaxone and Ciprofloxacin (both 60.52%) and also Trimethoprime/Sulfamethoxazole (63.15%) (Table 3).

We commonly use cotrimoxazole and fluoroquinolones as drugs ofchoice to treat common bacterial infections including community acquired UTI but they havelost their effectiveness against most frequent uropathogens [5]. In this study, the resistance of uropathogens to fluoroquinolones was high (42–68%) in gram negative bacteria and (46–94%) among gram positive bacteria.Indiscriminate usage and over the counter availability of antibiotics could explain emergence of drug resistant. This finding seriously limits choice of easy and effective antibiotic options available for UTI. Nitrofurantoin, an oral narrow spectrum antibiotic with no systemic action, is a popular therapeutic option for UTI treatment. High Nitrofurantoin sensitivity has been reported against all pathogens, including 90.6% against *E.coli* [8]. In our study we also found high Nitrofurantoin sensitivity in both gram positive and gram negative bacteria.

Conclusion

Emerging bacterial drug resistance has both clinical and financial implications for therapeutic purpose. Spectrum of bacterial drug resistance in an institution is important for epidemiological as well as clinical purposes. Physicians needs guidance for selection of antimicrobials for UTI by culture and sensitivity results and empirical therapy must be based on local epidemiological data, which should be constantly updated.

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Original Article

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Effectiveness of Demonstration Regarding Endotracheal Suctioning Among Staff Nurses Working in Selected Hospital

Pallavi Ashokrao Jambhulkar[1], Vidya Sahare[2]

Abstract

Introduction: Endotracheal suctioning (ETS) is one of the most common procedures performed in patients with artificial airways. It is a component of bronchial hygiene therapy and mechanical ventilation that involves the mechanical aspiration of pulmonary secretions from a patient's artificial airway to prevent its obstruction. The procedure includes patient preparation, the suctioning event, post procedure care. The objectives of the study were to (1) To observe the existing practice regarding endotracheal suctioning among staff nurses. (2) To evaluate practice regarding endotracheal suctioning among staff nurses after demonstration. (3) To find out association of practice with their selected demographic variables.

Method: One group pretest and post-test pre-experimental study design by using structured observation checklist to assess practice of endotracheal suctioning among staff nurses. The study was conducted among 30 staff nurses working in ICU of selected hospital by using non probability convenient sampling technique. The data was collected and analyzed based on objectives of the study using descriptive and inferential statistics.

Result: The overall comparison of pre-test practice score and post-test practice score of staff nurses regarding endotracheal suctioning mean of pre-test practice score was 7.57 and post-test practice score was 12.17. The tabulated 't' value was 1.69 and the calculated 't' value was 13.73 are much higher than the tabulated value at $p<0.05$ level of significance for overall practice score of subjects which was statistically acceptable level of significance. Hence it was statistically interpreted that the demonstration was an effective tool in improving the practice regarding endotracheal suctioning among subjects.

Conclusion: The investigator concludes that the demonstration was effective and will help to improve the practice of staff nurses.

Keywords: Effectiveness; Demonstration; Endotracheal Suctioning and Staff Nurses

Introduction

Surgery for Nurse

Our body needs a constant supply of oxygen to support metabolism. The respiratory system brings oxygen through the airways of lungs into the alveoli, where it diffuses into the blood for transport to the tissues. This process is so vital that difficulty in breathing is experienced as a threat to life itself. Oxygenation is one of the basic human needs.

Endotracheal suctioning (ETS) is one of the most common procedures performed in patients with artificial airways. It is a component of bronchial hygiene therapy and mechanical ventilation that involves the mechanical aspiration of pulmonary secretions from a patient's artificial airway to prevent its obstruction. The procedure includes patient preparation, the suctioning event, post procedure care. Because micro aspiration of secretions is a risk factor for Ventilator Associated Pneumonia (VAP), assessment of practices related to oral suctioning, oral care, and management of endotracheal tube is important.

The primary objective of mechanical ventilation are to decrease their work of breathing, relieve respiratory distress, rest the fatigued respiratory muscles, improve ventilation, stabilize the chest wall, and restore the acid-base balance. Therefore,

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the most common reasons for instituting mechanical ventilation are acute respiratory failure with hypoxemia (acute respiratory distress syndrome, heart failure with pulmonary edema, pneumonia, sepsis, and complications of surgery and trauma), which accounts for 65% of all ventilated cases, followed by the causes of hypercarbic ventilator failure such as coma (15%), exacerbations of chronic obstructive pulmonary disease (13%), and neuromuscular diseases (5%).

Need for the Study

Studies done by Day *et al.* and Pedersen *et al.* provided data on when and how to perform endotracheal suctioning reflecting that some patients may receive several times of endotracheal suctioning daily according to patient's need. In 2010 the American Association of Respiratory Care (AARC) published the AARC Clinical Practice Guidelines on endotracheal suctioning of mechanically ventilated patients with artificial airway as endotracheal suctioning is done if needed only; providing hyper oxygenation before, during and after endotracheal suctioning; endotracheal suctioning should be done without disconnection between patient and ventilator; avoiding routine normal saline instillation before endotracheal suctioning; use closed suction system for adults with high FiO_2, or PEEP; Suction tube diameter is less than 50% the lumen of the endotracheal tube in adults, maximum suction duration is from 10 to 15 seconds. Failure to meet the guidelines in implementation of this procedure can result in numerous side effects. A few studies examined if guidelines for endotracheal suctioning were tracked by nurses in intensive care unit. The results demonstrated that nurses were often not alert of these guidelines. Moreover, they found that there was a considerable difference reflected in nurses' performance between ideal standard endotracheal suctioning where nurses followed the recommended guidelines and actual routine technique when nurses didn't. Additionally, Day *et al*. and Sole *et al*. stated that practice of endotracheal suctioning was not always based on current research recommendations, which may lead to inconsistent practice among nurses, affecting patients' experience and increasing health risks associated with endotracheal suctioning. So, it is necessary to examine the actual routine method of endotracheal suctioning practiced by nurses in intensive care unit and its effect on patient's condition in comparison with the standard endotracheal suctioning that follows evidenced based recommendation.

Knowledge and experience can determine a nurse's ability to adequately perform endotracheal tube suctioning. All nurses who perform suction must receive approved training and demonstrate competencies under supervision. They should ensure that their knowledge and skills are maintained. Nurses should also make sure that they undertake role in accordance with their original protocols, policies and guidelines. But many researchers have identified that nurses are unaware of the current suctioning recommendations and practice is often based on ritual and tradition as opposed to empirical evidence. Hence the investigator has taken up the study to evaluate the effectiveness of endotracheal suctioning practice among nursing personnel.

Problem Statement

Effectiveness of demonstration regarding endotracheal suctioning among staff nurses working in selected hospital

Objectives

(1) To observe the existing practice regarding endotracheal suctioning among staff nurses.

(2) To evaluate practice regarding endotracheal suctioning among staff nurses after demonstration.

(3) To find out association of practice with their selected demographic variables.

Hypothesis

H_0: There is no significant difference in pre-test and post-test practice regarding endotracheal suctioning among staff nurses after demonstration measured at $p < 0.05$ level of significance.

H_1: There is a significant difference in the pre-test and post-test practice regarding endotracheal suctioning among staff nurses after demonstration measured at $p < 0.05$ level of significance.

Conceptual Framework

Conceptual Framework Based on Modified King's Goal Attainment Theory.

Review of Literature

Literature review is a critical summary of research on a topic of interest generally prepared

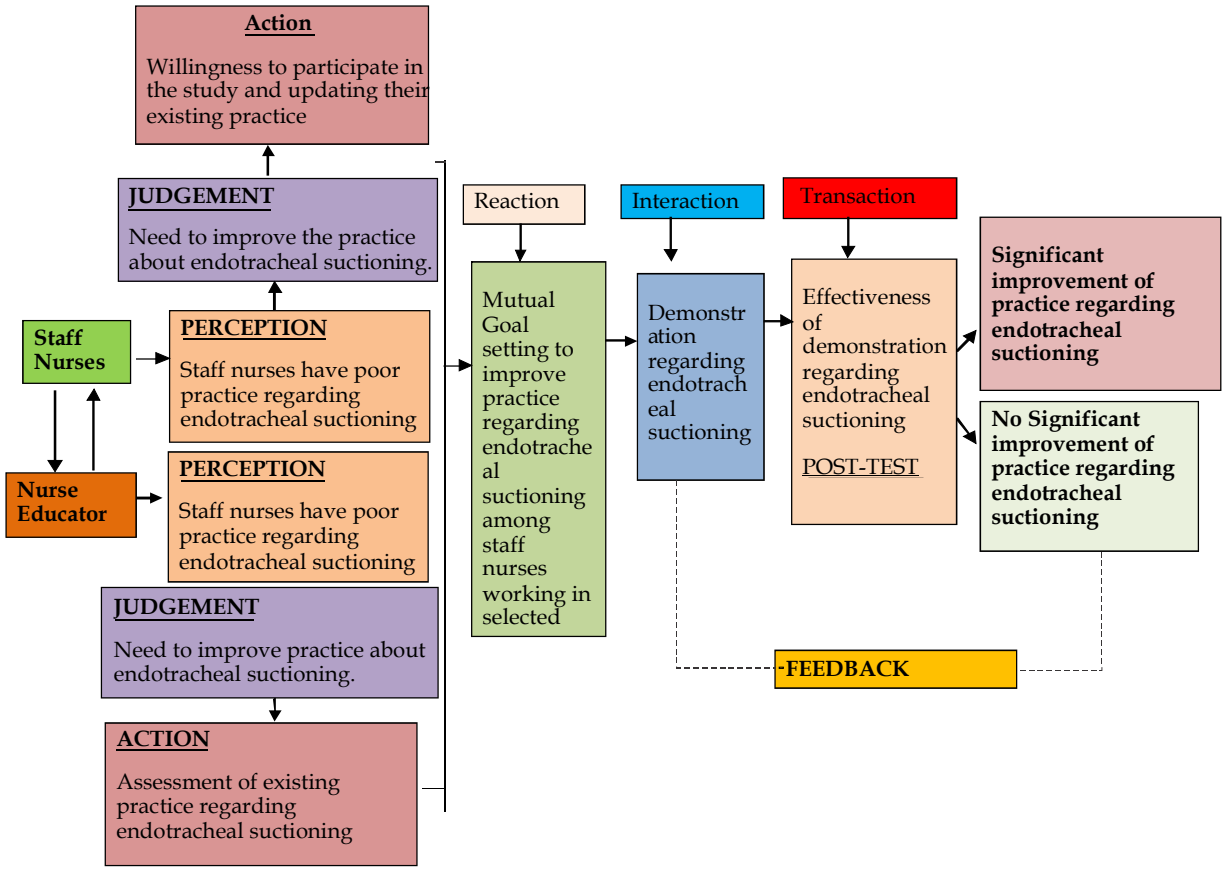

Fig. 1:

to put a research problem in context or to identify gaps and weakness in prior studies so as to justify a new investigation.

Studies reviewed have been arranged under the headings as

1. Review of Literature related to endotracheal suctioning.
2. Review of Literature related to effectiveness of demonstration regarding endotracheal suctioning

Materials and Methods

In this study effectiveness of demonstration regarding endotracheal suctioning among staff nurses working in selected hospital was studied by using structured observation checklist to assess practice of endotracheal suctioning. The research design used in the study was one group pretest and post-test pre-experimental design. The study was conducted among 30 staff nurses working in ICU of selected hospital by using non probability convenient sampling technique.

Inclusion Criteria

The study will include

1. Staff nurses working in the intensive care unit.
2. Staff nurses who are willing to participate in the study.

Exclusion Criteria

Nurses who have attended training programme on endotracheal suctioning.

Development of the Tool

The investigator used the procedure of endotracheal suctioning from National Accredited Board for Hospitals (NABH) guidelines and steps were used in the checklist.Structured observation checklist consists of two sections:

Part 1: Consists of demographic variables of study subjects such as age, professional qualification and years of experience.

Part 2: Structured observation checklist

Scoring Technique

Practice Score

Poor Practice	< 50%
Fair Practice	50%–75%
Good Practice	Above 75%

Results

Section-A

Distribution of subjects with regards to their demographic variables

Table 1 shows that the distribution of subjects according to their demographic variables. Regarding age, 18 (60%) subjects were between age group of 21–30 years, 12 (40%) subjects age group between 31–40 years. In relation to their professional qualification out of 30 subjects 12 (40%) subjects had done GNM, 12 (40%) subjects had done Basic B.Sc. nursing and 6 (20%) subjects had done Post B.Sc. nursing. In relation to their years of experience out of 30 subjects 17 (56.67%) subject had 0–5 years of experience, 9 (30%) subjects had 6–10 years of experience and 4 (13.33%) subject had 11–15 years of experience.

Section B

Distribution of subjects in relation to their existing practice regarding endotracheal suctioning

Table 2 reveals information about existing practice regarding endotracheal suctioning before demonstration. In that 14 (46.67%) subjects had poor practice and 16 53.33%) subjects had fair practice.

Frequency and percentage Distribution of subjects in relation to their practice regarding

Table 1: Frequency and percentage distribution of subjects with regards to their demographic variables.

(n = 30)

Demographic Variables	Frequency	Percentage %
Age		
21–30 years	18	60
31–40 years	12	40
41–50 years	0	0
>51 years	0	0
Professional Qualification		
Diploma in General Nursing and Midwifery	12	40
Basic B.Sc. Nursing	12	40
Post Basic B.Sc. Nursing	6	20
M.Sc. Nursing	0	0
Year of experience		
0 – 5 years	17	56.67
6 – 10 years	9	30
11 – 15 years	4	13.33
16 – 20 years	0	0

Table 2: Frequency and percentage distribution of subjects in relation to their existing practice regarding endotracheal suctioning

(n = 30)

Sr. No	Level of Practice	Poor		Fair		Good	
		Frequency	%	Frequency	%	Frequency	%
1	Pre-test	14	46.67	16	53.33%	0	0

Table 3: Shows information about existing practice regarding endotracheal suctioning after demonstration

(n = 30)

Sr. No	Level of Practice	Poor		Fair		Good	
		Frequency	%	Frequency	%	Frequency	%
1	Post-test	0	0	20	66.67%	10	33.33%

Table 4: Shows the mean, standard deviation and mean difference values are compared and student's paired 't' test

(n = 30)

Sr. No	Overall	Mean	SD	Mean Difference	t-value	p-value
1.	Pre Test	7.57	1.45	4.6	13.73(S)	p<0.05
2	Post Test	12.17	1.21			

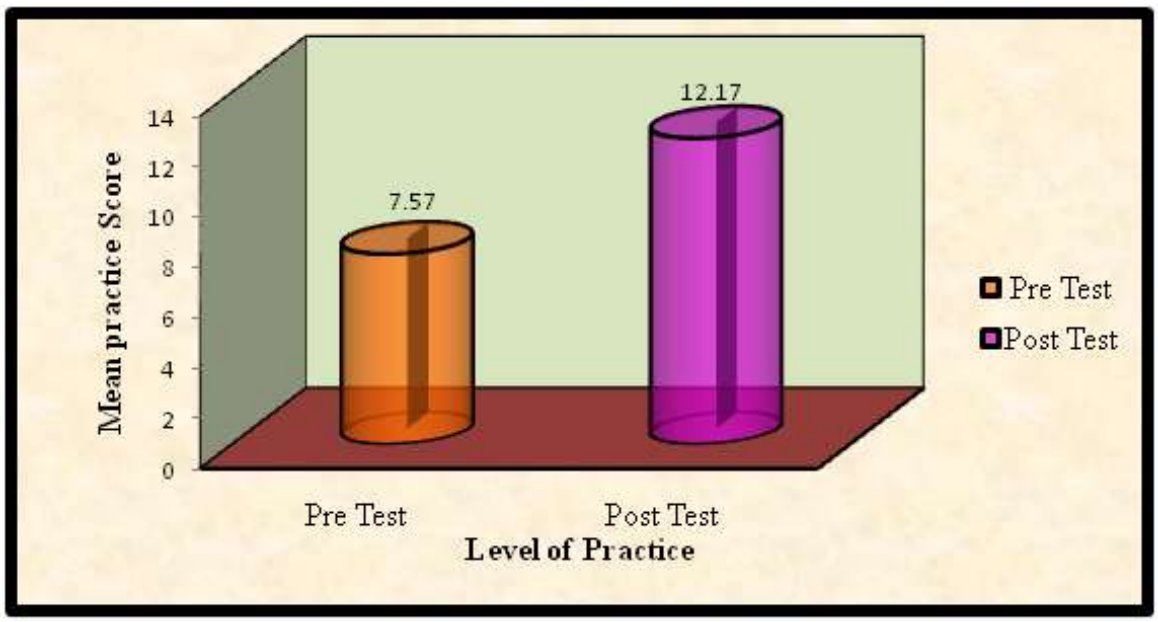

Fig. 1: Shows the mean, standard deviation and mean difference values are compared and student's paired 't' test

endotracheal suctioning after demonstration

Table 3 shows information about existing practice regarding endotracheal suctioning after demonstration. In that 20 (66.67%) subjects had fair practice and 10 (33.33%) subjects had good practice.

Section C

Significance of difference between practice score in pre and post-test of subjects

Table 4 shows the mean, standard deviation and mean difference values are compared and student's paired 't' test is applied at $p < 0.05$ level of significance. The tabulated value for df (n-1) was 1.69. The calculated 't' value was 13.73 are much higher than the tabulated value at $p < 0.05$ level of significance for overall practice score of subjects which was statistically acceptable level of significance. Hence it was statistically interpreted that the demonstration was an effective tool in improving the practice regarding endotracheal suctioning among subjects was effective. Thus the H_1 was accepted.

Section D

Association of existing level of practice score in relation to demographic variables

It was interpreted that demographic variables is statistically not associated with their practice score regarding endotracheal suctioning.

Discussion

The finding of the study was discussed with reference to the objective stated as below. The present study was undertaken as, "Effectiveness of demonstration regarding endotracheal suctioning among staff nurses working in selected hospital."

- To observe the existing practice regarding endotracheal suctioning among staff nurses.
- To evaluate practice regarding endotracheal suctioning among staff nurses after demonstration.
- To find out association of practice with their selected demographic variables.

A cross sectional descriptive study was conducted on the gap between knowledge and practices in standard endotracheal suctioning of intensive care unit (ICU) nurses in children's hospital Lahore in 2017 with an aim to assess the gap between knowledge and practice in standard endotracheal suctioning of intensive care unit nurses. The data collected from 118 nurses in the 11 ICU's of children hospital by using questionnaire and checklist. The findings showed that 42.9%had good level of practice, 44.5% had fair level of practice, and 14% had poor level of practice. The mean knowledge score of the nurses calculated to be 24 ± 3.0 (min-max = 10–31) and themean practice score was 17.85 ± 5.67. There is no relationship between knowledge and practice score. The study concluded that there is a need for training in this skill and continue feedback until desire level of skill achieved.

With regard to first objective of the study, the study result showed that among all subjects, in pre-test score 46.67% poor practice level and 53.33% had fair practice level. Mean practice score of pre-test was 7.57 ± 1.45 whereas in post-test score 66.67% had fair practice level and 33.33% had good practice level. Mean practice score of post-test was 12.17 ± 1.21. The study revealed that the level of practice regarding endotracheal suctioning among the subject in pre-test was poor and after the demonstration the mean post-test score improved.

A pre-experimental study was conducted on effectiveness ofplannedteaching programmeon theknowledgeof endotrachealsuctioningamong staff nurses working in intensive care unit at Mathuradas Mathur hospital in Jodhpur, Rajasthan in 2015 with an aim to assess the effectiveness of planned teaching programme on the knowledge regarding endotracheal suctioning among staff nurses working in intensive care unit. The data was collected from 26 staff nurses by using a structured knowledge questionnaire. The finding showed thatthe mean pre-test knowledge score (17.07)of the staff nurses have average knowledge regarding endotracheal suctioning. The mean post-testknowledge score (25.30) was higher than the pre-test score. The 't' test computed for knowledge 't' (25) = 8.1154, P ≤ 0.001 showed highly significant difference suggesting that a planned teaching programme is effective teaching strategy to increase their knowledge and improve their practices.

With regards to second objective of the study result showed that in pre-test mean score was 7.57 and standard deviation was 1.45. Post-test mean score was 12.17 and standard deviation was 1.21. Calculated't' value was 13.73 at $p < 0.05$ level of significance which was much higher than the tabulated value was 1.69 at $p < 0.05$ level of significance for overall practice score of staff nurses which was statistically acceptable level of significance. Hence it was statistically interpreted that the demonstration on overall practice regarding endotracheal suctioning among subjects was effective. Thus the H_1 was accepted.

With regards to third objective of study result showed that the association of existing level of practice score with age in years reveals that the tabulated chi-square value was 3.84 (df = 1) which was much higher than the calculated value was 1.32 at 0.05 level of significance. The association between practice score with their years of experience reveals that tabulated chi-square value was 5.99 (df = 2) which was much higher than the calculated value was 1.17 at $p < 0.05$ level of significance. There was no association between practice score with their demographic variables.

Conclusion

After the detailed analysis, this study leads to the following conclusion:

There was a significant increase in the level of practice among subjects after the demonstration. To find the effectiveness of demonstration 't' test was applied and 't' value was calculated, the mean post test score were significantly higher than their mean pre-test score as evidenced from demonstration which was measured that $p < 0.05$ level of significance. Thus it was concluded that demonstration was found to be effective teaching strategy.

Demographic variables did not show a major role in influencing the pre-test and post-test practice

score among staff nurses.

Hence, based on the above cited findings, it was concluded undoubtedly that the demonstration was effective regarding endotracheal suctioning.

Limitation

- This study was limited to the staff nurses working in intensive care unit in selected hospital.
- The study was limited to intubated patients.

Implications of the Study

The investigator has drawn the following implications from the studies which were of vital concern to the field of nursing education, nursing service, nursing administration and nursing research.

Nursing Practice

- The present study implies demonstration to be an effective strategy to improve the practice regarding endotracheal suctioning.
- The findings of the present study emphasis on demonstration regarding endotracheal suctioning which can be put into nursing practice to enhance the practice of staff nurses regarding endotracheal suctioning and to provide appropriate nursing care to the clients. Demonstration can be used as a basis for educating the staff.

Nursing Education

- Nursing may be defined as a dynamic, therapeutic and educative process in meeting health needs of the society.
- The present study emphasizes on demonstration regarding endotracheal suctioning among staff nurses. In order to educate the staff nurses, it is essential that the nurses have to be competent and have sound knowledge to improve the level of understanding which can be reflected to the public through education.

Nursing Administration

Nursing administration plays a pivotal role in supervision and management of nursing profession. The nurse administrators can utilize the present tool for assessing the practice of nurses and can implement measures to promote health on the finding of the study. Teaching modules, group discussions and periodical educational sessions can also be arranged for subjects.

Nursing Research

Research is a systematic attempt to obtain meaningful answers to phenomenon or events through the application of scientific procedures. It is an objective, impartial, empirical and logical analysis according to controlled observations that may lead to the development of generalizations, principles or theories resulting to some extent in prediction and control of events that may be the consequences or cause of specific phenomenon.

The finding of the study would add to the existing body of knowledge in the nursing profession. It would also provide a baseline data to educate staff and student nurses regarding endotracheal suctioning.

Personal Experience

The entire study gave an enriching experience to the investigator. It helped to develop her skill in critical thinking, analysis and realize the importance of effective communication with respondents. The entire study was varied and rich learning experience which enabled the investigator to develop her skill in dealing with different personalities. The concept clarity about research as a whole increased. At every stage, the investigator received guidance and support from her guide. This boosted confidence to go ahead and carry out the planned activities and the co-operation from study subject was remarkable. The research was a great learning opportunity for the investigator.

Recommendations

- On the basis of the findings of the study, it is recommended that the following studies can be conducted.
- Similar studies may be conducted on a larger population for generalization of findings.
- Studies may be conducted to evaluate the effectiveness of video assisted teaching on practice regarding endotracheal suctioning.
- A similar study can be conducted and evaluated using alternative teaching strategies like interactive learning sessions, structured teaching programme.
- Experimental studies can be conducted with recommendation.
- A study can be conducted to assess the knowledge regarding endotracheal suctioning.

- A study may be conducted to assess the existing knowledge and practice regarding endotracheal suctioning.

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Review Article

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TP53 as a Tumor Suppressor Gene

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Abstract

Recognition of *TP53*'s prominent role in protection from cancer has boosted a huge amount of scientific reports (around 40000) describing the function of *TP53* as a tumour suppressor. Quite an unusual feature of a tumour suppressor was noted – *TP53* is point mutated rather than inactivated in cancers and is highly expressed in tumours. Mutation of *TP53* gene confers novel oncogenic properties on *TP53* protein.

Keywords: Cancer; *TP53*; Tumor suppressor gene; Polymorphism

History of discovery

TP53 was identified in 1979 as a protein in complex with large T-antigen oncoprotein of the SV40 DNA tumour virus (Linzer *et al*., 1979). Another study reported high levels of *TP53* in transformed, but not normal cells, with no history of viral infection, suggesting it was coded by cellular genes (DeLeo *et al*., 1979). *TP53* gene was cloned (Oren *et al*., 1983; Zakut-Houri *et al*., 1985) and originally described as an oncogene, due to its ability to transform cells in cooperation with other H-Ras oncogene (Eliyahu *et al*., 1984; Parada *et al*., 1984). In support of this notion, expression of *TP53* then was shown to immortalize the cells (Jenkins *et al*., 1984) and enhance tumorigenic potential of cells injected in mice (Wolf *et al*., 1984). Later it was realized that the originally studied *TP53* protein was the product of a mutated *TP53* gene, which indeed promoted tumour genesis. However, after the wild type *TP53* gene was cloned it became evident that wild type *TP53* protein blocked the ability of oncogenes to transform cells (Eliyahu *et al*., 1989; Finlay *et al*., 1988; Hinds *et al*., 1989). Wild type *TP53* was then reclassified as a tumour suppressor gene and numerous studies since then have demonstrated its key role in protecting cells from cancer (Vogelstein *et al*., 2000). It was also declared as the molecule of the year. The fact that *TP53* is mutated in at least half of all human cancers indicates a strong selection for its loss during tumour progression (Hollstein *et al*., 1991). Additional support for its crucial role in tumour genesis came from the study of Li-Fraumeni patients, who inherit one allele of mutant *TP53* gene and are extremely pre-disposed to cancer (Malkin *et al*., 1990).

Structure of *TP53*

The *TP53* gene contains eleven exons with two alternative translation start sites in exon 2 and 4 (Gen Bank Accession Number: NC_000077) (Murray-Zmijewski *et al*., 2006). The *TP53* protein contains three major functional domains: N-terminal transcriptional activation domain (TA), the central sequence-specific DNA-binding domain (DBD) and the oligomerization domain (OD) in the C-terminus. There is also an N-terminal proline rich domain involved in protein interactions and regulatory domain in the C-terminus (*Figure 1*).

TP53 is active as a tetramer, with four identical chains of 393 residues. The N-terminal region consists of an intrinsically disordered trans-activation domain (TAD) and a proline-rich region. It is followed by the central, folded DNA-binding core domain that is responsible for sequence-specific DNA binding. Via a flexible linker, this domain

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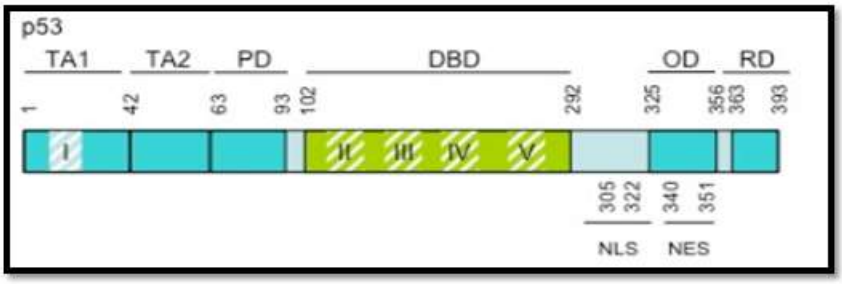

Fig. 1: Structure of *TP53* protein.

The main domains of TP53, nuclear export (NES), nuclear localization (NLS) signals and the location of the conserved boxes I, II, III, IV and V are shown. TA – transactivationdomain, PD - proline-rich domain, DBD - DNA binding domain, OD - oligomerization domain, RD – regulatory domain.

is connected to a short tetramerization domain that regulates the oligomerization state of *TP53 (Figure 2).* At its C terminus, *TP53* contains the so-called regulatory domain. This natively unfolded region is rich in basic amino acids (mainly lysine) and binds DNA non-specifically.

TP53 Isoforms

The human *TP53* gene is composed of 19, 200 bp, spanning over 11 exons on chromosome 17p13.1 (NC_000017). Until recently only 3 mRNA splice variants of *TP53* have been known, which encode full-length *TP53*, *TP53*i9 and *TP53*Δ40 (Ghosh *et al*., 2004). *TP53*i9 results from alternative splicing at exon 9 and encodes a protein truncated of the last 60 amino acids, which is defective in transcriptional activity. *TP53*Δ40 (other names p47 and Δ*NTP53*) protein is truncated of the first 40 amino acids and can be generated by two mechanisms: either by an alternative splicing of the intron 2 (Ghosh *et al*., 2004) or by alternative initiation of translation (Yin *et al*., 2002). *TP53*Δ40 contains the second transactivation domain and is capable of activating some of the *TP53* target genes. Interestingly, it can also inhibit transcriptional activity of the full-length *TP53* in a dominant-negative way (Ghosh *et al*., 2004). A recent study reports that the structure of the *TP53* gene is much more complex than previously thought and many more *TP53* isoforms exist (Bourdon *et al*., 2005). The structure of *TP53* gene and the currently known *TP53* isoforms are summarized in Figure 2. The *TP53* gene is transcribed from two distinct sites upstream of exon 1 and from an internal promoter located in intron 4. The alternative promoter leads to the expression of an N-terminally truncated *TP53* (Δ133*TP53*), which lacks the entire TA domain and part of the DNA binding domain. Usage of alternative promoter in intron 4 gives rise to Δ40*TP53* with truncation of N-terminal transactivation domain. In addition alternative splicing at intron 9 gives rise to α, β and γ isoforms. Therefore at least 9 different isoforms of *TP53* can be generated.

Function of *TP53*

TP53 is activated in response to oncogene activation, DNA damage and spindle damage, which can potentially increase the mutation

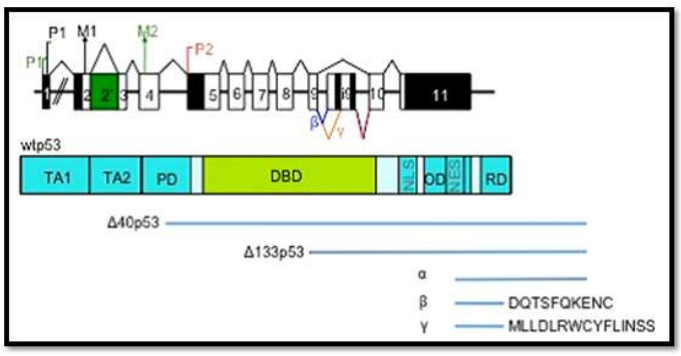

Fig. 2: Human *TP53* gene.

The structure of TP53 gene and the alternatively spliced TP53 isoforms are depicted.

occurrence in cells and increase the risk of becoming cancerous. *TP53* is also induced in response to other types of cellular stresses such as hypoxia, dNTP depletion and nutrient deprivation which can predispose cells to malignant transformation. Activated *TP53* can induce cell-cycle arrest, allowing DNA repair, or cause senescence, or promote apoptosis, eliminating the damaged cells (Vogelstein *et al*., 2000). Numerous studies have demonstrated that *TP53* can influence many other biological processes, such as invasion and motility, angiogenesis, differentiation, cell survival and more recently discovered glycolysis (Bensaad *et al*., 2006) and autophagy (Crighton *et al*., 2006) (Fig. 3).

TP53 is a Transcription Factor

The *TP53* gene encodes a transcription factor and mediates much of its biological activities by regulating the expression of numerous *TP53* target genes. *TP53* binds to the specific sequences– *TP53* responsive elements - in the regulatory region of its target genes and more than hundred different *TP53* target genes have been described with various biological functions and the list is likely to grow (Murray-Zmijewski *et al*., 2008). *TP53* activates transcription of most of its targets by recruiting general transcription factors (TATA-binding protein-associated factors) and histone acetyltransferases (HAT) CBP, p300 and PCAF to the promoter (Gu *et al*., 1997). One of the first discovered *TP53* target genes was the cyclin-dependent kinase inhibitor (CDK) p21, which induces a cell cycle arrest (el-Deiry *et al*., 1994). *TP53* induces apoptosis by activating genes mediating extrinsic and intrinsic apoptotic pathways (Chipuk *et al*., 2006). Such targets include genes encoding death receptors, Fas/CD95/Apo-1, Killer/R5, mitochondrial proteins Bax,Noxaand PUMA (Nakano *et al*., 2001).

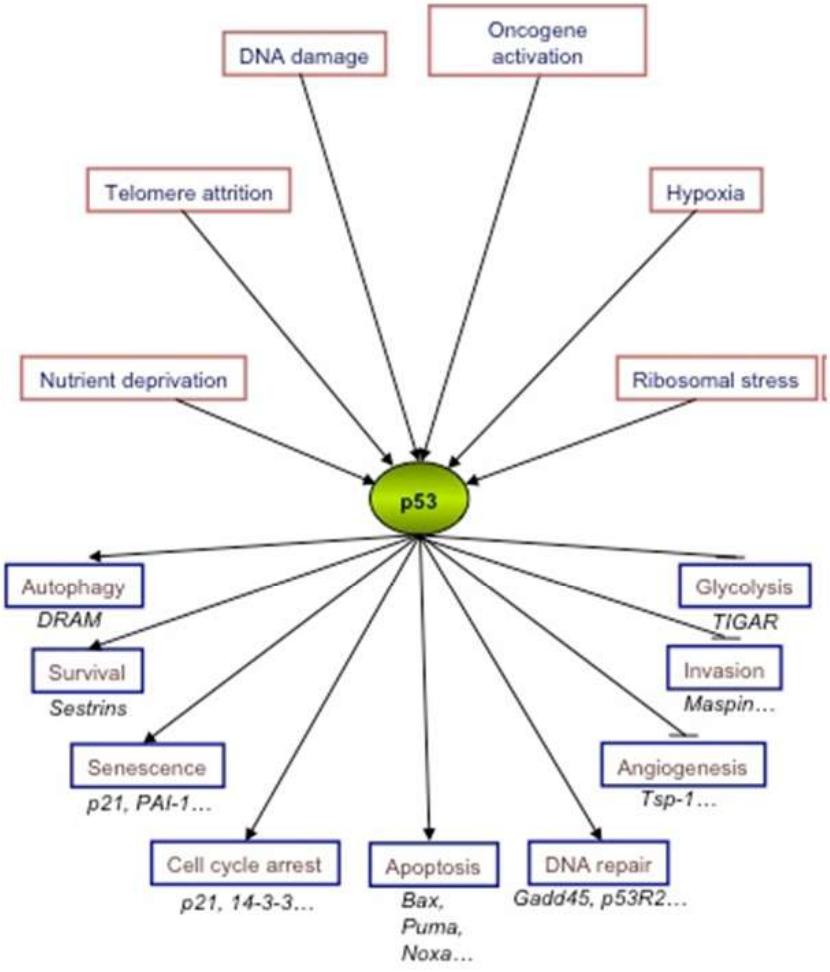

Fig. 3: Scheme of *TP53* response.

TP53 is activated by a number of cellular stresses (blue boxes) and regulates different biological processes (red boxes) via transcriptional activation of its target genes (marked in black).

Activation of autophagy via induction of novel gene DRAM by *TP53* also contributes to cell death (Crighton *et al*., 2007). Recent studies have identified microRNA miR-34 as a *TP53* target gene, adding a new twist on regulation of *TP53* gene network (Chang *et al*., 2007). MiRNAs are a class of small regulatory RNAs that mediate post-transcriptional silencing of specific target mRNAs (Bartel *et al*., 2004). The miR-34 family is directly induced by *TP53* in response to DNA damage and oncogenic stress, which can lead to induction of growth arrest and apoptosis through inhibiting gene expression of proliferative and anti-apoptotic genes (Chang *et al*., 2007). *TP53* can contribute to cell survival by allowing DNA repair by activating genes such as Gadd45, *TP53*R2 (Tanaka *et al*., 2000). *TP53* has also been suggested to play a direct role in mediating DNA repair by interacting with components of the repair machinery (Gatz *et al*., 2006). In addition, *TP53* plays a survival role by protecting the genome from damage by reactive oxygen species (ROS). This activity of *TP53* is mediated by activation of TIGAR, sestrins, aldehyde dehydrogenase-4 and Sco2 (Matoba *et al*., 2006), which can decrease the levels of intracellular ROS. The current model suggests that at low levels of stress *TP53* plays a survival role and helps the cell to cope with stress, by decreasing ROS and allowing DNA repair. When stress is severe and/or DNA damage is irrepairable, *TP53* triggers irreversible growth arrest or apoptosis, to eliminate the damaged cells from the healthy pool (Vousden *et al*., 2007). In light of the current data, the role of *TP53* therefore emerges as a master regulator of cells well-being, which prevents cancer development. Several *TP53* target genes inhibit *TP53* activity in a negative feedback loop. *TP53* transcriptionally activates its major negative regulator Mdm2 (mouse double minute) (Wu *et al*., 1993), a ubiquitin ligase, which inactivates *TP53* mainly by targeting it for proteasomal degradation and promoting its nuclear export. Similarly, to Mdm2, *TP53* target genes Cop1 and Pirh2 encode ubiquitin ligases which can degrade *TP53* (Leng *et al*., 2003). In addition, *TP53* can directly interact with the transcription factors, such as Sp1 and AP1 and others, preventing their binding to the target genes. By this mechanism *TP53* leads to repression of genes such as cyclin B1and TERT (Kanaya *et al*., 2000). *TP53* also recruits histone deacetylases (HDACs) to the promoters which is mediated by the interaction with SIN3A (Murphy *et al*., 1999). By this mechanism, *TP53* represses transcription of genes such as MAP4 and stathmin (Murphy *et al*., 1999). One of the novel target genes CD44 is inhibited by *TP53* under conditions of basal stress. *TP53* plays a key role in mediating tumour progression in cells lacking *TP53*. CD44 encodes a cell-surface molecule and can block *TP53*-dependent stress-induced apoptotic signals. The repertoire of *TP53* target genes is extremely broad and in addition to genes mentioned above also includes secreted proteins regulating migration and angiogenesis (Teodoro *et al*., 2006). Though some of these biological responses have sometimes opposing roles, they all seem to contribute to the tumour suppressive function of *TP53*.The choice of *TP53* response depends on the type of the particular stress and cellular context and is the active area of research (Murray-Zmijewski *et al*., 2008), which has mostly focused on the choice between the fundamental *TP53* responses – cell cycle arrest and apoptosis. Posttranslational modifications are involved in dictating the choice of transcriptional target genes by *TP53*. Upon UV and DNA damage HIPK2 and DYRK2 phosphorylate *TP53* on S46 (Taira *et al*., 2007). This promotes induction of apoptosis by *TP53* via activation of pro-apoptotic *TP53*AIP1 gene (Oda *et al*., 2000). Acetylation of *TP53* on lysine 120 by MOF and TIP60 also promotes *TP53*-dependent apoptosis in response to DNA damage, via recruitment of *TP53* to pro-apoptotic target genes, PUMA and Bax (Tang *et al*., 2006). Ubiquitination of *TP53* on Lys320 by E3 ligase E4F1 promotes cell cycle arrest function of *TP53* via activation of p21, Gadd45 and cyclin G1, while not affecting the pro-apoptotic target genes (Le Cam *et al*., 2006). *TP53* family members p63 and p73 can also selectively enhance the apoptotic activity of *TP53* in some cell types, by promoting transactivation of PERP and BAX but not p21 (Flores *et al*., 2002). *TP53* interacting partners play an important role in the outcome of *TP53* response. The members of the ASPP (ankyrin-repeat-SH3-domain- and proline-rich-region-containing) family play an important role in regulating the apoptotic function of *TP53*. ASPPs act by selectively enhancing the *TP53* binding and trans-activating promoters of pro-apoptotic target genes such as Bax, PIG3 (*TP53*-induced gene 3) and PUMA, while not affecting the promoters of the CDKN1A and mdm2 genes.

Mutations of *TP53* in Cancer

Fraumeni syndrome

Li-Fraumeni syndrome (LFS) is a rare inherited cancer pre-disposition syndrome, affecting individuals before the age of 45 years. Unlike other inherited cancer syndromes, LFS is characterized

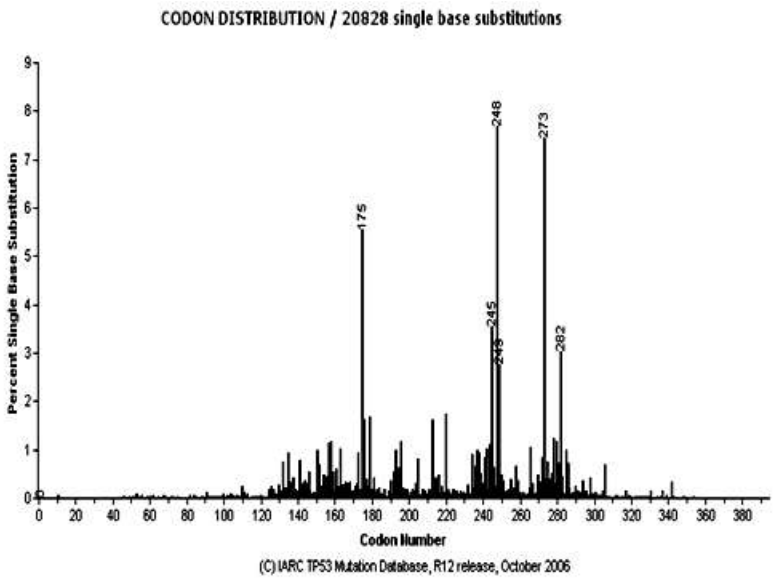

Fig. 4: Mutational frequency of *TP53*.

The frequency of the point mutations of each codon of TP53 found in tumors (IARC database, R12 release, 2006, www-TP53.iarc.fr).

by a variety of different cancers, predominantly sarcomas, breast cancers, brain tumours and adrenocortical carcinomas, though other cancers have also been reported. LFS is dominantly-inherited and is associated with high mortality. Analysis of the LFS families has shown that around 70% of these families have a germline mutation in the *TP53* gene. Li-Fraumeni-like syndrome (LFL) describes a similar syndrome, which does not have all features of the classical LFS and similarly has been found to have germ-line mutations in *TP53* gene (Olivier *et al*., 2003). From the database information it is revealed that most of the *TP53* mutations are missense mutations (72%) and some are deletions (10%). About 46% of the mutations were located at the codons 175, 213, 245, 248, 273 and 282 in the DBD of *TP53*, which correspond to hotspot mutations in sporadic cancers (Soussi *et al*., 2007).

TP53 *in sporadic cancers*

As already mentioned, *TP53* gene is found mutated in nearly half of all human cancers analyzed. In many other types of cancers *TP53*pathway is inactivated by other ways, such as inactivation of ARF or over expression of Mdm2. Unlike most of the tumour suppressor genes, more than 80% of the *TP53* alterations are missense mutations which lead to generation of full-length *TP53* with single amino acid substitution (Petitjean *et al*., 2007). The initial observations, which showed that *TP53* mutations are a frequent event in many tumour types, were made some twenty years ago (Takahashi *et al*., 1989). Those studies demonstrated that most of the mutations are localized in the exons 5–8, which lead to a single amino acid substitution of the DNA binding domain. Therefore, most of the later studies (40% of all) have focused on the characterization of these mutations, which mostly affect the DNA binding domain. The database of *TP53* mutations has been updated and includes the analysis of some of the recent studies have found that mutations also occur outside exons 5–8 (about 10%) (Figure 4) (Bastien *et al*., 2008). The current version of the *TP53* mutation database reports about 24000 different mutations most of which occur as single amino acid substitutions in the DNA binding domain of *TP53*. Most of the mutations locate within the highly evolutionary conserved regions of the DBD of *TP53*.

Properties of Mutant *TP53*

Loss-of-function

Biochemical studies have shown that *TP53* mutants exhibit certain heterogeneity in terms of structural alterations and loss of DNA-binding activity. The DNA-binding site recognized by *TP53* is highly degenerated and the affinity of *TP53* for target sites varies (Resnick *et al*., 2003). Though many *TP53* mutants exhibit total loss-of-function, some *TP53* mutants retain partial transactivation ability. Tumour-derived point mutants *TP53* 175Pro

and *TP53* 181Lys retain the ability to activate p21 and induce cell cycle arrest, however fail to induce other target genes, which impairs their ability to induce apoptosis (Ludwig *et al*., 1996). In addition to loss-of-function, *TP53* mutants acquire cancer promoting properties (Finlay *et al*., 1988), which have been attributed to the ability of mutant *TP53* to inhibit wild type *TP53* in a dominant-negative manner and by gain-of-function effect.

Dominant-negative effect

Over expression studies in cells have shown that mutant *TP53* inhibits the function of wild type *TP53* acting in a dominant-negative manner (Willis *et al*., 2004). This results in interference with several *TP53*-mediated biological processes, such as: apoptosis (Gottlieb *et al*., 1994), growth arrest, differentiation, genetic stability and transformation suppression (Unger *et al*., 1993). One of the explanations was that mutant *TP53* can induce a conformational change in wild type *TP53* (Milner *et al*., 1991). However, structural studies suggest that contact mutants do not have a gross change to their structure, though are capable of inhibiting wild type *TP53* when over expressed (Chene *et al*., 1998). The current mechanism of the dominant-negative effect suggests the formation of mixed tetramers of mutant and wild type *TP53* proteins, which reduces the level of fully active homotetramers of wild type *TP53* (Willis *et al*., 2004). One report suggests that at least three mutant molecules are required per tetramer to inactivate the transactivation ability of *TP53* (Chan *et al*., 2004). This suggests that dominant-negative effects of mutant *TP53* can be biologically relevant only when the levels of mutant *TP53* are high. It is possible that in tumour cells, where mutant *TP53* accumulates to high levels; it might lead to inhibition of the wild type *TP53*. In the course of tumour progression the wild type allele is often lost (Olive *et al*., 2004). This might imply that wild type *TP53* retains its function to some extent in the presence of mutant *TP53*, as there is a selective pressure to lose it.

Gain of function

Experimental systems on a *TP53*-null background have demonstrated novel tumour promoting properties of mutant *TP53*, which is known as "gain-of-function" effect. One of the early studies showed that mutant *TP53* expression in cells lacking *TP53* enhanced their tumourigenic potential (Wolf *et al*., 1984). Mutant *TP53* can enhance the transformation potential of *TP53*-null cells as assessed by colony formation assay and leads to enhanced growth of the cells. Several studies have shown that exogenously expressed mutant *TP53* confers tumourigenic potential in several *TP53*-null cell types: murine fibroblasts, murine L-12 pre-B cells and human osteosarcoma cell line (Wolf *et al*., 1984; Lanyi *et al*., 1998). Another gain-of-function property of mutant *TP53* is the ability to interfere with the induction of apoptosis in response to various stress signals, such as DNA damage and growth factor deprivation when over expressed in cells (Zalcenstein *et al*., 2006). However, the most convincing evidence for the gain-of-function effect is provided by the study of knock-in mice with "hot-spot" mutations in *TP53*. *TP53* mutant mice with mutation at either Arg172His (equivalent to 175 in humans) or Arg270His (equivalent to 273 in humans), belonging to structural and contact class of hot-spot mutants respectively, have been generated (Olive *et al*., 2004). Both mutants*TP53* knock-in and *TP53*-null mice develop tumours, however, mutant *TP53* knock-in mice exhibit different spectra of tumour spectrum, with predisposition to carcinomas and endothelial tumours. Tumours in mutant *TP53* knock-in mice display more aggressive phenotypes and metastasize with higher frequency. These findings provide the most physiologically relevant evidence for the gain-of-function effect of certain *TP53* mutants (Olive *et al*., 2004). The mechanism of the gain-of-function effect of *TP53* mutants has been proposed to be mediated via their interaction with p63/p73. However, the exact mechanism of gain-of-function of mutant *TP53* is still unknown. Recent study has addressed the gain-of-function effects of *TP53* hot spot mutations (R248W and R273H) by introducing them into the HUPKI allele (Song *et al*., 2007). Another mechanism of the gain-of-function of mutant *TP53* involves regulation of the expression of a specific set of genes. One of the first genes shown to be up regulated by mutant *TP53* was MDR-1, which was suggested as a mechanism underlying chemo resistance promoted by mutant *TP53* (Chin *et al*., 1992). Mutation of L22 and W23, required for transcriptional activity of *TP53*, abrogated the ability of mutant *TP53* to transactivate MDR-1 and enhancement of tumourigenic potential of the cells by mutant *TP53* (Lin *et al*., 1995). This study has provided the evidence for transcriptional regulation mechanism of the gain-of-function of mutant *TP53*.

TP53 Polymorphisms

As is true of the human genome as a whole (in which over 3.1 million sequence variations have

been mapped, which represent 25–35% of the total estimated SNPs (Frazer *et al*., 2007), numerous SNPs and other sequence variations are present at the *TP53*locus. Most of these variations are intronic and can be presumed to have no cancer-related biological consequences. Few of the many *TP53* polymorphisms have been assessed for altered biochemical and/or biological function, or for their effects on cancer risk in population studies.

Polymorphisms in non-coding sequences

More than 90% of the polymorphisms in *TP53*occur in the noncoding sequences. The well-characterized intronic*TP53* polymorphism is a 16 base pair insertion in intron 3 (Lazar *et al*., 1993). This is the only intronic polymorphism that has been associated with an increase in the risk of several types of cancer (Costa *et al*., 2008).

*Synonymous polymorphisms in **TP53** coding sequences*

Of the 19 exonic polymorphisms that have been reported in *TP53*, eight are synonymous. Although these polymorphisms do not change the amino acid sequence or structure of the protein, in theory, changes in base sequence and codon use could modify protein expression, folding and function, or provoke new splicing events (Candeias *et al*., 2008).A silent mutation at codon 36 (CCG to CCT) was shown to reduce the ability of *TP53* to activate apoptosis by lowering the affinity of the *TP53*mRNA for MDM2; consequently, reducing *TP53* levels (Candeias *et al*., 2008). Three synonymous polymorphisms—D21D (GAC to GAT), Pro34Pro (CCC to CCA) and Pro36Pro (CCG to CCA) — are located in the region that is crucial for *TP53* mRNA binding to MDM2 and their roles await functional analysis.

*Non-synonymous polymorphisms in **TP53** coding sequences*

The remaining 11 polymorphisms in *TP53* are non-synonymous, resulting in an amino acid change in the protein. Only four of these polymorphisms have been validated by multiple submissions of the polymorphism to *TP53* databases, reports on the frequency of the polymorphism, or inclusion of the polymorphism in the Hap Map database. In addition, they have not been reported as somatic mutations in tumours. Changes in the amino acid sequence can alter the ability of *TP53* to bind to response elements of target genes (as shown by tumour-associated *TP53* mutations alter recognition motifs for post-translational modifications, or alter the protein stability and interactions with other proteins (Li *et al*., 2007). For two of the polymorphisms, there is sufficient molecular evidence to suggest that the polymorphisms cause a functional change in the *TP53* pathway (Pro47Ser and Arg72Pro). The remaining two validated non-synonymous polymorphisms have not been associated with an altered cancer risk to date (Val217Met and Gly360Ala).

Codon 47 (Pro47Ser)

Pro47Ser, a rare polymorphism in the N-terminal transactivation domain of *TP53*, results from a C→T base substitution at position 1 of codon 47. It has only been reported in populations of African origin, in which it is found at an allele frequency of approximately 5% (Felley-Bosco *et al*., 1993). Phosphorylation of the N-terminal domain of *TP53* has been shown to regulate its transactivation properties (Kruse *et al*., 2008). P38 and homeodomain-interacting protein kinase 2 (HIPK2) phosphorylate Ser46, which enhances the transcription of apoptosis-related genes and hence promotes *TP53*-mediated apoptosis (Kruse *et al*., 2008). These two kinases are directed to phosphorylation sites by a proline residue adjacent to Ser46. Thus, replacement of Pro47, as occurs with the Per47Ser polymorphism, would be expected to decrease phosphorylation at Ser46, decrease transactivation of pro-apoptotic target genes and thus potentially increase cancer risk (Kurihara *et al*., 2007).

Codons 217 and 360 (Val217Met and Gly360Ala)

Val217Met (resulting from a G>A transition) is the only validated coding polymorphism that is located in the DBD of *TP53;* thus, in principle, it could dramatically affect the activity of *TP53*.Functional studies have been limited to transactivation assays in yeast (Kato *et al*., 2003), which indicate that this polymorphism results in little loss of activity The genes that show the most variation in activation are CDKN1A, BAX and PMAIP1 (also known as NoXA), but the *TP53*-Met217 variant leads to greater expression of these genes than the more common *TP53*-Val217 variant; extrapolating from this result, one can speculate that the Val217Met polymorphism might be protective against cancer.

Gly360Ala is located in the linker region adjacent to the tetramerization domain of *TP53*. Again, the functional data for this polymorphic variant have been provided by transactivation studies in yeast

(Kato *et al*., 2003), which showed a slight decrease in the transactivation of BAX, MDM2 and *TP53*AIP, and a more marked decrease in stratifin (SFN, also known as 14-3-3 sigma) and GADD45 (growth arrest and DNA damage-inducible (Gemignani, *et al*., 2004). Codon 72 (Arg72Pro) polymorphism in *TP53*

The codon 72 polymorphism

This common SNP results in a non-conservative changeof an arginine (R72) to a proline (P72) at amino acid72 that results in a structural change of the proteingiving rise to variants of distinct electrophoretic mobility (Matlashewski *et al*., 1987). This polymorphism occurs in a proline-richregion of *TP53*, which is known to be important forthe growth suppression and apoptotic functions ofthis protein (Sakamuro *et al*., 1997). Beckman and co-workers were the first todemonstrate a significant difference in the allelic distribution of the R72 and P72 variants. They first noted a significant difference in the P72 allele frequency between a Nigerian population (African Black) and a Swedish population (Western Europe), which were17 and 63%, respectively; in contrast, they did notnote any differences between populations living on the same geographical latitude (Beckman *et al*., 1994). The authors went on to demonstrate that the frequencyof the P72 allele differs with latitude, increasing ina linear manner as populations near the equator (Sjalander *et al*., 1995). These observations led the authors to suggest that the codon 72 variants differed inbiological activity, and further that these differences inactivity might be subject to selection in areas of high ultraviolet light exposure.

Banks and co-workers subsequently demonstrated the existence of biochemical and biological differences between the R72 and P72 isoforms of *TP53*. Noted are the conserved functional domains of *TP53*, with amino-acid residues for each functional domain listed below. Thelocations of the two coding region polymorphic variants (codon 47 and codon 72) are denoted with an asterisk. Figure 2 Amino-acid sequences of the *TP53* polymorphism atresidue 47. The two p38 MAPK sites of phosporylation (serines 33 and 46), adjacent to proline residues at amino acids 34 and 47, aredenoted. Figure 3 Amino-acid sequences of the *TP53* polymorphism atresidue 72. This region contains several SH3-binding motifs (PXXP), which are postulated to be important for the ability of *TP53* to induce apoptosis. In a subsequent study, the authors went on to demonstrate that the P72 form of *TP53* had enhanced ability to function as a sequence specific trans-activator, owing, in part, to its strongerinteraction with two TFIID-associated factors, TAFII32 and TAFII70 (Thomas *et al*., 1999). In contrast, the authors found that the R72 variant of *TP53* was amarkedly better suppressor of cellular transformation, an activity commonly associated with *TP53*'s apoptotic function. Differences in the biological activity of R72 and P72 proteins have also been described for certain tumor-derived mutant forms of *TP53*. Specifically, the *TP53*-homolog p73 has been reported to physically interactwith certain tumor-derived mutant forms of *TP53* (butnot wild-type *TP53*). More to the point, the authors demonstrated that these mutant forms of *TP53* interacted with p73 preferentially when they occurred in cis with the R72 *TP53* polymorphism (Marin *et al*., 2000). This study went on to show that, in tumours from individuals heterozygous for the codon 72 polymorphism (R72/P72), the R72 allele was most commonly subject tomutation, while the other allele (P72) was morefrequently lost by deletion (Marin *et al*., 2000). Thesedata suggested that the R72 variant of *TP53*, when in ciswith certain tumor-derived mutations, might haveenhanced tumor suppressive function owing to increased ability to inactivate p73. Subsequent studies suggest thatthe ability of R72 to target and inhibit p73 may be celltype dependent (Vikhanskaya *et al*., 2005). Specifically, these authors demonstrated that some of the *TP53* tumorderived mutants that are unable to bind and inhibit p73 are still able to confer resistance to drug treatment, suggesting that R72-containing mutants may possess other mechanisms to disrupt chemotherapy-induced apoptosis. Two groups found that, for non-mutated forms of *TP53*, the R72 variant has a significantly increased abilityto induce programmed cell death, in cells containinginducible versions of *TP53*, as well as in cells homozygousfor R72 and P72 (Dumont *et al*., 2003). The absence of differences in specific DNAbinding or transcriptional ability of these two polymorphic variants led our group to discover that theenhanced apoptotic potential of the R72 variant wasowing to increased trafficking to the mitochondria, resulting from enhanced interaction with, and ubiquitylation by, the MDM2 ubiquitin ligase (Dumont *et al*., 2003). Such mitochondrial localization of *TP53*, leading to cytochrome c release, was first described by Moll andco-workers, and later confirmed by our group (Dumont *et al*., 2003). Our group inassociation with the group of George has identified thepro-apoptotic protein BAK, an important member fromthe Bcl-2 family involved in cytochrome c release frommitochondria, as a mitochondrial *TP53*-interacting protein (Leu *et al*., 2004). Interestingly,

we found that thetwo *TP53* isoforms R72 and P72 demonstrate the same affinity for BAK, suggesting that the enhanced ubiquitylation and nuclear export of the R72 under liesits enhanced mitochondrial function in cell death. Insum, the combined data from several groups hasconfirmed the altered apoptotic potential of the codon72 polymorphic variants, with the R72 variant demonstrating enhanced apoptotic ability, and the P72 variant demonstrating enhanced growth arrest (Pim and Banks, 2004). Based on these findings, a number of studies have tried to establish a correlation between the *TP53*codon 72 polymorphism and the risk to develop certain types of cancer. In general, these studies have notyielded consistent results; this may be accounted for by the fact that the R72 variant, when found in mutantforms of *TP53*, might be predicted to enhance tumor development (increased inactivation of p73), but whenfound in the context of wild-type *TP53*, might be predicted to better inhibit tumor development (increased apoptotic ability)

One of the first studies to demonstrate a correlation between the codon 72 polymorphism of *TP53* and the riskto develop cancer was by Banks and co-workers, who reported that women with the R72 variant of *TP53* (better targeted for degradation by HPV E6 protein) had aseven-fold increased risk to develop cervical cancer (Storey *et al*., 1998). To date, dozens of studies have failed to confirm these results, possibly because of differences in subtypes of HPV, so an association between cervical cancer and the codon 72 polymorphism of *TP53* is not currently accepted.Several groups have reported an association betweenthe R72 *TP53* variant (binds and inactivates p73 better)and increased risk for epithelial cancer, including gastric cancer (Shen *et al*., 2004) and cancer of the breast, ovary oesophagus, skin (DeOliveira *et al*., 2004), lung, bladder, prostate and larynx (Sourvinos *et al*., 2001). In other studies, however, authors have found the opposite correlation,instead demonstrating an association between the P72 (lesser apoptotic) variant and increased risk forother cancer types, including cancer of the thyroid, nasopharynx, prostate, skin, urogenital region and lung (Zhang *et al*., 2003). Still other groups have failed to demonstrate any association between codon 72variants of *TP53* and cancer risk. Again, these discrepancies may be influenced by a failure to determine the mutational status of *TP53* in these tumours. Other researchers suggest that these discrepancies may beaccounted for by a failure to conduct meta-analyses, orowing to poorly controlled 'normal' populations that donot take into account the latitudinal differences in allele *TP53* polymorphisms. Oncogene frequency (Koushik *et al*., 2004).While correlations between cancer risk and the codon 72 polymorphism have been in consistent, more consistent have been the correlations between these polymorphic variants and cancer progression, survival, andage of on set of cancer. In particular, several groups havefound that patients homozygous for P72 (lesser apoptotic allele) were diagnosed at an earlier median ageof onset for their cancer. The median age varied from 6 years earlier for squamous cell carcinoma of thehead and neck, to 13 years earlier for non-polyposiscolorectal cancer, and between 10 and 11 years earlier for oral cancer (Jones *et al*., 2004). These data are consistent with the hypothesis that the R72 allele, which has greater apoptotic ability, consequently possesses enhanced tumor suppression function. Also consistent with thishypothesis are findings that individuals with the R72 genotype have higher response rates and better survival after receiving chemo- and radiation therapy foradvanced head and neck cancer and for cancers of the breast and lung (Xu *et al*., 2005). Therefore, while correlations between cancer risk and *TP53* polymorphic variants havenot been clear, more consistent correlations exist for cancer progression, survival, age of onset, and response to therapy.

In human populations, codon 72 of *TP53* has either the sequence CCC, which encodes proline, or CGC, which encodes arginine. The variants are hereafter abbreviated *TP53*-Pro72 and *TP53*-Arg 72. Comparative sequence analyses in non-human primates suggest that *TP53*-Pro72 is the ancestral form, although *TP53*-Arg 72 occurs at a high frequency (>50%) in some populations. A latitude gradient in variant frequency (an increasing frequency of the *TP53*–72 variant towards the equator (Sjalander *et al*., 1996) invited early speculation that *TP53*-Pro72 might protect against adverse consequences of sunlight or other environmental cancer risk factors.

The NIH genetic association database, which is not comprehensive, has records on over 230 studies evaluating the effect of the codon 72 polymorphism on susceptibility to a wide variety of cancers. Many of these studies have reported 'statistically significant' associations. Several formal meta-analyses combining data from multiple studies have been published on breast, gastric and lung cancer, and these do not support a role for this polymorphism in the risk of developing these cancers (Matakidou *et al*., 2003).

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Review Article

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Prevailing Hospital Acquired Infections a Challenge to Safety of Patients and Hospital Staff: An Overview

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Abstract

As a broad timeline, infections happening in excess of forty eight hours after admission to the medical health centres or hospitals are typically viewed as Hospital Associated Infections (HAI's)(WHO).These HAI's that patients gain throughout getting treatment for different medical conditions are likewise called nosocomial infections. Every year, numerous lives are lost in light of the spread of infections in hospitals. HAIs are a reason for noteworthy morbidity and mortality in patients receiving treatment, and the immediate and aberrant expenses of these infections drain the effectively restricted money related assets allotted to hospitals. It is evaluated by the Centers for Disease Control and Prevention that two million patients experience the ill effects of HAI's consistently and almost one lakh of them die.Annually HAI result in upto $4.5 billion extra medicinal services expenses. Therefore emergency clinics should concoct an inhouse mindfulness program where staff individuals, patients and their relatives can be taught on keeping up cleanliness and build up a comprehension of disease aversion and its financial ramifications which will permit disease control experts to settle on better educated choices.

Keywords: Infections; Hospital Associated Infections (HAI's); Intensive care units (ICU's).

Introduction

An infection or contamination is an illness brought about by microorganisms, for example, fungi, virus bacteria and parasites and medical healthcare centres are the breeding places for these diseases. Disease can be picked from gadgets, equipments, companions, and attendants amid a stay in hospital. These contaminations happen at an expense to the community and the patient since they cause ailment to the patient, a more extended stay in medical clinic, a more recovery time, costs related with extended stay in hospital and more recovery time (Chaudhuri, 1993). The most well-known kinds of HAI's or nosocomial diseases include diseases in lungs, wound, blood infections, pneumonia mostly ventilator-related pneumonia, urinary tract disease, and surgical site disease (Pratham *et al*., 2011; Richards *et al*., 2000). The most widely recognized bacteria and viruses causing HAIs are:

Acinetobacter baumannii: Intensive care units (ICU's) and regions with profoundly sick individuals are significantly infected by the episode of the *Acinetobacter* bacteria. Patients with compromised immune system and different comorbidities are increasingly susceptible to transmission of this microorganism. This organism is regularly resistant to normally endorsed antibiotics and principally causes blood contaminations, *Klebsiella pneumonia*, *Neisseria meningitis*, UTI and wound diseases (Dijkshoorn *et al*., 2007)

Bacteroides fragilis: *Bacteriodes fragilis* is an common microorganism found in the intestinal tract and the colon. However, it can cause diseases, most regularly in accomplice with other bacteria. This microorganism shows slow development, expanding antibiotic resistance and co-event with different pathogens which makes treatment increasingly difficult (Chia-Ying Liu *et al*., 2008).

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Burkholderia cepacia: *Burkholderia cepacia* is a gram-negative microorganism. They are essentially present in aquatic situations, found in colonized structure in intravenous arrangements. The bacteria cause pneumonia in patients with chronic lung illness, for example, cystic fibrosis. *Burkholderia cepacia* shows resistance to various antibiotic agents and spreads by means of infected medicines, infected medicinal gadgets, human to human contact or by contacting the infected surface (Lipowski *et al*., 2008).

Clostridium difficile: *Clostridium difficile* contamination causes irritation of the colon, making the manifestations from looseness of the bowels to life threatning colitis. These microscopic organisms are transmitted by means of the fecal-oral course, most normally being exchanged from a contaminated site to another patient via human hands. *Clostridium difficile* can live in clinical areas for expanded timeframe as it demonstrates protection from numerous normal cleaning items, including hand sanitizers (Dallal *et al*., 2002).

Clostridium sordellii: *Clostridium sordellii* is an uncommon bacterium, frequently causing infections like pneumonia, endocarditis, peritonitis and myonecrosis, and in extreme cases can prompt sepsis. *Clostridium sordellii* for the most part influences women and is frequently connected to end of pregnancy (Fischer *et al*., 2005).

Carbapenem-resistant Enterobacteriaceae (CRE): Enterobacteriaceae are ordinarily found in the gut yet causes serious illness if they spread to different parts of the body. CRE spreads by means of contact transmission like human to human contact or interacting with a contaminated devices, for example, a catheter. The microorganism show protection against antibiotic carbapenems.CRE contaminations can have upto a fifty percent of death rate (Chitnis *et al*., 2012).

Enterococcus faecalis: The bacteria eminently causes urinary tract diseases, sepsis and wound contaminations. *Enterococcus faecalis* is a versatile microscopic organisms, with the capacity to get by in a temperature scope of 50 degrees to 115 degrees fahrenheit. *Enterococcus* microbes demonstrates protection from antibiotic vancomycin, leaving only a couple of treatment alternatives for patients (Top *et al*., 2008).

Escherichia coli: *Escherichia coli* is generally found in the gut however can likewise become pathogenic. *Escherichia coli* contaimination causes UTI in patients, and can likewise cause gastroenteritis, pneumonia or even neonatal meningitis. Serious *Escherichia coli* contaimination can prompt hemolytic-uremic disorder (Poolman *et al*., 2018).

Hepatitis A Virus (HAV): The Hepatitis A infection is minimal regular of the three noteworthy hepatitis infections found in hospital settings. The infection spreads through the fecal-oral course, and medicinal services workers gets frequently contaiminated while taking care of a patient in whom the disease isn't yet perceived, is fecal incontinent or has looseness of the bowels (Meyers *et al*., 1975).

Hepatitis B Virus (HBV): HBV regularly spread through body fluids of a contaminated individual which in medicinal services settings is frequently through contaminated needles, syringes or other sharp objects.HBV can cause acute or chronic liver diseases. An acute disease commonly includes liver inflammation, vomiting and jaundice. Some acute cases can develope into chronic Hepatitis B, causing long lasting infections, cirrhosis, liver malignant growth, liver failure and death (Jessica *et al*., 2015).

Hepatitis C Virus (HCV): HCV is principally transmitted through intravenous medication use in the community.In the clinic setting HCV transmits through infected syringes, needles or sharps, contaminated blood transfusions and once in a while even organ transplants that have not undergone satisfactory HCV screening (Mazurek, 2000).

Human immunodeficiency Virus (HIV): HIV transmission in healthcare centres is uncommon, it is conceivable to be spread to patients through improper contamination control methodology, for example, cleansing and sterilization. The HIV infection harms T cells that are significant in helping the body against diseases. Hence HIV patients are at the danger of numerous kinds of infections.HIV is exchanged through body fluids, so appropriate alert must be taken for HIV infection as that with other blood borne pathogens (Ganczak and Barss, 2008).

Influenza: The H1N1 strain or swine flu, a standout amongst the latest destructive variants of the influenza A infection.The influenza infection is a typical one, yet novel strains, strains not before found in people, and variant strains regularly develop. The virus has ability to adapt into new strains. Some extreme instances of influenza can lead to death (Vanhems *et al*., 2016).

Klebsiella pneumoniae: In the clinic setting, *Klebsiella pneumoniae*, regularly causes UTI, wound contaminations, upper respiratory tract diseases, osteomyelitis and even meningitis. If the patients requires intrusive medicinal devices, urinary catheters, ventilators and antibiotics, risk of disease with *Klebsiella pneumoniae* increases. *Klebsiella pneumoniae* spread through the air, rather is predominantly spreads through contact with a contaminated individual. *Klebsiella pneumoniae* disease happens much of the time in premature newborn children and in the neonatal emergency unit (Podschun *et al*., 1998).

Methicillin-Resistant Staphylococcus aureus (MRSA): MRSA contaminations for the most part show up on the skin, however they can spread to organs and into the circulation system, causing sepsis, pneumonia and surgical site diseases. The microscopic organisms are transmitted through direct contact, more often through an open injury or infected hands. The best resistance against MRSA contamination is the best possible hand cleanliness (Diekema *et al*., 2001).

Morganella morganii: This microorganisms represents roughly one percent of nosocomial diseases, regularly experienced in postoperative settings. It causes UTI, sepsis, pneumonia, inflammation of the eye and musculoskeletal diseases. *Morganella morganii* is normally resistant to specific antimicrobial agents like penicillin, however is as yet treatable with different antibiotics (Williams *et al*., 1983).

Mycobacterium abscessus: *Mycobacterium abscessus* found in water, soil and dust, is known to infect drugs and clinical devices. Generally *Mycobacterium abscessus* moreover of causing contaminations of the skin or soft tissue under the skin, causes lung infections in individuals with chronic lung ailments. Transmission of the microorganisms more usually happens by means of contaiminated equipments or material in intrusive therapeutic strategies or when contaminated substances are infused into a patients (Ghosh *et al*., 2017).

Norovirus: Norovirus is the most widely recognized reason for gastroenteritis. Norovirus spreads quickly from individual to individual. Individuals with other medical sickness are at more risk of contamination of norovirus. Health service centres and other institutional settings are especially at risk of episodes of Norovirus infections in light of increased individual to individual contacts. Legitimate hand cleanliness is a successful method to abstain from transmitting norovirus (Sukhrie *et al*., 2012).

Psuedomonas aeruginosa: *Pseudomonas aeruginosa* contamination most generally happens in patients hospitalized for the time period of more than a weak. Patients with catheters or on ventilators are at increased risk of contamination in light of the fact that the microbes blossoms on moist surfaces. Although the contamination is treatable and reparable with anti-microbials, yet serious illness, for example, bacteremic pneumonia, sepsis, wound contaminations and meningitis from *Pseudomonas aeruginosa* are connected to high death rate (Fazie *et al*., 2012).

Staphylococcus aureus: *Staphylococcus aureus* when identified as the reason for sepsis, pneumonia, endocarditis or osteomyelitis in hospital settings can be fatal. Improper cleanliness protocol adherence is one of the greatest passages for *Staphylococcus* to be transmitted in the medicinal services setting (Valaperta *et al*., 2010).

Stenotrophomonas maltophilia: Patients requiring catheters, breathing cylinders and intravenous liquids in clinic settings are at increased risk of contamination by *Stenotrophomonas maltophilia* in light of its favored aquatic habitat. In patients without invulnerable immune system, *Stenotrophomonas maltophilia* may cause pneumonia, UTI or sepsis, although the threat of infection is minimal without the presence of intrusive medical devices (Looney, 2005).

Mycobacterium tuberculosis: *Mycobacterium tuberculosis* is one of the main sources of infection caused deaths worldwide. In healthcare settings, the disease isn't very common. However, it tends to be spread through the air from close contact to a infected individual (Cookson and Jarvis, 1997).

Routes of Transmission

Routes of transmission of infections in Admitted patients.

Contact transmission: Contact transmission includes transmission by contact or by means of contact with blood or body fluids and is the most widely recognized method of transmission. Contact might be direct or indirect (i) Direct transmission happens when infectious agents are exchanged from one individual to another for instance, a patient's blood entering an body of worker at hospital through an unprotected cut in the skin. (ii) Indirect transmission includes the exchange of an infection causing agent through infected object or infected individual for instance, hands transmitting infectious agents in the wake of contacting a infected body site of one patient and not performing hand cleanliness before contacting another patient. Multi drug resistant organism (MDROs), carbapenem resistant gram negative microbes, *Clostridium difficile*, norovirus, ebola infection, HIV, HBV and HCV infections, and exceedingly infectious skin contaminations (for example impetigo, scabies) and so forth are the instances of infections transmitted by means of contact (WHO, 2002).

Droplet transmission: Infectious particles larger than 5 microns in size are called droplets. Droplet dissemination is constrained by the force of expulsion and gravity and is more often not more than one meter. The actions of infected person like coughing, wheezing and talking can result in droplet transmission. In any case, indirectly droplet can likewise be transmitted to mucosal surfaces by means of hands. Instances of infections that are transmitted by means of droplets include influenza infection and *Meningococcus* (WHO, 2002).

Airborne transmission: Airborne transmission happens through particles containing infectious agents that stay suspended in air. Breathing, talking, coughing or wheezing and optionally evaporation of larger droplets in states of low humidity results in formation of small particles less than 5 microns in size. Certain methodologies, especially those that incite coughing, can advance airborne transmission for example diagnostic sputum induction, bronchoscopy, airway suctioning, and endotracheal intubation, positive pressure ventilation by means of face mask and high-frequency oscillatory ventilation. Infectious aerosols can be scattered over long distance via air (e.g.) ventilation or air conditioning frameworks and breathed in by vulnerable people who have not had any contact with the contaminated individual. Examples of infections that are transmitted by means of the airborne course include measles, chickenpox and *Mycobacterium tuberculosis* (WHO, 2002; Nosocominal infection, 2007).

Vector-borne Transmission: Vector-borne transmission alludes to transmission by means of vectors. Vector based transmission can be prohibited by proper construction and maintanence of health service offices, properly screened windows, and appropriate housekeeping. At the point when vectors, for example, mosquitoes, flies and rodents transmit infectious microorganisms into another living life form is called vector-borne transmission (WHO, 2002; Bonten *et al*., 1998; Lancet, 1996).

Routes of transmission of disease amid research center work at clinics

The most widely recognized courses of exposure associated with research center work at medical hospital includes intake of microorganisms occuring through mouth pipetting, transfer of infection causing microorganisms to the mouth by means of polluted things, for example, pencils, pens or hands, consumption of eatables in the lab, and incidental sprinkles that fall into the mouth. Routine laboratory work like collection and processing of specimen, manipulation of cultures regularly contaminate various containers, equipments, working tables etc. In the research facility, exercises like consumable eatables and applying cosmetics should be generally denied as they are significantly associated with lab related infections. Eating and drinking material should not be preserved in freezers utilized for the storage of clinical samples. One of the main sources of research centre related diseases is the accidental intramuscular or intravenous exposure of infection causing agents (Collins, 1993; Fleming *et al*., 1995; Pike, 1976). The uncut or intact skin is an astounding hindrance to most pathogenic microorganisms. The vast majority of the diseases happen following entrance of microorganism into the skin through contaminated needles, surgical blades, or broken glass. The mucous films of the eyes, mouth, and nasal hole are particularly vulnerable to sprinkles, splashes, and transmission via hand to eye, mouth and nose. Aerosol concentrates that are produced in research centre through various techniques cause disease when breathed in (Gilchrist *et al*., 1992; Kenny and sable, 1968; Rawal, 1959).With the assistance of ventilation systems that creates

an air exchange, these particles can be expelled from a room within 30 to 60 minutes (Gilchrist *et al*., 1993). The significant outbreak of research facility procured diseases ventured to be brought about by these infected particles have been related with *Brucella*, *Coxiella burnetii* or Q fever, *Chlamydia psittaci* or psittacosis, and *Mycobacterium tuberculosis* (Gilchrist *et al*., 1993; Kenny and sable,1968: Rawal, 1959)

General Measures of Infection Control

Isolation: Isolating a patient includes evaluating the requirement for detachment, screening of all ICU's for the patients with neutropenia and immunological issue, loose bowels, skin rashes, known communicable infection, known carriers of a epidemic species of bacterium and choosing the kind of isolation required for the specific patient. There are two ways the patients can be isolated in the ICU: Protective confinement and Source disengagement. Protective Confinement is for neutropenic or other immunocompromised patients to lessen the chances of procuring diseases from other contaminated patients. Source confinement of contaminated patients is to limit potential transmission to different patients or staff. Separation rooms should have tight-fitting entryways, glass segments for perception and both negative pressure (for source segregation) and positive weight (for protective confinement) ventilations (Guideline for isolation precautions, 2014).

Patient at high risk of nosocomial diseases: Development of nosocomial contamination relies on certain factors like age over seventy years, shock, injury, acute renal failure, coma, prior antimicrobials, mechanical ventilation, drugs influencing the immune framework (steroids, chemotherapy), indewelling catheters, prolonged ICU stay of over three days (Guideline for isolation precautions, 2014). These risk factors make patients increasingly prone for acquiring nosocomial diseases.

Observe hand cleanliness: Hand cleanliness is the absolute best methods for preventing the transmission of diseases among medical clinic patients and medicinal services laborers as the hands are the most widely recognized hotspot for transmission of pathogenic microorganism (WHO, 2014). Hand cleanliness is an absolute necessity, before contacting a patient to shield the patient from harmful agents carried on the hands of individual managing patients, before aseptic strategies to secure the patient against destructive germs, including the patient's own germs, after body fluid exposure to ensure protection of caretaker from the unsafe patient germs.

Standard safeguards: Standard precautionary measures incorporate preventive estimates that must be followed every time, independent of a patient's disease status (WHO, 2014).

Gloves: While contacting mucous membrane and injured area on skin and performing sterile procedures for example arterial, central line, foley catheter insertion and during laboratory and research work at hospitals clean gloves must be worn after hand cleanliness procedure. Clean, non-sterile gloves are safe for contacting blood, other body fluids and infected material. Changing gloves over and again while perfoming procedures in same patient particularly while moving from a infected body zone to a clean body region is mandatory. Same pair of gloves should not be utilized more than once for the consideration of more than one patient. At whatever point gloves are expelled hand cleanliness convention must be practiced (WHO, 2014).

Gown: Wearing an outfit to avoid contamination of garments and skin during methodologies that are probably going to produce sprinkles of blood, body fluids and secretions is a measure of contamination control. The sterile outfit is required just for aseptic methodology and for the rest, a clean, non-sterile outfit can be utilized. Contaminated outfit must be expelled with consideration at the earliest opportunity, to stay away from infections (WHO, 2014).

Mask, Eye protection and face shield: Wearing a mask, utilizing satisfactory eye protection or a face cover to ensure protection to mucous layers of the eyes, nose and mouth during techniques and procedures that are probably going to produce sprinkles of blood and body fluids of patient can help in disease control.Patients, relatives and hospital workers showing respiratory manifestations for instance cough should dependably utilize masks (WHO, 2014).

Shoe and head covers: Shoe and head covers must be used while entering in operation theatres and ICU's (WHO, 2014).

Patient-care equipments: Used patient-care equipment sullied with blood, body fluids, secretions should be taken care of cautiously

to prevent exposure to skin and mucous membrane, contamination of attire and exchange of microorganisms to health care workers, different patients or the hospital environment. Reusable equipments must not be utilized for the consideration of another patient until it has been cleaned and sanitized suitably. Single use things and sharps should be disposed of appropriately (WHO, 2014).

Transmission-based precautionary measures: Transmission-based safeguards are the safety measures that must be observed in the patients known or suspected to have airborne, contact or droplet contaminations (WHO, 2014).

Airborne precautions: Disease-causing microorganisms might be suspended in the air as minute particles which stay infective over time and distance, for instance, mycobacterium tuberculosis(pulmonary/laryngeal),varicella zoster infection (chickenpox), herpes zoster (shingles), rubella infection and measles. These patients must be confined with negative-pressure ventilation. Respiratory security like utilization of dispensable N-95 respiratory veil must be utilized when entering the isolated room. N-95 cover fits firmly around the nose and mouth to ensure security against both huge and little droplets. This must to be worn by all people going into the room, including guests and attendants (WHO, 2014).

Contact safety measures: Infections can be spread by direct or indirect contact with a contaminated individual or with patient care material, for instance, flu infection disease, respiratory syncytial infection, varicella (chickenpox), herpes zoster, hepatitis A and rotavirus infections. Isolation for such patients is required to stay away from transmission of disease. Non critical patient-care equipment should ideally be utilized once. If unavoidable, at that point equipment must be cleaned and sanitized sufficiently before utilizing to another patient. Transport of the patient must be restricted to avoid transmission of malady (WHO, 2014).

Droplet safety measures: Pathogenic microorganisms are likewise transmitted through droplets that is large particles >5 µm in size. These particles are created during coughing, wheezing and talking for instance, flu infection, *Bordetella pertussis*, *Hemophilus influenzae* (meningitis, pneumonia), *Neisseria meningitides* (meningitis, pneumonia and bacteremia), *Mycoplasma pneumoniae*, extreme intense respiratory disorder related coronavirus, Group A streptococcus, adenovirus and rhinovirus (WHO, 2014). Respiratory protection like utilization of disposable N-95 respiratory masks when entering the rooms in which such patients are confined. N-95 cover fits firmly around the nose and mouth to secure against both enormous and little droplets. This should be worn by all people going into the room, including guests. Seclusion for such patients is required to dodge transmission of sickness. High quality cleaning and purification of all patient-care territories is significant, particularly surfaces near the patient (for example bedrails, bedside tables, doorknobs and equipments). Transport of the patient must be constrained to dodge transmission of sickness (Circulation of disinfection and sterilization in healthcare facilities, 2008).

Immunization and inoculation: Hospital strategy for yearly immunization of human services experts covering for flu, hepatitis and other infective malady flare-ups must be joined in HAI avoidance guideline (Rakita *et al*., 2010).

Management of Laboratory Accidents: The most judicious way of management of lab mishaps and aversion of exposures to infectious agents is a safety plan that recognizes potential hazard or risk assesment and limits or controls the potential for exposure or accident.The management of an exposure to an pathogenic organism depends on the specific microorganism and an assesment of the potential danger of infection (National committee for clinical laboratory standards, 1991). All mishaps and potential exposures should be accounted quickly to the suitable safety officer. Follow-up to the incident should include quick medicinal consideration coordinated toward expulsion of the infectious material and institution of first aid, accident examination that includes recognizable proof of the source patient and risk factors in case of blood-borne pathogens, confidential medical consultations with the worker to address his or her inquiries in regards to danger of contamination, need of prophylaxis, probability of potential transmission to relatives, future treatment and observation; and restorative activity to counteract future mishaps or exposures. Following presentation to a blood-borne pathogen for instance hepatitis infections or HIV, the action plan should be reliant on determination of the contamination status of the source patient. The management of mishaps and exposures should be clarified in the employee health manual.

Conclusion

HAIs are a noteworthy safety matter for both medicinal services suppliers and the patients. Taking into consideration about increasing incidences of diseases, increased death rate, expanded time of stay at hospitals and the additional cost associated, endeavours must be made to make the hospitals protected against the infections. Conventions and projects should be created and executed vivaciously in individual ICUs across the world, yet change is desperately likewise required at the authoritative and regulatory dimensions regarding incorporating all factors that go into powerful and prudent contamination control rehearses. Infection prevention and control should be a noteworthy spotlight on hospital clinic score, alongside the financial reports.

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Article in supplement or special issue

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