

Athens Journal of Health and Medical Sciences



Volume 7, Issue 3, September 2020 Articles

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The current issue is the third of the seventh volume of the *Athens Journal of Health and Medical Sciences* (AJHMS), published by the <u>Health</u> & <u>Medical Sciences Division</u> of ATINER.

Gregory T. Papanikos
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20th Annual International Conference on Health Economics, Management & Policy, 21-24 June 2021, Athens, Greece

The Health Economics & Management Unit of ATINER will hold its 20th Annual International Conference on Health Economics, Management & Policy, 21-24 June 2020, Athens, Greece sponsored by the Athens Journal of Health and Medical Sciences. The aim of the conference is to bring together academics, researchers and professionals in health economics, management and policy. You may participate as stream leader, presenter of one paper, chair of a session or observer. Please submit a proposal using the form available (https://www.atiner.gr/2021/FORM-HEA.doc).

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- **Dr. Paul Contoyannis**, Head, <u>Health Economics & Management Unit</u>, ATINER & Associate Professor, McMaster University, Canada.
- **Dr. Vickie Hughes**, Director, <u>Health & Medical Sciences Division</u>, ATINER & Assistant Professor, School of Nursing, Johns Hopkins University, USA.

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• Abstract Submission: 23 November 2020

• Acceptance of Abstract: 4 Weeks after Submission

• Submission of Paper: 24 May 2021

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Important Dates

• Abstract Submission: 5 October 2020

• Acceptance of Abstract: 4 Weeks after Submission

• Submission of Paper: 5 April 2021

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LEAN System Management in Hospitals

By Ivan Bošnjak* & Marija Bošnjak*

Statement of problem: Healthcare industry is struggling under an increasing pressure of constantly rising costs as the science opens new horizons in the development of new drugs and technologies making thus the task of employing resources in an effective manner more challenging than ever before. LEAN system management in hospitals can contribute to effective costs management and better results. We analyzed industrial LEAN model management and its implementation in hospitals. LEAN management has its roots in Just-In- time management implemented by the company Toyota that has provided for this company to become a fierce competitor to the United States car industry. The aim of LEAN is to eliminate waste and reduce production time. The basic principle of LEAN philosophy is to determine where the value is added in the process and where it is not. LEAN consists of several tools: five S, Kaizen events, standardized work, kanbans, spaghetti diagrams. Spaghetti diagrams are used to track the movement of employees, materials and patients. Effective implementation can reduce the time used for different needs of patients and tasks of employees, so this is an example of lost effectiveness that can be eliminated. Kaizen events include a project team selected from hospital staff, whose goal is to solve efficacy problem by defining the problem and reasonable output and then implement new ideas. An example may be a disorganized inventory of hospital pharmacy that consequently prolongs the time of drug delivery. The project team can locate the problem and suggest inventory changes. Competitive market companies must constantly innovate and implement new ideas to win a market share. Such innovations can sometimes be used in healthcare industry, and effective implementation can increase the quality of health service provided by hospitals, and also reduce never ending rising costs, a challenge that hospital management encounters.

Keywords: LEAN, rising costs, hospital management, waste elimination

Introduction

The process of management, controlling of the costs of hospitals and of other health institutions is a very challenging part of quality management. The main question is how we can provide the best health care to patients and achieve the highest healthcare standards in spite of constantly rising costs based on new diagnostic and therapeutic possibilities. Hence, the objective of this study is to present modern managerial method, LEAN management introduced by manufacturing companies, as well as the possibilities and results of LEAN management implementation in a complex hospital environment (Centauri et al. 2018). In the year 1999, the Medical Institute in the United States of America published a paper reporting that 98,000 patients died in hospitals because of medical errors that could have been prevented. In 2012, the report of the Institute of Medicine titled Best Care at Lower Cost: The Path to Continuously Learning Health Care in America showed the underperformance in healthcare system: 750

^{*}General Practitioner, Clinical Hospital Centre Sisters of Mercy, Croatia.

^{*}Brand, Marketing and Communications, Ernst & Young and University of Zagreb, Croatia.

billion dollars were needlessly spent in the year 2009. There were 75,000 needless deaths that could have been averted in the year 2005 if every state had performed at its best (Graban and Swartz 2014).

The quality problem in healthcare institutions can be seen in the quality care for patients provided by employees and in a number of errors that could be prevented. Errors done by physicians can have profound effect on patients' health, as well as clinician's confidence on practicing medicine. Healthcare institutions have rigid policies in dealing with those issues (Rodziewicz and Hipskind 2020). The difference in quality management between healthcare system and other industries is that, for example, car industry quality is based on the object of production, like cars and individual parts, and a buyer pays for the product. In healthcare system, a buyer of services is at the same time an object the service is provided for, so two services are related to one person. The process can be observed from several angles. One of them is the purchase of material and equipment at lower costs. However, the equipment management requires experts. The other possibility is based on creating the economic process value through efficient healthcare management in health institutions and by removing, remaking process inefficiencies, and thus creates better and more efficient process chain system. LEAN management system is one of modern management methods in industrial sector and service industries (McLaughlin and Hays 2008).

The history of LEAN system is based on Toyota Just-In-Time model that includes cost minimisation and waste reduction. LEAN system implemented in a process chain provides improvement at all levels, which gives the company competitive edge over other competitors. The goal is to eliminate dead weight loss and process inefficiencies. Lean system is based on a few basic principles: muda, muri, mura. Muri stands for planning the business process. Muda is based on efficiency of business process, product quality and quality design of business process and lack of efficiency elimination. Muda (waste) is the resulting output of the process. The role of management is seen mainly in muda, in other words, muda is affected by muri and mura. Muri and mura are parts of Porter chain of value, the process elements which have the function of adding value to output in health industry, the patient health (Womack et al. 1990). Original seven mudas are: transport, inventory, people and product movement, time of waiting, overproduction, over processing and defects. In healthcare industry, the industries that do not have product part like car industry, the seven types of wastes are defined as follows: 1. waiting time of service buyer 2. duplicating (now and again information writing, cross information taking, taking same information more than once) 3. unnecessary movement (ergonomic science) 4. lack of quality communication 5. inventory errors (lack of supplies, badly organized supplies) 6. loss of opportunity of keeping a customer, or winning a new customer (ignoring customer, rudeness toward customer, lack of contact) 7. errors in transaction of service (lost or damaged equipment) 8. providing a service below expected standards (McLaughlin and Hays 2008).

Methodology

Problem statement: Along with the progress of medicine, hospitals are constantly facing the requirement to provide the best quality medical service, but also the increased costs based on new treatments. All of that puts pressures on hospitals.

Research: Through the research of relevant managerial and healthcare management literature, the review of scientific papers, and meta-analysis in healthcare management, we have analyzed modern management tools that can improve hospital effectiveness and give added value to hospital services. Hypothesis: There are management systems and tools that can improve the quality of healthcare management and the quality of service. We have analyzed the data of LEAN implementation in different hospitals and found the results of hospital cost-effectiveness.

Conclusion: Based on data analysis, we conclude that the management model according to LEAN philosophy improves the cost-effectiveness of hospitals and the outcomes of their daily operations, which contributes to the health and quality of patients' life. This scientific paper has been written by combining the information from various literature sources.

Kaizen (Continuous Improvement)

The term continuous improvement is not mentioned and important only in LEAN philosophy, but also in models like Six Sigma and Total Quality Management. The philosophy of Kaizen is based on continuous improvement of business process and chain value of all hospital employees. LEAN philosophy is a basic mechanism with health as a final output. Incremental changes, incremental improvements bring added value to the improvement of value chain. The focus should not be based only on defects of value chain, or elements that do not bring added value or cause the loss of values in value chain, but also on normal integral parts of value chain that can be improved. So the place of adding value is extended to all elements of improvement process. Baptist Health Care (Florida) had a Kaizen program established in 1995. In their programme every employee is expected to implement three ideas per year that will improve patients' outcome. More than 50,000 ideas have been implemented since the year 2000 and the estimated cost savings are 50 million dollars (Graban and Swartz 2012). The hierarchical structure is not vertical, but more horizontal and cross functional. Organization is seen through the chains of value in different elements of organization. These value chains interfere with each other in providing certain value to the input, in the care of patients in a hospital setting. The final outcome is based on all effects of inputs. It is important to note that this is a decentralized system of management in which the lowest ranking employees are seen as important factors in value adding mechanism. Kaizen philosophy is based on a few elements: 1. value specification means identifying what gives the biggest value to the patient 2. mapping of process map means identifying activities that give most value and write them down in order 3. flow means making the advancement of input through value chain without unnecessary stops 4. continuous improvement means continual repetition and focus on the process improvement so progress is constantly being made (Aij and Teunissen 2017).

Quick and easy Kaizen is a method that has the function of implementing improvements and it is divided into several steps: 1. find 2. discuss 3. implement 4. document 5. share. Finding means to actively search for opportunities for continual improvement. One should start from all levels of organisation, especially from the lowest level. The employees should be slowly introduced to implementation of Kaizen methodology with the focus on incremental improvements. It is usually suggested that employees should start with themselves by analyzing their work process and finding methods to improve it. By focusing on continuous improvement, work is more fun, interesting and challenging. As an example of Kaizen implementation, we can consider the allocation of rooms and doctor offices in a hospital. If the doctors have to walk a long way from hospital ward to their office to examine patients, it can be seen as a defect in the chain of value. By focusing on better room, hospital wards and doctor offices, the improvement value measured over time can be added to the chain of value. Taichi Ohno said: 'Why not make the work easier and more interesting so that people do not have to swear? The Toyota style is not to create results by working hard. It is a system that says that there is no limit to people's creativity. People do not go to Toyota to work, they go there to think.' Many Kaizen events function in such a way that boring and self-repetitive jobs are removed, which then provides the time for more rewarding and creative jobs and direct patient care. The example may be the automation of covering the test tubes. The process of automation saves time unlike the process in which a technician covers each test tube himself (Graban and Swartz 2014).

Value Stream Mapping

Value stream mapping is a process that includes the analysis of each component of business process and breaks it down to individual elements. Individual process elements are then divided further to smaller individual elements. These steps are described in details in a value map with successive mechanism. It is important to highlight which steps contribute to value adding and the ones that do not add value. Value stream mapping with its analytical mechanism effect provides for the organization the ability to focus on each individual process element. By focusing on process elements, the part that does not add value or subtracts it should be improved to focus on improving each process element. In healthcare hospital system, value stream mapping explains the patient flow through hospital (Figure 1). The process consists of elements like admission to hospital, taking their medical history, hospitalization, patient treatment, transfer to surgical department, reception in intensive care unit, administration of medication, follow-up progress and releasing a patient. All elements are parts of a business process (Gellad and Day 2016).

If we consider hospital setting as a whole Porter value chain that consists of various elements of individual business processes that are intertwined, the importance of each element in removing the inefficiencies and improving the mechanism of process elements, the improvement of flow in vertical pyramidal organizational structure can be observed. Value stream mapping points to a competitive advantage and improvement of its final output, patient health, and progress of each employee (Buttigieg et al. 2016).

It can be further considered whether this element of chain of value adds some value or not: 'Is the buyer of service willing to pay for the individual activity?' Patient waiting time could be used as an example. Long waiting time is not something a patient is willing to pay for and it is therefore not added to value chain, but subtracted, because the patient may go to another hospital (Lawal et al. 2014).

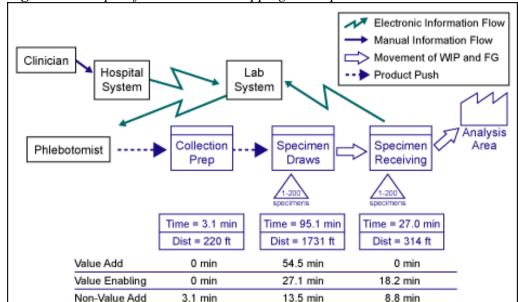


Figure 1. Example of Value Stream Mapping in Hospital Lab

Source: Blaha.

Spaghetti Diagram

Spaghetti diagram is a visual representation of material, employee movement within hospital settings. Its purpose is to use documentation of employee movement and patients within the system and to improve them. Typically, employees do a lot of movements that are duplicated and unnecessary (Figure 2). Movement analysis can be used to find most effective diagram that can contribute to the value chain (McLaughlin and Hays 2008).

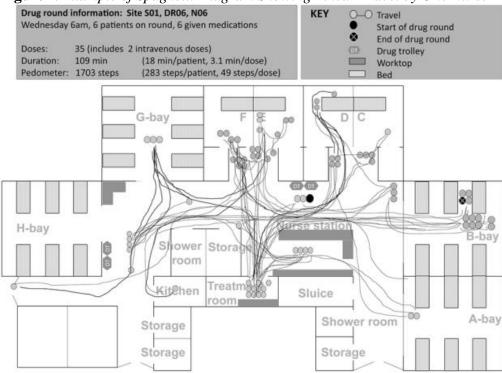


Figure 2. Example of Spaghetti Diagram Showing Linear Travel by One Nurse

Kaizen Event or Blitz

Source: Mcleod at al. 2015.

Kaizen event is a project task organized for the purpose of improving the individual parts of business process; it includes 8-10 members. A team consists of cross-functional members. The following elements are included into Kaizen event: 1. selection and definition of objectives 2. determination of the current state of value map 3. determination of the time from the input coming into the system, the time needed for the process until output is created 4. making the implementation plan: who, when, how 5. implementation of improvements 6. checking the efficacies of improvement 7. documenting and standardizing a newly made process 8. continuation of the cycle through the newly made value chain process (Graban and Swartz 2012).

Work Standardization

Work standardization is a written document that explains the ways each element of the process functions. It is based on recent documentation and analysis and has the function to explain the best way of performing certain activity (Tate and Panteghini 2007).

The examples of standardization in healthcare system are the healthcare guidelines provided both for diseases or hospital processes. Massachusetts General Hospital has implemented a guideline related to coronary artery bypass in cardiac surgery that has resulted in reducing the length of hospital stay to 1.5 days. The

contents of guidelines for hospitals advise on what should be done with a patient on admission day, operation day and the day after operation. The goal is to reduce the variability and discrepancies in the business process (Graban and Swartz 2014).

Jidoka and Andon

Jidoka is a Japanese term referring to the possibility for a worker to stop a process in case of some problem or detection of a defect. The role of Jidoka in LEAN philosophy is to detect and correct mistakes. If a mistake is found in the flow of process, the process should be stopped and all employees should try to identify and correct the mistake that may fall beyond the standard deviation framework. Andon is a system of signalization intended to notify that the process is stopped because an error has occurred (Soliman 2016).

Kanban

Kanban is a Japanese word for signal. Kanban in industrial product sectors is determined as an upstream container where workers would signalize that they have finished their job. In this way, empty kanbans are moved upstream toward the beginning of business process so they could signal additional work flow (Sugimori et al. 1977). Hospital pharmacy can be used as an example. It can have two kanbans. After emptying the first one, a signal is sent to notify that additional orders of drugs are needed. The second kanban is being emptied until the ordered items arrive. The number and size of kanbans determines the size of drug stock.

Single Minute Exchange of Die (SMED)

In healthcare system, Single minute exchange of die represents time spent between one and the other procedure of business process. Single minute exchange of die consists of three steps: 1. separating internal from external activities 2. converting internal in external activities. 3. streaming of all activities. Internal activities are such activities that have to be done in a system, they cannot be done offline (Karstoft and Tarp 2011).

The example of internal activities is cleaning the operating room before the next operation. Organization of surgical instruments is an example of external activity. It can be performed outside the operating room so the number of surgeries can increase.

Flow and Pull

The term flow refers to continuing movement of jobs, patients and products through business process without waiting and stoppages. Pull is a system in which products and services are not provided if a buyer does not ask for them. LEAN philosophy is continuously working on the improvement of both goals. In recent years the importance of patient flow has been recognized by a hospital system. To

satisfy optimal patient flow, hospitals must implement standards and business process to ensure continual improvement and flow of inputs in the system (Pinkney et al. 2016).

Heijunka and Advanced Access

Heijunka is a system that provides the elimination of the diversity in volume and types of waste. In healthcare system it is referred to levelling showing patient demands for services. If the demand can be quantified over different time periods based on previous data analysis and future prognostic data, hospitals can be more agile in reacting to changes and different expectations in the future. The basic example of Heijunka is related to scheduling patient examination in specific time period. Heijunka and Advanced Access are used in primary health care, especially family medicine. Ordering and examining patients in appointed time provides improvement in patient flow through the system, as well as the satisfaction of patients. It is basically required to predict the demand for services related to specific diseases in different yearly time intervals. It is important to note that hospitals must be ready for the upcoming demand, and the change in demand should be expected and prepared properly. The application of proactive policy will allow the reduction of waste in the system and the improvement of patient flow. This results in adding value to the patients and hospital value chain (Witt 2006).

Tools Used for Data Analysis

Source: Taner et al. 2007.

Tools used in process analysis are the following: fishbone diagram, check sheet, Pareto chart, flowchart, run chart (Figures 3-5).

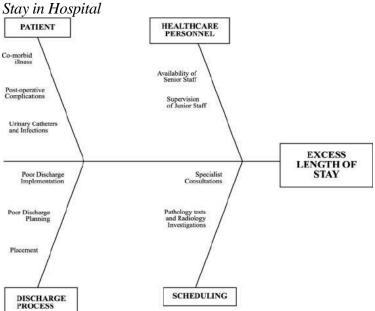
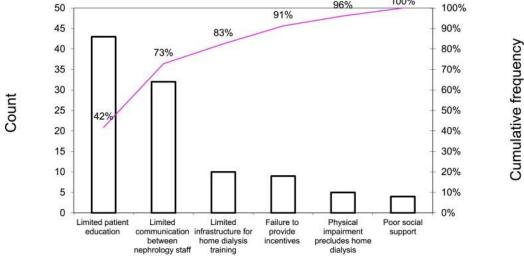


Figure 3. Example of Fishbone Diagram for Possible Causes of Excess Length

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Figure 4. Histogram Represents Visual Representation of Data Divided in Classes

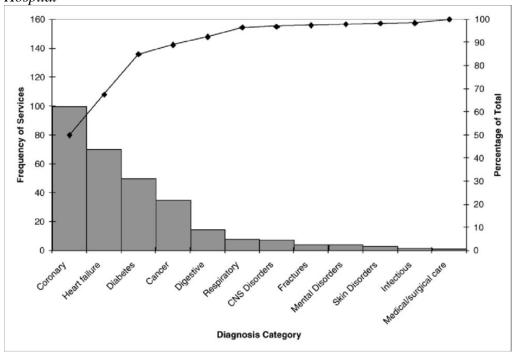
50 91% 100% 100%



Cause of the Quality of Care Problem

Source: Taner et al. 2007.

Figure 5. Pareto Chart Illustrating Frequency of Health Services Utilization in Hospital

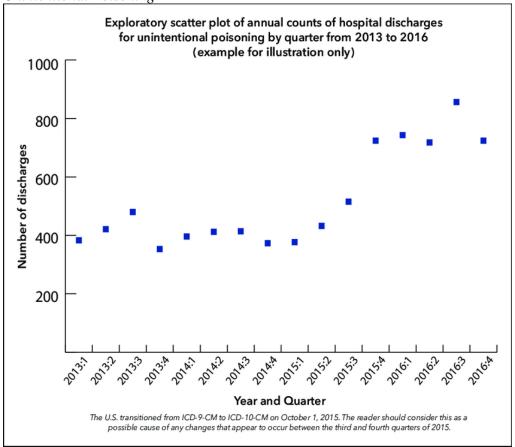


Source: Harel et al. 2016.

Scatter Plot

Scatter plot is a two dimensional data visualization diagram that shows data distribution between two numerical quantitative variables (Figure 6). Two variables can be in three different relationships: linear, nonlinear and curved relationship (Friendly and Denis 2005).

Figure 6. Example of Scatter Plot of Annual Counts of Hospital Discharges for Unintentional Poisoning

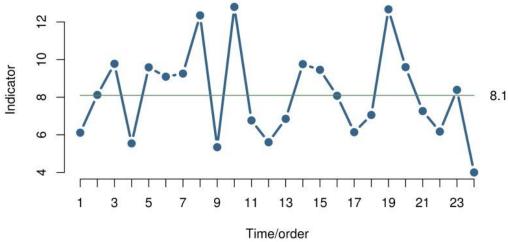


Source: Safe States 2016.

Run Chart

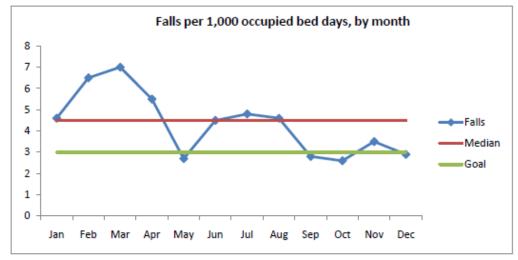
Run chart is a graph that shows the data recorded over time. Using the acquired data, the line graph can show different trends through time (Figure 7). It is important because it can show if trends are out of or within given limits (Figure 8).

Figure 7. Run Chart



Source: Anhoj and Olesen 2014.

Figure 8. Example of Run Chart Showing Falls per 1000 Occupied Bed Days



Source: Agency for Healthcare Research and Quality 2013.

Difference between LEAN and Parkinson Law in Hospital

Parkinson law states that administrative units always have tendency to increase the number of their employees. Parkinson law can give an explanation why there has been an increase in hierarchical vertical structure of hospitals throughout the history. Hierarchical structure can be unnecessarily increased by promotion of employees, which eventually urges the employment of new workers. If a hospital has several consultants and subordinates, and all of them feel they work to the limit of their capacity, they can reach an agreement with director of hospital to promote the existing consultants to hospital directors, and senior registrars to consultants. New employees will be needed soon. Lean philosophy does not give support to this level of thinking simply by focusing on system efficiency (The Economist 1955).

Results

Example of LEAN Hospital

St. Francis Health System is a hospital system established in Indianapolis, Indiana, divided in thirteen hospitals located all over Indiana and north-eastern Illinois that has used Lean philosophy, Kaizen and continuous improvement methodologies to improve its results. In the year 2012, they were granted the clinical excellence award for being in the top 5% in the nation overall clinical quality. In the year 2007, four thousand individuals in the hospitals generated over 17,000 ideas with estimated dollar savings over 4,700,000 million dollars. The crucial factor in being able to obtain such a result is the implementation of LEAN and Kaizen culture in organisations. Kaizen gives employees the chance to participate and contribute to hospital operations. If the employees are given the opportunity to present their ideas and if their opinion is appreciated, their performance is higher, as well as job satisfaction.

The next example presents a summary of Lean methods used by St. Francis Health System. Paula's husband had open-heart surgery in Franciscan St. Francis Health Centre. Paula is a nurse, and she and her husband found it hard to communicate in the recovery room after he woke up. Paula communicated with her husband by observing his eyebrows and squinting. Her husband could not use his hands as he wanted to. Paula started panicking when she found out that her husband could not use his hands properly. Both of them were deeply distressed until the anaesthetics wore off and they could speak normally again. After realizing that her husband's hands were numb, she later noticed the same symptoms with other patients being operated by cardiac surgeons. She found out the surgeons leaned on patient's hands reducing thus blood supply and causing numbness. She found sled positioners that could be used to reduce pressure on patient's arm. This is an example of how the process can be improved by an employee. Her idea added value to all patients who were taken care of after her husband. The ultrasound technician in Franciscan St. Francis Health Centre noticed that paediatric patients felt uncomfortable when she pressed ultrasound probe to their skin. Children would not stand still during the examination. She had an idea how to distract her patients. She told parents to bring small bottles of bubbles and asked parents to blow them over the child to entertain them. Children were distracted and technicians were better and faster in capturing quality images for radiologist making the job easier for technicians, radiologists, parents and patients. This small improvement adds a lot of value to increasing the patient volume. Another example of small improvement in Franciscan St. Francis Health Center is the replacement of manual paper towel dispensers with hands-free automatic paper towel dispensers in paediatric departments. Once the automated dispensers were mounted in rooms, nurses noticed that more babies made grinding noises and started crying when the automated dispenser was activated. The noise of a dispenser produced reduced resting times for babies. Nurses suggested going back to manual dispensers. After measuring the loudness of automatic dispensers, it was found out that the noise was 50 decibels. The staff concluded they should bring back the manual paper dispensers. After returning to manual dispensers, the babies were less distressed, as well as the nurses, which all added value to young patients as well as to nurses. Another example of Kaizen is when an X-ray technician created a shield for patients by moving a shielding device from X-rays device to i.v. pole to support a shield. The i.v. pole could be raised and lowered according to the height of a patient. The technicians no longer needed to wrap up the patients with Velcro straps. This idea provided for technicians a considerable amount of saved time (Graban and Swartz 2014).

Hospital Organisational Structure

Hospitals usually have functional organisational structure. Functional organisational structure groups the workers based on specific skill and knowledge (Figure 9). Employees are supervised by their superior in the same field (Fiorio et al. 2018).

An example in hospitals would be a resident and chief in cardiac surgery. Employees are classified into specific areas to utilize their skills and help the organisation in achieving its goal. Organisational chart is divided into functional departments like board of directors, financial sector, surgery, internal medicine, pharmacy. Advantages of functional organizational structures are related to grouping the employees having the same skills, to the development of specific skills, fixed and defined responsibilities; one instead of more. There is no job duplication, employee careers have a clear growth path. Disadvantages of functional organisational structure are: employees feel bored at work because their job becomes monotonous, conflicts arise if appraisal system is not adequately managed, short-sightedness of functional managers and care just for their department, one-dimensional thinking of employees just about their department, functional manager makes decisions autocratically. The classical organizational structure in hospitals is based on board of directors, clinic managers, department chiefs, doctors, nurses, administrative departments and human resource management. Functional organizational structure is usually found in organizations with traditional organizational structures. Functional organizational structures can have different process efficacy due to different levels of verticality or horizontality. In Eastern Europe, hospitals have more vertical organizational structure, while in western societies like the United States of America they have less vertical structures. Modern organisation theoreticians propose horizontal and less vertical structures instead of vertical organizational structures (Baligh 2006).

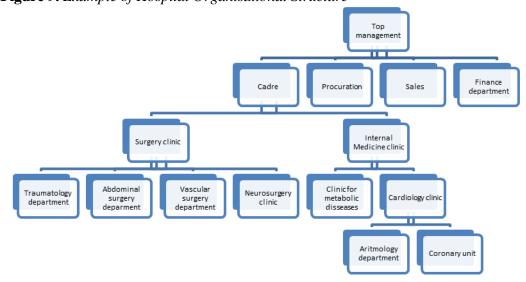


Figure 9. Example of Hospital Organisational Structure

Hospitals usually have 5-7 vertical levels. LEAN philosophy integrates the needed organisational structures into its business process to produce best possible output.

When LEAN Philosophy cannot be applied

Lean philosophy cannot be applied universally. When there is no even flow of demand throughout a year, it becomes challenging to apply LEAN philosophy. This is especially true with seasonal demand. It also does not work if an organisation produces very different products, provides very different services, because kanbans will be colliding. It also cannot be applied to specific demand requests, because the service of production is not standardised in organisations. Lean philosophy is best used in repetitive systems without mass production of many different models.

Discussion

The purpose of this paper is to find best ways for hospital quality management. Since the beginning of 20 the century and the development of scientific management, there were great leaps in management considerations. Firstly, the focus was mostly on organisation and efficacy, and employees were seen just as labourers. A different approach has been developed over time. Managers started to see the value of different employees and their connection with competitive advantage of company and its success. After prioritization of organizational structure design and human resource management, quality management was accepted. Quality management like LEAN management added great value to production companies that started implementing it (Maijala et al. 2018). Since then, lean philosophy has been implemented in service industry. Hospitals are very complex institutions with large requirements for highly educated employees and

with great need for capitalization because of great demand for different medical devices and drugs. We have shown that LEAN management can reduce costs by focusing on hospital business processes and implementing new ideas from LEAN philosophy. By developing the quality of management, more value can be added to patients and medical staff. The purpose of LEAN philosophy is to give the employees at lower levels of organisational structure more decision making power, and the power to develop and apply new ideas that make organisation more efficient.

Conclusion

LEAN philosophy is a philosophy invented by Toyota company. It is a management tool used to reduce waste and add value to process and final output. In recent years more healthcare institutions, especially private hospitals have been implementing LEAN philosophy. By analyzing and creating a business process, managers can establish supervision in each part of business process. Business process consists of a value chain which has many smaller components. Value chain is analyzed. After performing the analysis, managers can, together with employees, find parts that do not function optimally. By focusing on these parts with decentralized decision making, the parts of chain of value can be improved. By improving them, patient value is created and transferred to patients. Time of waiting is reduced, the flow of patients and business processes is more effective, and the satisfaction of employees, as well as the satisfaction of patients, is significantly improved. There is a growing number of hospitals that are using LEAN philosophy, and significant cost reduction and patient satisfaction has been documented. LEAN philosophy can and will be implemented in a growing number of hospitals facing increasing costs in ever more competitive environment.

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The Manual Dexterity of Nurses and Factors that Affect It

By Yıldız Denat* & Hürmüs Kuzgun[±]

The purpose of this descriptive and analytical study was to define the manual dexterity of nurses and factors that affect it. The sample for this descriptive and analytical study consisted of 96 nurses who worked in an education and research hospital in the south region of Turkey and were willing to participate in the study. The data collection tools were a survey and the Purdue pegboard test. The results of this study indicated that gender and lack of hobby affect hands dexterity and that some types of manual dexterity decreased as age, years of working as a nurse, and BMI increased. The results of this study may constitute a normative data for future studies which would be conducted on this issue.

Keywords: Manual dexterity, nursing, Purdue pegboard test

Introduction

Nursing is a branch of arts and sciences (Denat and Eşer 2006) that require the understanding and application of specialized knowledge and skills to provide comprehensive patient care. Professional nursing practices are founded upon cultural and professional knowledge, clinical and conceptual skill, and the value system of the individual (Denat and Eşer 2006).

Nurses go through an education system that covers cognitive, sensory and psychomotor learning fields during their nursing education (Morgan 2006, Goldsmith et al. 2006, Mete and Uysal 2009). Psychomotor learning has an important place at the stage of implementation of what has been learned during the education process. Psychomotor field comprises skills, movement, muscle movement, and hand manipulation (National Association of EMS Educators 2002, Denat and Eser 2006). Skill is the ability to perform a task or a group of tasks, applications that require tools and equipment, by using motor functions, at a specially defined level of competence (Mamakli 2010). Skills primarily include movement-based activities, psychomotor skills can be grouped as skills that require attention, manipulative skills, and skills that require excessive movement. Skills that need attention include attention-based sensitive functions such as IV injection. Manipulative skills are the functions that require eye and arm to work together, as well as manual dexterity (for example physical examination, aspiration, dressing, etc.). As for the skills that require excessive movement include the functions that require movement of large muscle groups (Moore 2001, Denat and Eşer 2006). In many nursing practices, it is important to acquire all of these three groups of psychomotor skills.

^{*}Associate Professor, Nursing Faculty, Aydın Adnan Menderes University, Turkey.

[†]Research Assistant, Nursing Department, Faculty of Health Sciences, Nevşehir Hacı Bektaş Veli University, Turkey.

In the literature, there are studies on manual dexterity and effective factors in many professions that require hand and eye coordination. When the studies aiming to determine the effect of demographic properties on manual dexterity are examined, Yücel and Bumin (2010) found that hand function decreased significantly with age, and women's manual dexterity was better than men. In another study where the grip strength and anthropometric measurement results were compared according to gender, the difference was found to be significant in favor of men, whereas female students were found to be more successful than the boys in the manual dexterity test (Yücel and Kayıhan 2008). In the study by Çalışkan and Gökbel (1997) which investigated the relations between hand preference, manual dexterity and grip strength in both sexes, left-hand dexterity was observed to decrease as the degree of right-handedness increased. In another study conducted by İlmezli (2011) on manual dexterity, the manual dexterity test performed with the dominant hand was found to be completed in a shorter time than the non-dominant hand, and the manual dexterity of the dominant hand was better than the non-dominant hand. In the study conducted by Genç et al. (2002) which compared the hand functions of musicians and non-musicians, nonmusicians were found to be able to perform manual dexterity tests in a shorter duration than musicians.

In studies conducted in the field of dentistry, Weinstein et al. (1979) determined that general practitioner dentists who completed the skill test in a long time received high scores in restorative quality; Orbak et al. (2002) found that in terms of coordination between two hands and dexterity, left-handed dentists were superior to those who were right-handed, Ojimba et al. (2004) determined the fact that dentistry students' way of sitting and holding tools had a facilitating effect on gaining manual dexterity. Gansky et al. (2004) found that through a manual dexterity test applied to dentistry students, it would not be able to predict the clinical success grade. Besides, Giuliani et al. (2007) found that basic manual dexterity is not required for the selection of dentistry students, and the manual dexterity of students who carry on with the education are significantly improved.

There are also studies in the literature that examine the effect of glove type and thickness on dexterity. As a result of their study, Sawyer and Bennett (2006) found that using nitrile type gloves in jobs requiring fine skills may hinder the skill. Drabek et al. (2010) stated that health workers should wear gloves of appropriate size when performing manual work. Fry et al. (2010) stated that the use of double gloves does not have a significant effect on dexterity and touch sensitivity when compared to cases without gloves or with single gloves; Bensel (1993) stated that preferring the finest glove is the most effective selection for hand performance, as well as chemical protection. Neiburger (1992) also stated that the use of gloves in dental operations significantly reduced dexterity.

In Turkey, relevant studies in the nursing field that the researchers have reached are that of Bakır et al. (2013) which examines the relationship between nursing students' dexterity and nursing course mid-year success grades, as well as the grades received at the entrance exam of nursing school, and that of Kuzgun and Denat (2020) which aims to determine manual dexterity of nursing students and effective factors. As a result of the study by Bakır et al. (2013), manual

dexterity was found to display no parallels with the knowledge level. Kuzgun and Denat (2020) determined that the manual dexterity of senior nursing students was relatively high, and that girls, those with a normal body structure, and those who chose the profession voluntarily had better manual dexterity.

As is seen, the studies in the field of manual dexterity were about the effect of demographic properties and wearing gloves on manual dexterity, and they mostly focused on dentistry and dentistry students. In the field of nursing, the researchers could not reach a sufficient amount of studies. However, in professions as nursing where hand manipulation is used, manual dexterity and its level of development are important. The purpose of this study was to define the manual dexterity of nurses and factors that affect it.

Methodology

Design and Sample of the Research

The purpose of this descriptive and analytical study was to define the manual dexterity of nurses and factors that affect it.

In according to Republic of Turkey Ministry of Health Health Statistics Yearbook 2018 data, the total number of nurses in turkey is 190.499 and the number of nurses working in University teaching and research hospital is 29.263 (Başara et al. 2019). The population of the research consisted of 400 nurses working in a training and research hospital in the southern region of Turkey. This number constitutes 1.4% of the general population.

In this research, a sample size of 95% reliability level was estimated using the "G. Power-3.1.9.2" computer program. Based on the study by Kuzgun and Denat (2020), the effect size was calculated as 0.53, α =0.05, and the total sample size 90 to attain a power level of 0.80. Taking into account the sample losses, the study was completed with 96 nurses volunteering to participate in the study.

Data Collection Tools

In the research, the data collection tools were through PurduePegboard Test and a survey form created by scanning the literature (Demirel 2005, Giuliani et al. 2007, Yücel and Kayıhan 2008, Sezer et al. 2009, Bakır et al. 2013).

The survey consisted of two parts; the first part contains introductory information about the participant and questions concerning the factors which are thought to affect manual dexterity. The second part includes the Purdue Pegboard Test results. Introductory information and questions concerning the factors that are thought to affect manual dexterity include age, gender, educational status, the clinic worked in, working experience, dominant hand, the status of suffering from a chronic disease, the status of medication use, existence of a physical case that cause a finger loss or holding and gripping problem, having a hobby, doing sports, the status of voluntarily choosing the profession, and satisfaction with the profession.

Purdue Pegboard Test was developed by Tiffin and Asher (1948) for measuring manual dexterity. Validity and reliability studies concerning the test have been completed (Tiffin and Asher 1948). The test comprises five subtests: (a) right hand; (b) left hand; (c) both hands; (d) right + left + both hands; (e) assembly. The test board consists of a board with four cups across the top row and two vertical rows comprising 25 small holes towards the center. Each of the two outside cups contains 25 pins; the cup at the immediate left of the center contains 40 washers and the cup at the right of the center contains 20 collars.

Each phase is repeated three times. The mean scores for each subtest consist of the average scores of these 3 applications (Lafayette Instrument 2015).

Data Collection

The study was completed with 96 nurses volunteering to participate in the study. Before the data collection process, nurses were informed about the aim of the study. The survey was conducted through a face-to-face interview with 96 nurses.

Purdue Pegboard Test is based upon the principle of applying manual skills at a certain time interval. It measures two kinds of skills. The first is the gross motions of the whole hand, fingers, and arms; the other one is the fine manual dexterity which is required in the assembly tasks. The application comprises 4 stages: right hand, left hand, both hands, and the assembly. In general, at the end of the application 4 distinct scores are obtained: right-hand score, left-hand score, both hands score, right hand + left hand + both hands score, and assembly score. The performance of the right-hand subtest requires participants to place as many pins as possible within 30 seconds using their right hands. The left-hand phase is also the same. The score of each of these subtests is the total number of pins placed by each hand within the given time. Both hands subtest is a bimanual test where the participants use both hands simultaneously to place as many pins as possible in both rows in 30 seconds. The score of this subtest is the total number of pairs of pins placed in 30 seconds. For the right hand+left hand+both hands score there is no separate test, it is the arithmetical sum of the scores of the right hand, left hand and both hands subtests. The assembly phase comprises the placement of a nail, washer, ring, and a washer again into a gap. The score of this subtest is the total number of pins, washers, and rings placed using both hands simultaneously in 60 seconds. The data were collected by only one researcher. Data collection took about 20 minutes for each participant

Statistics

The data were assessed using SPSS version 18.0. Since the data showed normal distribution, the T-test for independent groups, One-Way Analysis of Variance (ANOVA) and Pearson Correlation Analysis were also used for data analysis. For the results, we accepted p < 0.05 as statistically significant. *Ethics Approval*

To conduct the study, we obtained approval from the Adnan Menderes University Faculty of Medicine Non-interventional Clinical Research Ethical Committee (Approval no: 53043469-050.04.04) and the informed consent forms were signed earlier by individuals to participate in the research.

Results

The mean age of the nurses participating in the study was 27.48 ± 4.52 ; 67.7% of the nurses were female, 84.4% had bachelor's degree, 38.5% were working in Surgical Service, and had an average working experience of 60.29 ± 47.95 months (approximately 5 years); 88.5% of the nurses used their right hand predominantly, 71.9% of them did not have a chronic disease and 89.6% of them did not use medication regularly. None of the nurses had a physical problem that would affect their ability to hold and grasp such as finger loss, injury, etc.; 64.6% did not have any hobbies and 71.9% did not do sports. 46.9% of the nurses stated that they preferred the nursing profession voluntarily and 53.1% stated that they were satisfied with their profession (Table 1).

Table 1. Comparison of the Characteristics of Nurses with their Purdue Pegboard Test Scores

						Phase of	of test				
		Domin han		Non-don han		Both ha	ands	Right ha left har both ha	ıd +	Assem	bly
Characteristics	n	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Gender											
Female	65	19.02	1.40	17.38	1.40	14.89	1.25	51.32	3.57	42.37	6.59
Male	31	18.39	1.20	16.64	1.34	14.10	1.26	49.14	3.38	38.94	7.12
t/p		t=2.15, p	p=0.03	t=2.44, p	=0.01	t=2.90, p	=0.00	t=2.83, p	=0.00	t=2.32, p	=0.02
Educational Statu	S										
Vocational High School of Health	15	18.53	1.18	17.08	1.59	14.53	1.03	50.26	3.47	39.77	5.08
Bachelor Education	81	18.87	1.40	17.15	1.39	14.66	1.35	50.68	3.68	41.53	7.20
t/p		t=-0.18, p=0.37		t=-0.17, p=0.86		=0.71	t=-0.40, p=0.68		t=-0.90, p=0.36		
Currently Workin	g Clin	ic									
Intensive Care	33	18.69	1.28	17:05	1.45	14.71	1.39	50.47	3.62	40.95	6.31
Internal Clinics	37	18.81	1.44	17.21	1.30	14.54	1.29	50.61	3.61	41.37	7.77
Surgical Clinics	26	18.99	1.40	17.15	1.57	14.68	1.24	50.81	3.83	41.49	6.60
F/p		F=0.35,	p=0.70	F=0.10, p	p=0.90	F=0.16, p	=0.84	F=0.06, p	=0.93	F=0.05, p	=0.95
Choosing the nurs	ing pr	ofession w	illingly								
Yes	45	18.52	1.39	16.98	1.36	14.47	1.22	49.99	3.44	39.95	6.36
No	26	18.86	1.29	16.86	1.43	14.52	1.31	50.29	3.55	41.80	7.30
Partially	25	19.30	1.32	17.71	1.40	15.06	1.38	52.07	3.80	43.06	7.27
F/p		F=2.67,	p=0.07	F=2.92, 1	=2.92, p=0.05 F=1.80, p=2.87 F=2.87, p=0.06 F=		F=1.76, p=0.17				
Being satisfied wit	h the 1	nursing pr	ofession					_			
Yes	51	18.87	1.36	17.32	1.21	14.74	1.23	50.95	3.27	41.08	7.13
No	16	18.95	1.14	17.33	1.40	14.72	1.63	51.03	3.85	42.26	6.68
Partially	29	18.66	1.52	16.71	1.70	14.42	1.24	49.80	4.11	41.02	6.86
F/p		F=0.30,	p=0.73	F=1.96, p	p=0.14	F=0.58, p	=0.55	F=1.04, p	=0.35	F=0.19, p	=0.82
Having a hobby											
Yeah	34	18.52	1.17	16.71	1.33	14.36	1.18	49.63	3.27	39.26	7.48
No	62	18.98	1.45	17.37	1.42	17.79	1.34	51.15	3.74	42.35	6.39
t/p		t=-1.58,	p=0.11	t=-2.24, 1	p=0.02	t=-1.53, p	=0.12	t=-1.99, p	=0.04	t=-2.12, p	=0.03
Doing Sports						· · · · · · · ·					
Yes	27	18.81	1.39	17.18	1.59	14.60	1.05	50.57	3.65	39.99	7.36
					•						

ŀ	t/n	- 0,	t=-0.04, 1		t=0.16, p		t=-0.18, p		t=-0.06, p		t=-1.12, p	
	No	69	18.82	1.37	17.12	1.36	14.65	1.39	50.63	3.66	41.76	6.72

Nurses were determined to work for an average of 7.12 ± 3.12 hours a day when the Purdue Pegboard Test was applied. The mean dexterity scores of the nurses were 18.82 ± 1.37 for the dominant hand, 17.14 ± 1.42 for the non-dominant hand, 14.64 ± 1.30 for both hands, 50.61 ± 3.64 for right + left + both hands, and 41.26 ± 6.92 for assembly skill.

According to the results of the study, all kinds of mean dexterity scores of female participants were found to be significantly higher than the male, and those who did not have a hobby were found to have higher non-dominant hand, right + left + both hands, and assembly mean scores (p <0.05) (Table 2).

Table 2. The Relationship between the Characteristics of Nurses and Purdue Pegboard Mean Scores

	Domi ha	inant nd	dom	on- inant and	Both 1	hands	Right l left ha both l	and +	Assei	nbly
	r	р	r	p	r	p	r	p	r	p
Age	-0.18	0.07	-0.15	0.13	-0.22	0.02	-0.21	0.03	-0.24	0.01
Working year as a nurse	-0.21	0.03	-0.17	0.09	-0.23	0.01	-0.23	0.02	-0.31	0.00
BMI	-0.34	0.00	-0.16	0.11	-0.23	0.02	-0.28	0.00	-0.31	0.00
Working duration when the test was applied	-0.14	0.16	-0.10	0.29	-0.17	0.08	-0.15	0.12	-0.15	0.14

A negative correlation was found between the dominant hand mean scores and working duration as a nurse (r = -0.21), as well as BMI (r = -0.35). No significant correlation was found between the non-dominant hand dexterity, age, working duration as a nurse, and BMI. A negative correlation was found between both hands dexterity mean scores, age (r = -0.22), working duration as a nurse (r = -0.24), and BMI (r = -0.24). A negative correlation was found between the mean scores of right + left + both hands dexterity, age (r = -0.22), working duration as a nurse (r = -0.24), and BMI (r = -0.28). A negative correlation was found between the mean scores of assembly skill, age (r = -0.24), working duration as a nurse (r = -0.31), and BMI (r = -0.31).

Discussion

In the literature, it is emphasized that the genes and genetic structure of the individual play a role in the development and differentiation of the hand. Also the external factors faced by the hand in the development process and the work or the occupation that the individual deals with affect the hand structure (Demirel 2005). In this study, which was carried out to determine the manual dexterity of the nurses and effective factors, the mean manual dexterity scores of nurses were

found 18.82 ± 1.37 for the dominant hand, 17.14 ± 1.42 for the non-dominant hand, 14.64 ± 1.30 for both hands, 50.61 ± 3.64 for right + left + both hands, and 41.26 ± 6.92 for assembly skill. In a study conducted to evaluate hand function according to professions, differences were found between office workers and industrial workers in all of the gripping, dexterity and functionality tests; industrial workers were found to have greater hand strength, and lower manual dexterity, while office workers lower hand strength, and greater manual dexterity (Doğan 2012). Besides, in a study by Kuzgun and Denat (2020) which examines the manual dexterity of nursing students, mean dominant hand dexterity scores of the students were found to be 19.16 ± 1.36 , mean non-dominant hand dexterity scores 17.04 ± 1.43 , mean both hands dexterity scores 14.58 ± 1.35 , mean right hand + left hand + both hands dexterity scores 50.70 ± 4.20 , and mean assembly skill scores 38.55 ± 6.02 . For every stage of the test, the findings of this study are similar to that of Kuzgun and Denat (2020).

When the effect of age on manual dexterity was analyzed, hand functions were found to decrease significantly with age (Yücel and Bumin 2010), and as a result of this study a significant negative relation was found between age, both hands, right hand + left hand + both hands, and assembly mean scores. According to the result of the study, as the age increases the manual dexterity of individuals can be said to decrease. In the study, all kinds of manual dexterity mean scores of female participants were found to be significantly higher than that of the male; many other studies also determined that women's manual dexterity is better than that of men (Dokuztuğ et al. 1991, Agnew et al. 1988, Çakıt 2008, Yücel and Bumin 2010, Yücel and Kayıhan 2008, Kuzgun and Denat 2020).

When the literature was examined, manual dexterity was observed to be associated with many factors such as hand anthropometry, hand preference, gender, and demographic properties; there was not a sufficient amount of studies on hobby/pursuit factor, a limited number of studies on sports factor was encountered by the researchers as well. Hobby/pursuit means a work, activity or occupation that someone does voluntarily and with pleasure. It is an activity that is repeated at different time intervals depending on the will of the individual, and repetitive motor activities are well-known to form the basis for motor learning (Higgins et al. 2005, Beydoğan 2008). For this reason, in our study, the hobbies/pursuits were examined which the nurses were interested in and which are thought likely to improve their manual dexterity. As a result of the study, those who do not have a hobby were found to have higher dominant hand, right + left + both hands and assembly mean scores (p <0.05), and doing sports was found not to cause any change in manual dexterity. When similar studies are examined, considering the relationship between sports and manual dexterity, Soyupek et al. (2006) found that aerobic exercise had a positive effect on dexterity, while Gündoğan et al. (2009) determined that short-term motor activity positively affected the pace of manual dexterity. In another study conducted by Ölçücü et al. (2010), tennis training was found to produce important developments in nondominant hand coordination. As for the studies comparing music and manual dexterity, Wagner (1988) found that pianists had higher manual mobility compared

¹http://www.tdk.gov.tr.

to those who do not actively engage in music, Genç et al. (2002) found that non-musicians managed to perform manual dexterity tests in a shorter duration than musicians. The literature shows that sports activities and musical instrument playing are the most examined factors regarding their relationship with manual dexterity. The results of this study displayed exactly the opposite effect. Most of the nurses participating in the study are not interested in any hobby or sports activities, while those who are interested in such activities focus rather on applications that require gross motor activities.

When the effect of years working as a nurse on manual dexterity was examined, a negative relationship was found between working years as a nurse, dominant hand, both hands, right hand + left hand + both hands, and assembly mean scores. In the literature, there were not found any studies examining the effects of working duration in different occupations on manual dexterity, whereas in the studies conducted with nursing and dentistry students there are findings showing that as the education progresses the manual dexterity of students develops (Bakır et al. 2013, Kuzgun and Denat 2020, Giuliani et al. 2007). In the training processes of practical occupations, the manual dexterity of students improves because of a certain degree of discipline and repeated applications that the training process entails, while in the professional practice no short-term changes are observed in manual dexterity which is thought to arise from a decrease in the repetitive improving activities. Indeed, the nurses who participated in the study had approximately 5-years of working. This fact, limits arriving at a general judgment on the effect of working duration on manual dexterity. Conducting and evaluating similar studies with nurses who have a longer-term working experience could be recommended.

In the study, a significant negative relationship was found between the BMI of the nurses and their dominant hand, both hands, right + left + both hands, and assembly scores. In the study by Kuzgun and Denat (2020), nursing students with a normal body type (18.5–24.99 kg/m²) were determined to have greater assembly mean scores than the ones with a pre-obese body type (>25.00 kg/m²). In their study, D'Hondt et al. (2009) found that obese students' general motor skills (including manual dexterity) were lower than that of normal weight and pre-obese students. This study supports other research results in this respect, showing that manual dexterity decreases as the BMI increases.

Educational status, the clinic worked in, the status of voluntarily choosing the profession, the satisfaction with the occupation, and the working year at the time of the application of the test were determined not to cause any significant change in the manual dexterity of nurses. In the literature, no other study was encountered which investigates the relationship between willingly choosing the profession and manual dexterity. However, psychomotor skills are stated to require not only the use of muscles in a coordinated way but also the verbal knowledge about the skill, strategy, as well as the enjoyment during the application of the skill (Senemoğlu 2011). In the study conducted with the nursing students by Kuzgun and Denat (2020), the students who had voluntarily chosen the profession had significantly higher dominant hand scores than those who had not. The results of this study do not support the literature. This is thought to be due to the fact that the nurses in the

population were young and had an average of 5-year working experience, and that most of the nurses had chosen the profession voluntarily or partially voluntarily, and were satisfied with the profession.

Conclusion

As the conclusion of the study, gender and not having a hobby were found to affect the manual dexterity; certain kinds of manual dexterity were determined to decrease as the age, years of working as a nurse, and BMI increase. According to the results of the study, the assignment of female, young nurses with normal (or below) body mass index could be recommended in jobs that require manual dexterity more. The results of this study might constitute normative data for future studies on the subject. Besides, repeating the study with nurses having longer-term work experience and working in different institutions could also be recommended.

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mRNA Expressions of Specific Gamma-Glutamyl Transferases in Molecular Subtypes of Breast Cancer

By Dilek Gelen-Güngör*, Ece Miser-Salihoglu[±], Semra Demokan[‡], Karanlik Hasan[‡] & Sevgi Yardim-Akaydin •

An increased risk of breast cancer has been reported in individuals with elevated levels of gamma-glutamyl transferase (GGT). GGT1 was the only enzyme used for diagnosis in clinic and human genome contains additional related genes or sequences besides GGT1. From the perspective of amino acid sequences, genes showing substantial similarity (GGT5, GGT6, and GGT7) to GGT1 have been identified. The aim of this study was to investigate the mRNA expressions of GGT1, GGT5, GGT6, and GGT7 in 58 breast cancer patients' tissue samples by qRT-PCR method. In total, mRNA expressions of GGT5 and GGT7 increased and GGT6 decreased in tumor tissues than those in normal tissues of the same patients (p<0.145, p<0.003 and p<0.05, respectively). Among molecular subtypes, GGT7 expressions were significantly higher in tumor tissues than those in normal tissues of the patients in Luminal A group (p<0.009). Over-expression of GGT7 was observed in almost half of the patients. The research showed mRNA expressions of GGT1, GGT5, GGT6, and GGT7 in breast cancer. Among the four genes, we obtained surprising results for GGT7 and we believe that the activity of this gene should be examined in breast cancer.

Keywords: GGT1, GGT5, GGT6, GGT7, breast cancer, mRNA expressions

Introduction

Among the most common cancers in women, breast cancer is seen in one out of every four females. A total of 17,571 Turkish women with breast cancer, which is the first-line cancer type in women all around the world, was diagnosed in 2013. Breast cancer incidence in Turkish women was observed as 45% between 50–69 years of age and 40% between 25–49 years of age (Türkyilmaz et al. 2018).

Breast carcinomas are highly heterogeneous tumors with clinical signs/symptoms/treatment responses as well as biological behaviors. According to recent research, immunophenotypic and molecular classification have been shown to be much more prognostic and predictive than classification based on basic clinicopathological parameters such as morphology, tumor histological subtype, and histologic grade applied for many years (Banerji et al. 2012, Carey et al. 2006, Rouzier et al. 2005, Tran and Bedard 2011).

^{*}Research Assistant, Gazi University, Turkey.

^{*}Research Assistant, Gazi University, Turkey.

[‡]Professor, Istanbul University, Turkey.

⁺Professor, Istanbul University, Turkey.

Professor, Gazi University, Turkey.

The first molecular classification of breast carcinomas was performed by Perou et al. by using DNA microarray (microarray) method in 2000 (Perou et al. 2000). According to this classification, breast carcinomas are divided into 4 subtypes; i. Luminal, ii. HER2 (+), iii. Basal-like, and iv. Normal breast-like. In the light of advanced molecular knowledge up to date, breast carcinomas are divided into 5 subgroups (Luminal A, Luminal B, HER (+), Luminal B-HER (+), triple negative) based on the levels of hormones (estrogen, ER and progesterone, PR) and HER2 expression. In recent years, the Ki-67 proliferation index has also been added to this classification, especially in the clinical-oncological predictive direction (Carey et al. 2006, Tran and Bedard 2011, Cheang et al. 2009, Dent et al. 2007, Yang et al. 2007)

Gamma-glutamyl transferase (5-L-glutamyl-peptide: amino acid 5-glutamyl transferase; GGT; EC 2.3.2.2) is an enzyme with ecto-activity located on the outer surface of plasma membranes of cells. GGT is a dimeric glycoprotein composed of a heavy and light subunit bound to noncovalent bonds and is processed from a single chain precursor by an autocatalytic cleavage in prokaryotes and eukaryotes (MyBioSource 2006, InterPro 2017, Fornaciari et al. 2014). The enzyme has an auto-cleavage function and this function is linked to the nucleophilic threonine (Thr 381) in the peptide sequence (Brenda 2019). GGT is found in the structure of membranes of almost all cells, mainly in epithelial tissues with secretory or absorptive functions. While the enzyme is expressed by the cells of many organs, the highest GGT activity is found in the kidney, duodenum, small intestine, and bile duct cells. However, plasma GGT is thought to be derived from the liver (Fornaciari et al. 2014). It has critical functions in the glutathione metabolism and the conversion of Leukotriene C4 (LTC4) to Leukotriene D4 (LTD4) (Hanigan 2014). The glutathione synthesized in the cell is transported extracellularly by GGT. GGT can break the glutamyl peptide bond in glutathione and other proteins and transfer glutamyl residues to an acceptance such as amino acid, peptide or water (MyBioSource 2006, InterPro 2017, Hanigan 2014).

An increased risk of breast cancer has been reported in individuals with elevated levels of GGT. In a recent study, serum GGT activity was found to be slightly higher in breast cancer patients compared to the control group (Shackshaft et al. 2017) In addition, positive associations were found between serum GGT activity and development of ER+, ER- and PR+ breast cancers compared to controls and inverse associations between GGT levels and PR- breast cancers compared to PR+. Staudigl et al. did not found any relationship between GGT enzyme activity and hormone receptor and HER2-status (Staudigl 2015). On the other hand, a positive correlation was reported between increased GGT activity and breast cancer incidence in only premenopausal women (Fentiman and Allen 2010) However, increased GGT levels were explained an independent risk-factor for breast cancer by Van Hemelrijck et al. (2011). Despite the accumulation of evidence that increased GGT levels may be a risk factor for breast cancer, it is not known which activity or type of GGT is responsible for this. In collaboration with the HUGO (Human Genome Organization) and Human Genome Nomenclature Committee (HGNC), possible active genes resembling GGT1, the only enzyme used for clinical diagnosis, with nucleotide and amino acid sequences have been identified (Heisterkamp et al. 2008). 13 genes of GGT family were detected when GGT associated human gene sequences were searched by using genomic and cDNA databases. A real protein entity could not be shown for other genes except for GGT1, GGT5 (formerly *GGL*, *GGTLA1/GGTrel*) and GGT7 (formerly GGTL3, GGT4). Experimentally, it has been shown that only GGT1 and GGT5 turn into a protein with enzymatic activity. GGT6 (formerly rat *ggt6* homologue) and GGT7 carries 47% and 52% amino acid sequence identity to GGT1 and GGT5, respectively, which are better characterized than other family members (Heisterkamp et al. 2008).

In studies with GGT1 and GGT5 null mutants, GGT1 has been shown to play a role mainly in glutathione metabolism (Carter et al. 1997, 1998) and GGT5 in leukotriene metabolism (Han et al. 2002). In a study on glioblastoma, the demonstration that GGT7 reduction increases the amount of cellular reactive oxygen species suggests that it may be related to GSH metabolism (Bui et al. 2015). The function of GGT6 has not yet been described.

In our previous study with a small group of various types of cancer, we achieved interesting results in GGT1, GGT5 and GGT6 mRNA expressions in breast cancer (Yardım-Akaydın et al. 2017), and our main goal in this study was to examine the expressions of the same GGT genes by including GGT7 in a larger breast cancer patient population. For this purpose, we examined the mRNA expression levels of GGT1, GGT5, GGT6 and GGT7 genes in tumor and matchednormal tissues of patients with breast cancer and the expression differences of these genes among the molecular subtypes of the breast cancer.

Materials and Methods

Fifty-eight patients, who applied to Istanbul University, Oncology Institute, Clinical Oncology Department, Oncology Surgical Unit and were diagnosed with breast cancer and had operation due to their illness, were included in the study. The patients were informed for participation in the study with approval prior to the operation date and their voluntary approvals were obtained. One cm³ size (100) mg) tissue samples (tumor and matched-normal tissues) were taken during the operation from patients. Eight healthy women who applied to Istanbul University, Oncology Institute, Clinical Oncology Department, Oncology Surgical Unit for macromastia and for breast reduction surgery and without a history of breast cancer story in family, were included as the control group. The main characteristics and laboratory results of patients were given in Table 1. While the tumor and matched-normal tissues were taken from breast cancer patients in surgery, pathological examination of the tissues were performed simultaneously and excised tissue is stored at -80°C immediately. This study was approved by the Clinical Research Ethics Committee of Istanbul, Faculty of Medicine (2016/419-106748).

Demographic Characteristics and Laboratory Tests of the Patients and Controls

Table 1. The Main Characteristics and Laboratory Results of Patients

Parameters	Patients (n=58)	Controls (n=8)
Age, mean (SD)	53.1 (12.0)	36.3 (9.6)
Menopause Status		
Premenopausal, n (%)	33 (56.9)	6 (75)
Postmenopausal, n (%)	25 (43.1)	2 (25)
Stage, n (%)		
I	5 (8.6)	-
II	23 (39.7)	-
III	30 (51.7)	-
Lymph Node Involvement, n (%)	5 (8.6)	-
Tumor Location, n (%)		-
Right side	31 (53.5)	-
Left side	26 (44.8)	-
right +left sides	1 (1.7)	-
Laboratory tests		
Estrogen Receptor, mean (SD)	43.5 (43.3)	-
Progesterone Receptor, mean (SD)	21.5 (32.8)	-
Ki67, mean (SD)	40.8 (26.2)	-

Molecular classification of the tumor tissues was performed according to the presence of estrogen/progesterone hormone receptor, Ki67, and c-erbB2 (HER2), which are given below (Table 2).

Table 2. Parameters Used in the Classification of Breast Cancer Patients

Molecular Subtype	Parameter	N
Luminal A	ER(+)/PR(+)/Ki67 less-than 25	16 (27.6)
Luminal B	ER(+)/PR(+)/Ki67 more-than 25	8 (13.8)
Luminal B-Her2	ER(+)/PR(+)/Ki67 more-than 25, c-erbB2(+3)	9 (15.5)
HER2 positive	ER(-)/PR(-)/c-erbB2(+3)	9 (15.5)
Triple negative	ER(-)/PR(-)/c-erbB2(-)	16 (27.6)

Quantitative Real-Time PCR (qRT-PCR) Analysis

To obtain RNA, all tumor and matched-normal tissues were homogenized in TRIzol Reagent (Invitrogen, Carlsbad, CA, USA). After RNA isolation, cDNA synthesis reactions were performed with SensiFAST cDNA Synthesis Kit (Bioline USA Inc., USA). Both of two methods were applied according to the manufacturer's instructions. The primer sequences used were as follows:

GGT1: Fw-5'- TGACCTTCAGGAGAACGAGA -3', Rv-5'- TCTTCTTCA TGGCTCTGCGT -3'

GGT5: Fw-5'-CTCCAAGGTCTGCTCGGAT-3', Rv-5'-GTTGTCACATTGTAGATGGTG-3'

GGT6: Fw-5'-ATTCCACGGCCCTGACATCA-3', Rv-5'-CCATCAGCATGGCAAAGTAGT-3' GGT7: Fw-5'- ACACCGACCCGGACTCCTT -3', Rv-5'-ACGGGTCTTTGCGCGTCTC-3' Internal reference, β-actin: Fw-5'-GTCTTCCCCTCCATCGTG-3' Rv-5'-AGGGTGAGGATGCCTCTCTT-3'

PCR conditions: 95°C for 2 min, 95°C for 5 sec, 65°C for 10 sec, 72°C for 20 sec, for 40 cycles. Measurements of GGTs mRNA expression levels in tumor and matched-normal tissues were carried out in parallel. qRT-PCR was done in a AriaMx Real-Time PCR System (Agilent Technologies, Santa Clara, CA, USA). The experiments were performed in triplicate. Target gene mRNA expressions were quantified and standardized according to the β -actin reference gene signal. Relative quantification values were calculated by the formula of the Pfaffl method shown below (Pfaffl 2001).

$$\mathbf{RQ} = 2^{[C}_{T}^{\text{(tumor, ref. gene)}} - C_{T}^{\text{(tumor, targ. gene)}} / 2^{[C}_{T}^{\text{(calibrator, ref. gene)}} - C_{T}^{\text{(calibrator, targ. gene)}}$$

Target mRNA expressions were calculated in tumor and matched-normal tissues (calibrator sample), compared to reference mRNA expressions on the basis of the difference between CT values of the target and reference genes (Δ CT) (as proportional).

Statistical Analysis

All data was expressed as mean (standard deviation, SD). The homogeneity of the data was evaluated with the Kolmogorov-Smirnov test. For non-homogenous (non-normal distribution) data, matched-normal tissue and tumor tissue changes of the each gene in the same patient were analyzed by Wilcoxon signed rank test. P values of less than 0.05 were regarded as statistically significant. Statistical analyzes were performed using the SPSS 22 Trial Package Program (SPSS Inc, USA).

Results

mRNA Expression Levels of GGTs

According to relative quantification values of GGTs, tumor mRNA expression greater than 1.5 fold relative to the corresponding gene expression in matched-normal tissues was considered to be an overexpression.

According to the qRT-PCR results, comparison of normal tissue and tumor tissue mRNA expression levels were presented in Table 3. The tumor tissue expression levels of GGT1 was found to be significantly higher than those of matched-normal tissues (p=0.02) in the total breast group. Among the sub-groups, mean expression levels of GGT1 was higher in matched-normal tissues than those

in tumor tissues in Luminal B-Her2 (+) group [0.39 (0.46) vs 0.08 (0.17), respectively, p=0.028]. Although GGT5 mRNA levels were generally higher in tumor tissues, no statistically significant difference was observed between matchednormal and tumor tissue expression levels (p=0.145). Mean values of GGT6 mRNA expression levels were found to be higher in matched-normal tissues than those in tumor tissues in the total breast group (p=0.045). When subgroups were evaluated, tumor tissue expression levels were higher in the Her2 (+) group (n=9), but statistical significance was borderline (p=0.069). In both of total breast and the Luminal A groups, mean GGT7 expression values were significantly higher in tumors than those in the matched-normal tissues [0.2132 (0.2500) vs 0.11349 (0.1192), respectively, p=0.003 for the total group and 0.3690 (0.3543) vs 0.2060 (0.2435), respectively, p=0.009 for Luminal A group]. Similarly, higher tumor tissue expression levels were also observed in Triple-negative (n=15) and Her2positive (n=9) groups, but statistical significance was borderline (p=0.069 and p=0.063, respectively). When the normal tissue mRNA expression of the patient and healthy controls were compared, no statistically significant difference was observed in any of the four GGT genes (p>0.05).

GGT1, GGT5 and GGT6 mRNA expressions were not observed in normal tissues of 16, 23 and 16 of 58 patients (respectively), and in tumor tissues of 16, 16 and 16 of 58 patients. All 3 genes were expressed in the tissues of 4 out of 8 healthy controls. Except for only one normal tissue of the patients, all normal and tumor tissues had GGT7 expressions. For all the patients, 25.8% (15/58) of patients for GGT1, 15.5% (9/58) of patients for GGT5, 15.5% (9/58) of patients for GGT6, and 46.6% (27/58) of patients for GGT7 showed higher mRNA expression fold changes (Threshold for fold change is greater than and equal to 1.5) (Figure1).

According to the subgroups, GGT1 overexpressions were observed as 35.7% for Luminal A, 50% for Luminal B, 22.2% for Luminal B+Her2(+), 33.3% for Her2(+), and 26.7% for Triple(-) groups (Figure 2a). GGT5 overexpressions were observed as 57.1% for Luminal A, 40.0% for Luminal B, 62.5% for Luminal B+Her2(+), 55.6% for Her2(+), and 38.5% for Triple(-) groups (Figure 2b). GGT6 overexpressions were observed as 41.6% for Luminal A, 50.0% for Luminal B, 28.6% for Luminal B+Her2(+), 33.3% for Her2(+), and 62.5% for Triple(-) groups (Figure 2c). GGT7 overexpressions were observed as 56.3% for Luminal A, 37.7% for Luminal B, 28.6% for Luminal B+Her2(+), 77.8% for Her2(+), and 56.3% for Triple(-) groups (Figure 2d).

GGT1 GGT5 GGT6 GGT7

Figure 1. Scatter Plot of GGTs' Expressions in All Breast Cancer Patients

The Y-axis indicates the fold change in gene expression, and the X-axis represents the patients. a 1.5 fold increase in gene expression in tumor tissue was considered as overexpression.

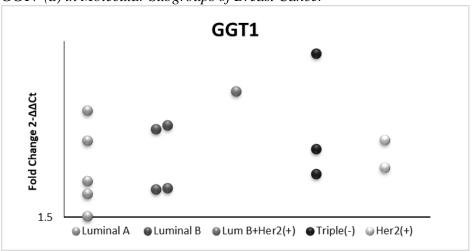
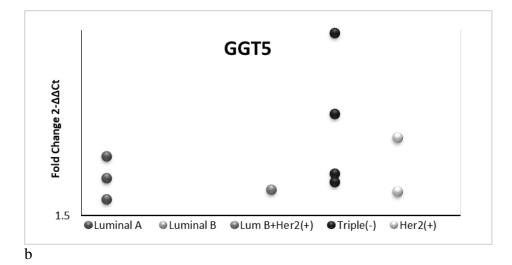


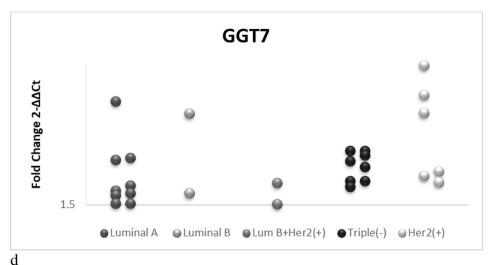
Figure 2. Scatter Plot of Expressions of GGT1 (a), GGT5 (b), GGT6 (c), and GGT7 (d) in Molecular Subgroups of Breast Cancer

a



GGT6

Luminal A Luminal B Lum B+Her2(+) Triple(-) Her2(+)



The Y-axis indicates the fold change in gene expression, and the X-axis represents the patients. A 1.5 fold increase in gene expression in tumor tissue was considered as overexpression.

Table 3. Comparison of Median (± Standard Deviation, SD) GGT5 and GGT7 Expressions in Normal and Tumor Tissues in Breast Cancer (Wilcoxon Rank-Sum Test, P-Value < 0.05)

	mRNA Expression Levels		
	Matched-Normal Tissue	P	
GGT1	0.1414 (0.2500)	0.2048 (0.9422)	0.020
GGT5	0.0187 (0.0390)	0.0328 (0.1350)	0.145
GGT6	0.1942 (0.3287)	0.1366 (0.3619)	0.045
GGT7	0.1349 (0.1872)	0.2132 (0.2500)	0.003

Discussion

In this study, we examined the expression of GGT genes in the tissues of breast cancer patients and evaluated their potential as biomarkers in detection strategies. For this purpose, we compared mRNA expression in normal and tumor tissues of the same patients.

GGT1, which has a precursor peptide sequence containing 569 amino acids, is an enzyme with important functions in extracellular glutathione metabolism, LTC4 catabolism, and glutathione homeostasis. GGT1 is the most expressed in the normal tissues of kidney, duodenum, small intestine, and prostate (Heisterkamp et al. 2008). In this study it was observed that GGT1 was significantly expressed in breast cancer when compared with the control. The expression of tumor tissue GGT1 has also been shown in various cancers such as prostate (Kawakami et al. 2017), epithelial (Lukic et al. 2016), lung (Hino et al. 2016), colorectal (Palaniappan et al. 2016), overian (Mahata 2006), liver (Pavesi et al. 1989), and breast (Banneau et al. 2010).

GGT5 is a protein that is clearly homologous to GGT1 at the amino acid level, with significant deletion due to nucleotide identity. GGT5 also had a protein with enzymatic activity (Heisterkamp et al. 2008). Previous studies using GGT1 and GGT5 null mutants showed that GGT1 is the main enzyme involved in glutathione metabolism (Carter et al. 1997, 1998), whereas GGT5 is mainly involved in LTC4 metabolism (Han et al. 2002). Studies in cDNA libraries have shown that the mRNA of GGT5 is extensively expressed in normal tissues such as adrenal glands, adipose tissue, lymph nodes, kidneys, and bile ducts (NCBI 2019a). In addition, increased expression of GGT5 has also been observed in kidney, glioma, and esophageal cancers (Heisterkamp et al. 2008). GGT6 was identified in rats by Puente and Lopez-Otin and was included in the threonine protease family (2004). The function of GGT6 as an enzyme has not yet been described and there are no studies showing its translation into a potential protein (Heisterkamp et al. 2008). In normal tissues, GGT6 expression is most abundant in the colon, kidney, duodenum, and small intestine. On the other hand, expression of GGT6 has been observed to increase in the adrenal, colorectal, and breast cancers (NCBI 2019b).

GGT7 is the nucleotide sequence encoding the peptide containing 662 amino acids (Kyoto Encyclopedia of Genes and Genomes 2019, NCBI 2018a). Although GGT7 shows significant similarity to GGT1 in terms of amino acid sequencing,

there is a significant lack of nucleotide identity, and GGT1 and GGT7 are therefore included in separate families (Heisterkamp et al. 2008). Its functions have not yet been fully elucidated and are thought to be involved in enzymatic activities regulated by leukotriene synthesis, glutathione metabolism, or glutamyl transfer. GGT7 is extensively expressed in normal tissues such as brain, thyroid, ovarian, and prostate (NCBI 2018b). However, expression of GGT7 has been observed to increase in bladder, glioma, head and neck, lung, and PNET cancers (Bui et al. 2015).

There is only one previous publication from our group, showing the expressions of GGT1, GGT5, and GGT6 mRNA in a small group of different types of cancer, including breast cancer (Yardım-Akaydın et al. 2017).

This study was designed to examine these three GGT genes, by adding GGT7, in only breast cancer patients according to molecular subtypes. Two reports have been published focusing on GGT1 expression in molecular apocrine breast cancer (MABC) subtype of breast cancer (Banneau et al. 2010, Guo et al. 2015). Furthermore, it was observed that most patients in MABC subtype, which included tumors with ER-/PR-/HER2- (triple-negative breast cancer, TNBC) and ER-/PR-/HER2+ (HER2-overexpression) (Liu et al. 2016), showed GGT1 expression, while its expression was observed in only 1.5-9.6% of non-MABC cases. Except ours, there is no published clinical study showing GGT5 and GGT6 expressions in breast cancer or any other cancer. However, in a study examining the expression of GGT7 in glioblastoma, which is an aggressive malignant tumor, it was determined that patients with high GGT7 expression had a better prognosis than patients with low expression (Bui et al. 2015). It is also reported that, GGT7 played a role in tumorigenesis with an anti-oxidative regulating effect and GGT7 reduction has been shown to increase the amount of cellular reactive oxygen species and thus induce tumor formation and growth (Bui et al. 2015). According to the results of our study, GGT1, GGT5, and GGT7 expressions increased in tumor tissue compared to matched-normal tissues, whereas GGT6 decreased. On the other hand, GGT7 overexpression was observed in most of the patients in all molecular subgroups, except for Luminal B groups.

Conclusion

GGT is an enzyme that plays important roles in both glutathione metabolism, which is associated with oxidative stress and drug resistance, and leukotriene synthesis. Therefore, it is important to determine the type of GGT responsible for the increase in GGT activity, which is considered a risk factor in breast cancer. This study showed that there were GGT1, GGT5, GGT6, and GGT7 mRNA expressions in molecular subtypes of breast cancer. According to the results, it is suggested that GGT7 may have marker potency in breast cancer, especially in the luminal A, HER2 positive, and triple negative groups. In our research laboratory, we continue our studies to examine potential functions of GGT7 gene in breast cancer.

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Practices and Determinants of Exclusive Breastfeeding among Young Mothers Attending a Secondary Health Care Facility - A Cross Sectional Study

By Hemant Kumar* & Ruchita Satish Gaonkar[±]

The benefits of exclusive breastfeeding (EBF) cannot be over emphasized, especially in a country like India, where nearly 600,000 newborns die within 28 days of their birth every year while only 54.9% infants are exclusively breast fed. Lives of 820,000 children under-five, could be saved if all children aged 0-23 months were optimally breastfed. Present study tried to assess the prevalence of EBF among study subjects and its socio-demographic determinants, in rural South India. This was a cross-sectional study that employed a structured questionnaire to collect data from 182 mothers, attending a rural hospital in South India, from April 2019 to September 2019 selected through convenience sampling. The study reveals that less than half of the respondent mothers (48.3%) practiced exclusive breastfeeding. Four socio-demographic factors were found to be significantly associated with EBF practices and these were - age of mother (p = 0.004753), gender of the infant (P < 0.000634), number of antenatal visits (p>0.01148) by respondents and caesarean Section delivery (P<0.027847). In our study, EBF practices were found to be suboptimal giving rise to a need to educate every pregnant or lactating mother during their antenatal or post-natal visits by our health care workers about EBF and its benefits.

Keywords: Exclusive breastfeeding, Complementary food, Infant feeding, Determinants, Barriers

Introduction

Breastfeeding is one of the most effective ways to ensure child health and survival (WHO 2017a). Colostrum, the yellowish, sticky breast milk produced at the end of pregnancy, is recommended by the World Health Organization (WHO) as the perfect food for the newborn, and feeding should be initiated within the first hour after birth (WHO 2020a). Breastfeeding is potentially one of the top nutrition interventions for reducing under-five mortality. Over 820,000 children's lives could be saved every year, if all children 0-23 months were optimally breastfed. Improving child development and reducing health costs through breastfeeding results in economic gains for individual families as well as at the national level (WHO and UNICEF 2003). Further, increased breastfeeding is associated with US\$302 billion annually in additional income – nearly 0.5 per cent of world gross national income (WHO 2017b, c). World Health Assembly had set a target of increasing the rate of exclusive breastfeeding in the first 6 months up to

^{*}Professor & Head, Department of Community Medicine, A.J. Institute of Medical Sciences & Research Center, India.

[±]Clinical Tutor, Department of Community Medicine, A.J. Institute of Medical Sciences & Research Center, India.

at least 50 per cent compared to the prevalent rate of 40 per cent by 2025 globally (WHO 2020b).

While breastfeeding rates have improved globally, disparities in breastfeeding practices persist particularly in rural and low resource settings. In low and middle income countries (LMICs), only 37% of children are breastfed exclusively for the first 6 months of life (Victora et al. 2016). Situation in India is no better, as National Family Health Survey-2015-16 (NFHS-4), brings out that only 42.6% mothers initiated breastfeeding within one hour of birth, while only 54.9% children were exclusively breastfed (urban=52.1%, rural=56%). While majority of the states have registered improvement in EBF practices, the trends in Kerala and Karnataka have shown a decline i.e., from 56.2% to 53.3% and from 58.6% to 54.2% respectively (MHFW 2017, POSHAN 2017).

As India leads the world in the number of preterm births and neonatal mortality, understanding the factors associated with EBF can help in improving the nutritional status of millions of infants, and reducing neonatal mortality rate (UNICEF 2019a). Keeping in view the declining trends of EBF in Karnataka, present study was conceived and conducted among rural mothers attending a subdistrict (SDH) Hospital located in Bantwal, Dakshina Kannada District, Karnataka, India, with an aim to determine prevalence of EBF and the socio-demographic variables which may have an association with it, as these findings may be useful later on, in planning and implementation of EBF intervention programs in the community.

Literature Review

Breastfeeding, also called nursing, is the process of feeding mother's breast milk to her infant, either directly from the breast or by expressing (pumping out) the milk from the breast and bottle-feeding it. Breast milk provides the infant with essential calories, vitamins, minerals, and other nutrients for optimal growth, health, and development. Breastfeeding is beneficial to both, the mother and her infant, and also offers an important opportunity for the pair to bond (NIH 2017).

WHO, as well as UNICEF recommend initiation of breastfeeding within the first hour after the birth; exclusive breastfeeding for the first six months; and continued breastfeeding for two years or more, together with safe, nutritionally adequate, age appropriate, responsive complementary feeding starting in the sixth month. Similar recommendations have also been made by American Academy of Paediatrics on breastfeeding (UNICEF 2015, NIH 2017).

Studies reveal that newborns that started breastfeeding between two and 23 hours after birth had a 33% greater risk of dying as compared to those who began breastfeeding within one hour of birth. Among newborns that started breastfeeding a day or more after birth, the risk was more than twice as high. Further, an exclusively breastfed child is 14 times less likely to die in the first six months of life than a non-breastfed child, as breastfeeding drastically reduces deaths from acute respiratory infection and diarrhea, the two major child killers (WHO 2018). Sadly, only 44% of new-born are put to the breast within the first hour of birth

globally and only 2 in 5 infants less than 6 months of age are exclusively breastfed (UNICEF 2019b). WHO (2012) recommends that a new mother should have at least 16 weeks of absence from work after delivery, to be able to rest and breastfeed her child (WHO 2012).

Studies also bring out that exclusive breastfeeding helps children support healthy brain development, improves cognitive performance and is associated with better educational achievement at the age of five years (UNICEF 2015). Research further indicates that, breastfeeding supports infants' immune system and may also protect them later in life from chronic conditions such as obesity and diabetes (WikiLectures 2014). Besides, breastfeeding also benefits the mothers in many ways - it lowers their risks of breast and ovarian cancer, helps them return to their pre-pregnancy weight faster, reduces the rates of obesity and lowers the incidence of postpartum depression (WHO 2013, Hamdan and Tamim 2012).

Questions have been asked as to why not to use infant formula? The answer is that infant formula does not contain the antibodies found in breast milk and is also linked to some inherent risks, such as water-borne diseases that arise from mixing powdered formula with water which may not be safe sometimes, over-diluting formula to "stretch" supplies and the cost of formula may not be affordable to many poor families. Infants who receive formula feedings are also at a higher risk for acute otitis media, asthma, diabetes, eczema, lower respiratory tract and infections. Besides, formula is harder to digest for a new born baby and stays in the stomach longer than breast milk, which may cause the baby to feed less often and cause a decrease in milk production of the mother (Dartmouth-Hitchcock 2020).

Studies in India and abroad bring out that EBF practices are sub-optimal in most of the developing countries while India is no exception. Research indicates that the main modifying variables to EBF practices are-the age of the mother, her educational status, economic status of the family, occupation/employment of the mother, parity, antenatal care, multiple births, cue to action/self-efficacy, type of delivery, birth weight of infant, previous experiences with breastfeeding, support from family and friends, support from health workers, knowledge of feeding babies, maternal prenatal intention, lack of awareness about benefits of EBF, personal motivation and perception of having insufficient milk secretion (Andy 2015).

Some of the studies undertaken in India and abroad on EBF and the various factors which influence it are given below:

Tarrant et al. (2010) conducted a prospective study on antenatal women who delivered healthy, term singleton infants, at 6 weeks and 6 months postpartum. Results brought out that breastfeeding initiation rates of the Irish-national and non-Irish-nationals were 47% and 79.6%, respectively, while the factors which were significantly associated with both breastfeeding initiation and 'any' breastfeeding at 6 weeks included age of the mothers (>35 years) and educational status. The negative perception that breastfeeding is an embarrassing way to feed an infant was demonstrated as a major barrier to initiation. The author recommended that health campaigns that focus on increasing the social acceptability of breastfeeding may prove effective in addressing this cultural barrier (Tarrant et al. 2010).

Bakoula et al. (2007) conducted a longitudinal study among 3734 Greek mothers to determine the prevalence and socio-demographic, psychosocial and environmental factors associated with maternal infants feeding intention. The results showed that any breastfeeding at 3 to 6 months were 52% and 24% respectively. The corresponding rates of exclusive breastfeeding were 37% and 17%. The author recommended health education programmes to support breastfeeding were necessary with special focus on non-working mothers and mothers who did not have previous breastfeeding experience (Bakoula et al. 2007).

Edmond et al. (2006) in his study among 10947 breastfed babies brought out that breastfeeding was initiated within the first day of birth in 71% of infants and by the end of day 3 in all but 1.3% of them, while 70% were exclusively breastfed during the neonatal period. Delay in the time of repair of episiotomy and labor duration less than 12 hours were associated with early breastfeeding initiation. Early contact between baby and mother, help received on the delivery table and the presence of more than one delivery assistant, positively influenced breastfeeding initiation (Edmond et al. 2006).

Behzadifar et al. (2018) in a systematic review and meta-analysis in Iran brought out an overall prevalence of EBF to be 53%. The OR for breastfeeding education received before pregnancy was 1.13, for mother's job -1.01, for education level -1.12, for type of delivery -1.16 and for gender of child -1.03 (Behzadifar et al. 2018).

Oakley et al. (2013) in their study in England (2010-2011), which included all the 151 primary care trusts (PCTs) in England, observed considerable variations in breastfeeding with breastfeeding initiation mean -72%, any breastfeeding at 6-8 weeks mean -45%, and exclusive breastfeeding at 6-8 weeks mean -32%. Maternal age was strongly associated with breastfeeding. Weaker associations were observed between socio-demographic factors and breastfeeding in London PCTs (Oakley et al. 2013).

Raveendran et al. (2020) in their study in Kerala (India) brought out rather low prevalence of EBF i.e., 21.9%, with a median duration of four months. Main factors which influenced the EBF were observed to be maternal education, occupation of mother and advice on exclusive breastfeeding during antenatal visits. Perception of inadequacy of breast milk was found to be the major barrier to non-exclusive breastfeeding (Raveendran et al. 2020).

According to Hayden et al. (2009) health behavior is determined by personal beliefs and perceptions which are based on four constructs -perceived susceptibility, perceived severity or seriousness, perceived barriers and perceived benefits. The individual perception together with cues to action and self-efficacy determine the health behavior or action. Studies bring out that the success of a breastfeeding promotion program will depends on understanding the major constructs which are modified by variables such as culture, educational level, past experiences, skill, socio-demographic variables and motivation (Hayden et al. 2009).

The review of literature thus brings out a huge scope for improvement of EBF practices globally as well as in our country, and also the need to understand

various socio-demographic characteristic like age, education, parity, economic status, and employment which may influence the these practices.

Methodology

Study Design: Present study was a cross-sectional descriptive study, conducted over a period of two months from 1 August 2019 to 30 September 2019; in a subdistrict (SDH) Hospital located in Bantwal, Dakshina Kannada District, Karnataka, India. The reason for selecting the ibid hospital was that our Medical College has memorandum of understanding (MoU) for training and research of our undergradduate and post-graduate students.

Study Population: The study included all lactating mothers, attending the ibid hospital outdoor patient department (OPD) and had at least one living child aged less than two year and were willing to participate in the study. Convenience sampling method was adopted keeping in view the time frame and the available resources. Finally a total of 182 mothers were enrolled in the study.

The Study Instrument and Data collection: A structured questionnaire was then administered to the study respondents through face to face interviews after taking written informed consent from the participants. Approval of Institutional Ethical Committee (IEC) was obtained before the conduct of study. The participants were asked questions related to current breastfeeding practices and recall as to how early they initiated breastfeeding after the delivery including questions on complementary feeding, bottle feeding, any other foods or liquids given to the infant during first six months. The questionnaire also collected information on socio-demographic characteristics of the mothers, type and place of delivery, and their knowledge about EBF.

Statistical Analysis: Data entry was done using Microsoft excel 2010 and analyzed using SPSS version 20.0. The descriptive parameters have been represented as frequencies and percentages. The chi-square test has been used for assessing the significance of breastfeeding practices and selected variables. The p-value less than 0.05 have been taken as significant.

Operational Definitions

Breastfeeding practices were assessed based on the World Health Organization (2008) definitions for assessing infant and young child feeding practices (WHO 2008).

Exclusive breastfeeding: Exclusive breastfeeding" is defined as no other food or drink, not even water, except breast milk (including milk expressed or from a wet nurse) for 6 months of life, but allows the infant to receive ORS, drops and syrups (vitamins, minerals and medicines).

Early initiation of breastfeeding: Proportion of children born in the last 24 months who were put to the breast within one hour of birth.

Exclusive Breastfeeding under 6 months: the proportion of infants 0-5 months of age who were exclusively breastfed in the last 24 h.

Continuous breastfeeding at 1 year: Proportion of children 12-15 months of age who are fed breast milk in the last 24 h.

Timely complementary feeding: Proportion of infants 6-8 months of age who were breastfeeding and receiving solid, semi-solid or soft foods.

Bottle feeding: The proportion of infants less than 24 months of age who were receiving any liquid (including breast milk) or semi-solid food from a bottle with nipple/teat including non-human milk and formula in the last 24 hours.

Results

Socio-Demographic Characteristics

Present study, included a total of 182 participants. The majority of the mothers, 146 (77.0%) belonged to 21-30 years age group, 13 (7.1%) mothers belonged to less than 20 years age group while remaining 23 (12.6%) were aged more than 30 years. The mean age of the mothers was 23.6 years. Among the respondents, 143 (78.5%) mothers were Hindus while remaining 39 (21.4%) belonged to other religions. Furthermore, 11 (6.0%) of the mothers were illiterate, 117 (64.2%) belonged to social class II/III, 153 (84.0%) were housewives, 97 (53.2%) stayed in joint families, 96 (52.7%) had male children, while 128 (70.3%) mothers had two or more children (Table 1).

Awareness on EBF and its Advantages

Table 2 brings out awareness among mothers about EBF and its advantages. It was observed that 166 (91.2%) of the respondents had heard of EBF, but only 98 (53.8%) actually knew that it meant feeding only breast milk for six months. Furthermore, only 44 (24.1%) mothers rightly brought out that initiation of breastfeeding should be within the first hour of delivery. Most of the mothers 126 (69.2%) felt that complementary feeding should be started around 6 months of age for the babies. The study brought out that 33 (18.1%) mothers were aware that breast milk protects the baby from many diseases, 21 (11.5%) were aware that breastfeeding creates a bond between mother and baby while 89 (48.9%) felt that breast milk is best food for babies. Furthermore, 63.7% mothers also felt that they may not be producing sufficient milk to meet the nutritional needs of the babies.

Table 1. Socio-Demographic Characters of Study Population (n=182)

Variables	Frequency	Percentage
Age in years		
<20	13	7.1
21-24	77	42.3
25-30	69	37.9
>30	23	12.6
Literacy status of mother		
Illiterate	11	6.0
Primary	51	28.0
Secondary	73	40.1
Above Secondary	47	25.8
Occupation		
House wife	153	84.0
Employed	29	15.9
Socio-economic status	•	
I	17	9.3
II	39	21.4
III	76	41.7
IV	41	22.5
V	09	4.9
Type of family		
Nuclear	85	46.7
Joint	97	53.2
Poverty line		
APL	23	12.6
BPL	159	87.3
Religion	•	1
Hindu	143	78.5
Muslim/Others	39	21.4
Gender of infant under su	II.	
Male	96	52.7
Female	86	47.2
Number of children in the		I
Single	54	29.6
U		
Two	79	43.4

Table 2. Awareness on Exclusive Breastfeeding and its Benefits of (n=182)

Statement	Frequency	Percentage
Ever heard of exclusive	166	91.2
breastfeeding		
EBF means only	98	53.8
breastfeeding for 6 months		
Breastfeeding should start after	delivery	
Within one hour	44	24.1
Within 24 hours	85	46.7
After 24 hours	47	25.8
Do not know	06	3.2
What is the period for exclusive	breastfeeding	
1- 2 months	24	13.1
3-4 months	17	9.3
5-6 months	35	19.2
6 months	98	53.8
Do not know	08	4.3
Age at which baby should be give	ven liquid/solid foods	
1- 2 months	19	10.4
3-4 months	21	11.5
5-6 months	126	69.2
Do not know	16	8.7
Do you know it protects your	33	18.1
baby from many dangerous		
diseases		
Breastfeeding creates a bond	21	11.5
between mother and baby		
Breast milk is best food for	89	48.9
babies?		
Do you think only your milk is suff	icient for the baby for firs	st 6 months
Yes	66	36.2
No	116	63.7

Breastfeeding Practices among Mothers

Table 3 brings out breastfeeding practices among the respondents. The study brings out that 168 (92.3%) mothers were breastfeeding their babies at the time of interview. It was further observed that, 136 (74.7%) mothers started breastfeeding within the first hour after delivery while 38 (20.8%) started between 1 h and 24 hours. Majority 161 (88.4%) of the new born babies were given colostrum while 56 (30.7%) were given pre-lacteal feed. Further, 138 (75.8%) mothers practiced breastfeeding on regular basis. Continuous breastfeeding rate at 1 year was found to be 77.3% while 57.1% babies were using a feeding bottle. However, timely complementary feeding was provided to only 35.1% infants.

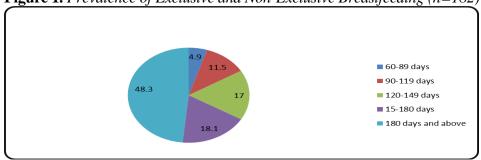
Table 3. *Breastfeeding Practices among Mothers (182)*

Feeding Practices	Frequency	Percentage		
Currently breastfeeding	168	92.3		
Initiation of breastfeeding				
Within one hour	136	74.7		
> one h - 24 h	38	20.8		
> 24 h	8	4.3		
Colostrum given to baby	161	88.4		
Timely complementary feeding	64	35.1		
Continuous breastfeeding at 1 year	144	79.1		
Bottle feeding	104	57.1		
Pre-lacteal feed	56	30.7		
Frequency of Breastfeeding				
Regularly	138	75.8		
On demand	35	19.2		
Randomly	9	4.9		

Exclusive Breastfeeding

Present study brings out that 88 (48.3%) mothers practiced EBF while 94 (51.6%) mothers did not. The study further brings out that 4.9% mothers breast fed their babies for duration of less than 90 days, 11.5% breast fed for 90 to 119 days, 17.0% breast fed for 120 to 149 days while 18.1% mothers breast fed their babies for 150 to 179 days (Figure 1).

Figure 1. Prevalence of Exclusive and Non-Exclusive Breastfeeding (n=182)



Determinants of Exclusive Breastfeeding

The present study brings out higher prevalence (58.6%) of EBF among mothers from higher age group (25 years and above), while mothers in the younger age group (24 years and below) were having lower prevalence (37.7%). Further, the EBF practices were found to be high (60.8%) among the families which were below poverty line, as compared to those who were above poverty line (46.5%). In our study, practice of EBF was found to be almost equal among nuclear as well as joint families i.e., 48.2% and 48.4% respectively. Further, the EBF practices were found to be 54.5% among illiterate mothers while it was 47.9% among literate mothers. The practice of EBF was found to be relatively

much higher (54.9%) among mothers who were house wives/ not working, while only 13.7% of working mothers practiced EBF.

Among Hindus, 45.4% and among Muslims, 58.9% mothers exclusively breast fed their babies. Among 96 male children, 48.9% while among 86 female children, 47.6% were provided EBF. The study further brings out that, mothers with a single child practiced EBF in 57.4% cases as compared to 44.5% with more than one child. The study reveals 50.8% prevalence of EBF among mothers who had four or more antenatal visits as compared to 44.2% among those who had three or less visits. Further, EBF was found to be 30.55% among mothers who had caesarean section as compared to 52.7% among those who had normal vaginal delivery.

We tried to establish an association between selected socio-demographic variables and the practice of EBF and found some of these to be significantly associated and these were-maternal age (p<0.004753) occupation of the mother (p<0.00049), gender of the infant (p<0.000634), number of antenatal visits (p<0.01148) and type of delivery, i.e. vaginal or caesarean (p<0.027847) (Table 4).

Table 4. *Determinants of Exclusive Breastfeeding n=182*

Variable	EBF(n=88)	NEBF(n=94)	Total(n=182)	χ2 / p value
	(%)	(%)	(%)	
Maternal age in	years			
< 25	34 (37.7)	56 (62.2)	90	7.9712
>25	54 (58.6)	38 (41.3)	92	p<0.004753
Literacy status	of mother			
Illiterate	06 (54.5)	05(45.4)	11	0.0127
Literate	82 (47.9)	89(52.0)	171	p>0.91014
Occupation of 1	mother			
House wife	84 (54.9)	69 (45.0)	153	16.4967
Employed	04 (13.7)	25 (86.2)	29	P< 0.000049
Socio-economi	c status			
BPL	14 (60.8)	09 (39.1)	23	1.652
APL	74 (46.5)	85(53.4)	159	p>0.198693
Type of family				
Nuclear	41 (48.2)	44 (51.7)	85	0.5574
Joint	47 (48.5)	50 (51.5)	97	p>0.453313
Gender of infar	nt under survey			
Male	67(69.7)	29 (30.2)	96	11.6726
Female	21(24.4)	65 (75.5)	86	P<0.000634
Number of chil	dren in the family			
One	31 (57.4)	23(42.5)	54	2.5214
>One	57 (44.5)	71 (55.4)	128	p>0.112313
Antenatal visits	}			
< four	21 (35.0)	39 (65.0)	60	6.3895
> four or	67(54.9)	55 (45.0)	122	p>0.01148
more				
Type of delivery				
Vaginal	77 (52.7)	69 (47.2)	146	4.8375
Caesarean	11 (30.5)	25 (69.4)	36	P<0.027847

Discussion

Present study brings out that 92.3% mothers were breastfeeding their babies at the time of interview, 74.7% mothers had initiated early breastfeeding, 88.4% infants were given colostrum, 30.7% were given pre-lacteal feed, 35.1% infants were given timely complementary feed and 57.1% babies were using a feeding bottle. In a similar study in a neighboring district in Karnataka, by Manjunatha Swamy et al. (2015), it was observed that only 17.17% of mothers intended to exclusively breastfeed their infants for six months while majority of mothers (36.13%) wanted to continue EBF only for four months. Their study also found that 34.13% mothers had initiated early breastfeeding while majority (75.25%) of the mothers had provided colostrum to their new born babies Manjunatha Swamy et al. (2015). In another study by Bernard Yeboah in Ghana, 74% of the mothers were found to be breastfeeding their children, more than half of all mothers (63.4%) had started early breastfeeding, about 81% of all mothers had offered colostrum to babies, EBF rate under 6 months was found to be 66%, continuous breastfeeding rate at 1 year was observed to be 77.3%, 43.5% of the infants aged 6-8 months were introduced to complementary feeding and among children less than 24 months, less than half (30.1%) were being bottle fed. These findings are similar to our findings (Yeboah-Asiamah Asare 2018).

In our study, less than half of the mothers (48.3%) practiced exclusive breastfeeding, which is lower than the national average of 54.9% as well as Karnataka average of 54.2%. Further, the mean duration of EBF among our respondent mothers was 107 days. The study brings out that 51.6% of the mothers did not complete EBF for 180 days. The study further brought out that 4.9%, mothers breast fed their babies for duration of less than 90 days, 11.5% mothers breast fed for 90 to 119 days, 17.0% mothers breast fed for 120 to 149 days while 18.1% mothers breast fed their babies for 150 to 179 days. In a similar study by Vijayalakshmi et al. (2015) 88.5% of the mothers were breastfeeders, but only 27% of the mothers were exclusive breastfeeders and only 36.9% initiated breastfeeding within an hour (Vijayalakshmi et al. 2015). In another study by Oche and Umar (2008) from in Sokoto, Nigeria, high prevalence of Exclusive breastfeeding was reported, as 78.7% of the mothers gave only breast milk up to six months after delivery, 71% of them continued breastfeeding for 19-24 months while majority of the mothers (76%) continued breastfeeding even when they felt their child was old enough to be weaned (Oche and Umar 2008).

We tried to identify major determinants of EBF in our study subjects. In our study prevalence of EBF was found to be relatively lower i.e., 37.7% among younger mothers (<25 years) as compared to 58.6% among the older mothers (>25 years) and this difference was also found to be statistically significant (p<0.004753). Nishimura et al. (2018) in their study from south India also reported increased EBF rates, with increase in maternal age (OR=1.04) (Nishimura et al. 2018). In a similar study, by Zielinska and Hamulka (2018) in Poland, the researchers also brought out that the highest risk factors for N-EBF were maternal age <20 years (Zielinska and Hamulka 2018).

Present study brings out that EBF practices were found to be slightly higher (54.5%) among illiterate mothers as compared to literate mothers (47.9%). Similar findings, have also been reported by Akpojene Ogbo et al. (2019) in their studies and brought out that mothers with higher level of education were less likely to exclusively breastfeed their infants (Akpojene Ogbo et al. 2019). However, contrary to our findings, Naik et al. (2019) in their study from Srinagar, India reported significantly higher rates of EBF among babies born to parents with higher education Naik et al. (2019).

In our study prevalence of EBF was found to be higher among housewives (54.9%) as compared to working mothers (13.7%) and this was found to be statistically highly significant. In a similar study, Al-Kohji et al. (2012) in Qatar also reported that EBF rates were higher among housewives in comparison with employed mothers, as the unemployed mothers (Al-Kohji et al. 2012). However, contrary to our findings, Basu et al. (2018) reported higher prevalence of EBF among working mothers (50.0%) as compared to housewives (33.3%) (Basu et al. 2018).

In our study EBF rate was found to be 60.8% among the families which were below poverty line (BPL), as compared to 46.5% among those, who were above poverty line (APL). However, this difference was not found to be statistically significant, (p>0.198693). In a similar study by Mawa et al. (2019) in Uganda, it was observed that odds ratios for exclusive breastfeeding by household wealth index were 2.38 (1.30-4.33), for the poorest, 2.16 (1.18-3.96) poorer, 1.91 (1.10-3.48) middle, and 1.41 (0.75-2.64), for richer households (Mawa et al. 2019).

In our study, practice of EBF was found to be almost same among nuclear as well as joint families i.e., 48.2 % and 48.4% respectively. However, contrary to our findings Gupta et al. (2006) in a study in urban slums of Rishikesh, (Uttar Pradesh) reported higher prevalence of EBF among mothers from Joint families (31.6%) as compared to mothers from nuclear families (24.7%); though this difference was not found to be significant (Gupta et al. 2006).

Gender of infant has been reported to an important determinant of EBF in India. In our study too, 69.7% male children were given EBF as compared to 24.4% female children and this difference was also found to be statistically significant (p<0.000634). However, Habtewold et al. (2019) in a meta-analysis and Vanderlinden and Van de Putte (2017) in their study in Belgium did not report any significant association between gender of infant and EBF practices (Habtewold et al. 2019, Vanderlinden and Van de Putte (2017).

Present study brought out that, mothers with a single child practiced EBF in 57.4% cases as compared to 44.5% with more than one child. Perera et al. (2012) in their study in Sri Lanka brought out that second born babies had a higher exclusive breastfeeding rate (73.6%) compared to first born (70%) while the EBF rate dropped again after the second baby to 66.6% (Perera et al. 2012).

Higher numbers of antenatal visits have been found to be associated with the highest odds of EBF. The benefits of breastfeeding should be emphasized during the initial antenatal visit to increase EBF rates among all mothers, though the studies on the association between EBF and number of antenatal visits in India and other countries are not consistent. Present study reveals 50.8% prevalence of EBF

among mothers who had four or more antenatal visits as compared to 44.2% among those who had three or less visits and this difference was also found to be statistically significant (p>0.01148). Bhanderi et al. (2019) in their study in Gujarat, also brought out similar findings and observed higher prevalence (52.7%) of EBF among those who had >4 antenatal visits as compared to those who had <4 antenatal visits (33.3%) (Bhanderi et al. 2019).

In majority of studies Caesarean section has been reported to be an important barrier to EBF. In our study too, this trend was observed as EBF was found to be only 30.55% among mothers who had caesarean section as against 52.7% among those who had normal vaginal delivery and this difference was also found to be statistically significant (P<0.027847). In a similar, but prospective cohort study from China, Chen et al. (2018) brought out exclusive breastfeeding rates at 1, 3, and 6 months as 80.2%, 67.4%, and 21.5%, respectively and also observed lower rates of EBF among women who had a cesarean delivery than those who had a vaginal delivery (p<0.05). The authors further observed that Cesarean delivery also shortened the breastfeeding duration (hazard ratio = 1.40, 95% confidence interval) (Chen et al. 2018).

Conclusions

In our study, EBF practices were found to be suboptimal and below the national as well as Karnataka state average, while these were influenced by multiple socio-demographic variables. The benefits inherent in the practice of EBF cannot be over emphasized, especially in a country like India, where a quarter of global neonatal deaths happen, i.e., nearly 600,000 newborns die within 28 days of their birth every year. Needless to say, that this study brings out an urgent need for health awareness interventions with special focus on the benefits of EBF for both, the infant and the mother. The health education drives should specifically target the new mothers and their family members as the studies indicate a strong influence of mother's parents and her in-laws on breastfeeding practices.

Limitations

The present study had the limitations which are inherent in all cross sectional studies as these make articulation of temporal association between the study factors and EBF difficult. Further, this was a hospital based study hence data obtained cannot be considered to be the true representative of general population. As the method of data collection in present study was face to face interview, recall bias due to lapse of time and information bias due to personal reasons may not be ruled out.

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