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About the Journal

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Aims & Scope

The Journal aims to publish research in all fields of clinical, diagnostic, experimental & preventive areas related to medical sciences to disseminate scholastic work among clinicians and scientists around the globe.

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Editorial

TELOMERE LENGTH- BIOLOGICAL MARKER OF AGEING

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ABSTRACT
Telomere length is an indicator of biological age, influenced mainly by oxidative stress and inflammatory conditions. Telomere length shortens with advancing age, however in certain situations this shortening expedites with early senile changes while in other situations it can be delayed resulting in slowing of ageing. Ageing is a factor associated with a number of diseases and also treatment decision of lethal diseases is directly influenced by the age. However, understanding the difference of chorological versus biological age is essential. It is also essential to determine cut-offs of the age by using telomere length.

INTRODUCTION

Telomere length is known as a biological marker of ageing, it is used to assess the cellular aging process in humans. Telomeres are repetitive DNA sequences that protect the ends of chromosomes from damage during the process of cell replication. Thus, telomere play a crucial role in preserving chromosome stability, replication, and gene regulation. As human cells divide, telomeres shorten due to incomplete replication, oxidative stress and environmental damage, and eventually reach a critical length that triggers cell senescence or death. Therefore, telomere length can suggest cellular aging, thereby predicting biological age and health status.

Telomere length influencing factors

Research studies have identified several factors that can affect telomere length, including age, diet, exercise, smoking, alcohol consumption, and chronic stress. There is evidence available which suggests that telomere length shortening was associated with insulin resistance (1). There was a multi-center randomized controlled trial reported that shortening of telomere length was linked with depression and cognitive decline in elderly population (2). There are studies which have found that chronic stress can expedite telomere shortening, raising risk of cardiovascular disease (3). While a healthy lifestyle and adaptation of relaxing strategies have shown to preserve telomere length. There was an open label single arm exploratory study which has linked meditation and yoga with improved cellular ageing (4). There was a women exclusive study which explored association of endogenous estrogen and telomere length, as it is already suggested that longer reproductive life has been shown to be associated with less number of senile diseases, thus it was reported that high endogenous oestrogen level was associated with longer telomere length(5). The DNA from CARDIOPREV study was explored for telomere length and intake of vitamin E and anti-oxidants. It was interesting that low vitamin E intake expedited the telomere length shortening (6). Similarly, PREDIMED-NAVARRA study showed that diet which triggers inflammation causing early telomere shortening, was associated with high risk of cardiovascular disease (7). It is interesting from explanation point of view that telomere length is influenced by the oxidative stress at cellular level. Thus, antioxidants like vitamins may improve cellular senescence. This hypothesis was attempted to be

tested in a rural community based cross-sectional study from China, which showed that the oxidative stress and inflammation was associated with early shortening of telomeres and mitochondrial dysfunction(8). There was an interventional study where micronutrients improved cellular ageing and 25% increase in telomere length by adopting antioxidant provision by micronutrient supplement diet(9).

Use of telomere length in clinical practice and caveats

The Helsinki's Birth cohort study has shown that the telomere length appeared to be associated with ageing (10). It was further elaborated that it be used as a marker of ageing in women (10). Till date the available literature suggests that telomere length can provide reliable information on an individual's biological age, disease risk, and overall health status. However, it gets influences by life style, stress, diet thus the biological age and chronological age differs between individuals. There are certain situations where it is utmost important to understand the biological age to advice interventions such as malignant diseases. There is a long debate for use of aggressive therapy in elderly women with breast cancer, given the chronological age of patients over 70 years, it is assumed they might not be fit, but clinically they fit are often enough to tolerate the therapy, other way round a 55 years old women might be biologically weak with a number of co-morbidities not allowing her to tolerate aggressive therapy. Thus American Society of clinical Oncology revised guidelines suggesting screening should be done till the women is a candidate to receive therapy. Now the question arises how to decide if the women is able to tolerate the therapy or she is fit enough. No such biological marker or test available in clinical practice till date. However telomere length has potential to determine. Thus, determining biological age appears to be the only answer. Since telomere length has shown its association with age it could be used. Nevertheless, till date the literature is so scare that clinical guidelines cannot be designed. Further research directed to make cut offs for ageing so that such novel marker can be used appropriately in clinical practice.

CONCLUSION

In conclusion, telomere length is an essential biological marker of aging that has gained increasing interest over the years. It can provide valuable insights into an individual's cellular aging and health status, as well as serve as a predictor of age-related diseases. Maintaining telomere length is likely to become an essential factor in future healthcare for age-related illnesses, especially for managing chronic diseases and extending lifespan.

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Research article

IMPACT OF COVID-19 PANDEMIC ON GENERAL SURGICAL PRACTICE AT TERTIARY CARE HOSPITAL IN PAKISTAN-A SINGLE CENTER ANALYSIS

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ABSTRACT

The Coronavirus Disease 2019 (COVID-19) has adversely affected the global healthcare system, especially the management of surgical diseases. Most guidelines issued during pandemic recommended deferral of elective surgeries to decrease transmission and conserve resources for COVID-19 management, which raised the risk of complications. This study was conducted to evaluate the impact of the COVID-19 pandemic on the general surgical practice of a tertiary healthcare facility in Sindh, Pakistan. The data were retrospectively retrieved from the operation room records for most common general surgical procedures performed between January 2019 to December 2020 (i.e. peak COVID-19 restriction period). Monthly frequencies of the enrolled procedures were compared to COVID-19-associated incidence, recoveries, and mortality in Sindh. The six enrolled procedures suffered a reduction of 23.9% from 2019 to 2020. However, the difference was not significant ($p > 0.05$) for the procedures collectively or individually, except for trucut biopsy ($p = 0.042$). COVID-19-associated mortality significantly influences the frequency of the surgical procedures, compared to the pre-COVID era ($p = 0.042$). However, the association was significant for the procedures collectively only, but in the individual procedure, only open inguinal hernia repair ($p = 0.011$) showed a significant difference. In conclusion, there was a significant reduction in surgical cases with the potential risk of complications. Therefore in such situations, there must be a developed system to that the cases may be decided on an individual basis.

Key Words: General Surgery, Elective Surgery, Coronavirus, COVID, Pandemic

INTRODUCTION

On 31 December 2019, the World Health Organization (WHO) China Country Office reported cases of pneumonia of unknown etiology in Wuhan City, Hubei Province of China. The Chinese authorities isolated and identified a novel type of coronavirus on 7 January 2020 (1). This novel virus has outreached worldwide and claimed millions of lives, including in Pakistan. According to the Government of Pakistan in May 2021 there were 850,131 confirmed cases were reported since January 2020, out of which 18,149(2.2%) deaths occurred and 728,044 (87.3%) were recovered from this disease(2).

The COVID-19 pandemic has changed human lives to the greatest degree all around the globe. Every field of life has been greatly affected, but the healthcare system was the worst hit. Tremendous burden has been placed by this viral outbreak on healthcare facilities across the globe (3). Low to Middle-Income Countries (LMICs), including Pakistan, have severely suffered consequences on the already strained healthcare resources due to the

disease burden (4, 5, 6). Given the nature of the symptoms and contiguous capacity the hospitals were restricted to a certain number of cases. Since the COVID-19 positive patients needed oxygen, thus large quantity of oxygen was required in all hospital and treatment facilities. Thus, In order to adjust the rising number of emergency admissions for respiratory syndrome, the majority of which required critical care, every healthcare center experienced considerable changes in their practices. In order to dispense this unprecedented disaster, many guidelines and procedures were proposed. Shortage of healthcare workers, personal protective instruments, increased oxygen demand and fear of excessive exposure of surgical and anesthesia staff to the virus, all the necessary measures were recommended at global and national levels (4). Postponement of elective surgical cases whenever possible was one of the crucial responses to the outbreak (7, 8, 9, 10). In addition to the reduced viral transmission, its advantages included decreased oxygen consumption, ICU admissions and ventilator usage. The conserved resources were then dedicated to deal with the high burden of COVID-19 associated respiratory diseases.

Healthcare institutions across Pakistan were recommended to hold their elective surgical cases, especially during the high positivity rates of their provinces. Despite widespread effects of the pandemic, relatively limited literature exists from the developing world for its impact on the surgical practices. Keeping in view this study was conducted to evaluate the impact of the COVID-19 pandemic on the performance of general surgical cases during peak COVID-19 restriction time (i.e. 2020) and compare it with the pre-COVID period (i.e. 2019).

METHODOLOGY

This study was a retrospective review of the surgical cases operated during two time periods:

1. Pre-COVID-19 (January 2019- December 2019)
2. COVID-19 restriction period (January 2020 – December 2020)

The data was retrospectively collected from operation room records at General Surgery Department, Dow University Hospital- Ojha Campus, Dow University of Health Sciences, Karachi, Pakistan. Only the most common procedures performed under care of general surgical service in 2019 were enrolled for analysis and the data of those procedures were retrieved for the period of 2020.

The data for COVID-19 incidence, recovery and mortality was collected from the official website by the Government of Pakistan (5). The data of all the common procedures performed were collected and compared. In addition, data of recoveries and deaths was also collected. The data of the most common general surgical procedures was divided as per each month of the years 2019 and 2020.

Statistical Methods

The data was collected and analyzed by using Statistical Package for Social Sciences (SPSS, IBM, version 26.0). Continuous data was evaluated as mean and standard deviation, whereas categorical data was evaluated as frequency distribution and percentages. The comparison was done by using regression analysis. A p-value <0.05 was considered significant.

RESULTS

A total of 1753 procedures were performed in 2019 while 1345 general surgical procedures were performed in the years 2020. The 23.9% reduction in the number of procedures for the year 2020 was observed.

Table 1 shows the most common operations performed under general surgical service at our hospital in years 2019 and compared with those performed in 2020. As observed for both years, laparoscopic cholecystectomy remained the most common procedure, followed by breast mass surgery and open inguinal hernia repair. The collective frequencies of enrolled procedures were 808 and 615 in 2019 and 2020 respectively, observing a 23.9% decrease. All surgical operations observed lower frequency in the year 2020, when compared to 2019. Five of the included six procedures were not performed at all for at least a month in 2020. However the significant decline was seen in tru-cut biopsies of breast lumps (Table 1).

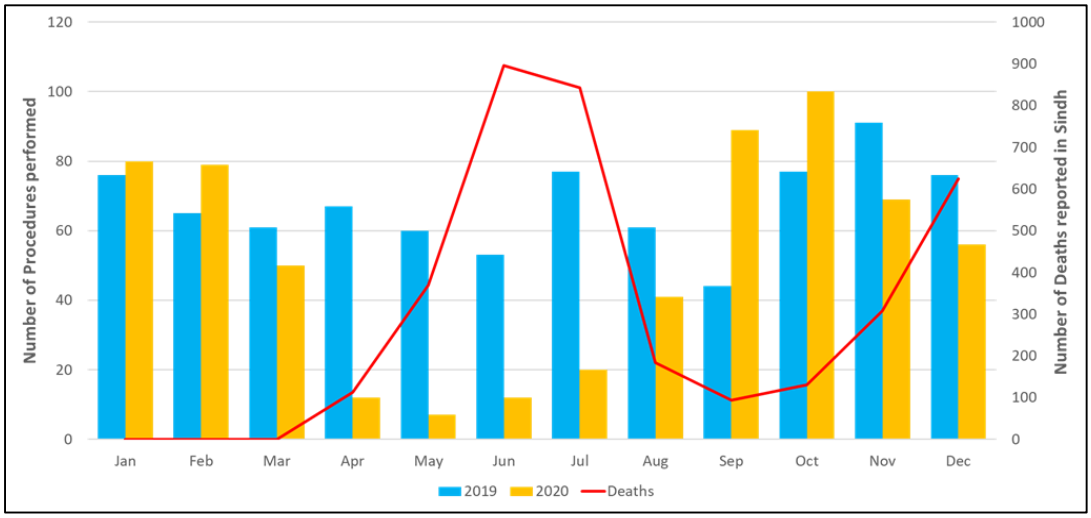
Table 1: The most common procedures performed under general surgical service at our hospital in years 2019-20.

S. No.	Procedures	Year	Month wise number of procedures												Total	*P-values
			Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec		
1	Breast Cancer Surgery	2019	17	9	10	9	13	10	10	11	11	22	21	14	157	0.278
		2020	16	10	12	8	6	10	8	7	17	18	16	9	137	
2	Laparoscopic Cholecystectomy	2019	34	22	29	28	22	15	34	20	12	30	40	31	317	0.374
		2020	33	29	17	2	0	0	2	21	49	43	30	29	255	
3	Open Inguinal Hernia Repair	2019	12	11	8	7	9	14	15	10	6	8	11	10	121	0.117
		2020	13	10	6	1	0	1	7	7	12	14	11	6	88	
4	Trucut Biopsy	2019	3	7	3	8	5	5	11	4	7	6	8	3	70	0.042
		2020	3	6	5	1	0	0	0	0	2	5	3	4	29	
5	Fistulectomy	2019	3	3	5	5	4	4	1	8	3	4	4	7	51	0.115
		2020	6	8	4	0	1	1	0	3	4	8	0	5	40	
6	Sebaceous Cyst Excision	2019	7	13	6	10	7	5	6	8	5	7	7	11	92	0.065
		2020	9	16	6	0	0	0	3	3	5	12	9	3	66	
7	Total Procedures**	2019	76	65	61	67	60	53	77	61	44	77	91	76	808	0.992
		2020	80	79	50	12	7	12	20	41	89	100	69	56	615	

*Significance for differences in number of general surgical procedures conducted between April to December in 2019 and 2020. ** Sum of all the six procedures enrolled in the study.

The periods of January to March for both years were excluded from the annual comparative analysis as Sindh observed its first case of COVID-19 infection in April 2020. A compensatory rise in number of procedures during the periods of low disease prevalence was observed. As for example, the cases of May 2020 were only 11.7% of those in same month in 2019, whereas the cases of September 2020 were 20.3% of those in same month of 2019. Graphical image (Figure 1) shows monthly COVID-19 mortality and frequencies of the common general surgical procedures in 2019 and 2020. COVID-19 associated mortality was observed to primarily influence the monthly frequencies of procedures collectively, although only open inguinal hernia repair observed significant association separately. The COVID-19 incidence only influenced the monthly cases of open inguinal hernia repair, whereas the recoveries played no role in affecting the operation room routine at our facility.

Figure 1. Summary of the monthly frequency of surgical procedures in the year 2019 and 2020 and COVID-19 mortality in Sindh



DISCUSSION

The study has shown considerable decline in the elective surgical procedures during COVID-19 peak period. Among them tru-cut biopsies of breast lumps were significantly reduced or deferred. Developing countries, like Pakistan, remain highly vulnerable to its devastating economic as well as healthcare burdens. It has led to upgrading the local healthcare practices to deal with the pandemic (3,4,7). In this study we evaluated the impact of COVID-19 pandemic and its factors on the general surgical practices at our institution. The pandemic restricted the surgical procedures to mainly emergency cases only, which led to decrease in surgeries conducted at our tertiary healthcare facility in 2020 (3,7). All major guidelines, including American College of Surgeons (ACS), British National Health Service (NHS), and European Society for Medical Oncology (ESMO), recommended prioritization of elective surgeries to defer cases which were not urgent (4, 9, 12, 13). As a result, the number of elective surgeries performed by our department decreased in 2020, especially during the high provincial positivity rates. Similar observations were made in other surgical departments and institutions as well (14, 15). These guidelines also assisted surgeons with amending the local protocols for surgical decision making. Such improvised protocols usually allow the patients to undergo procedures depending on their risk of developing complications (4). Oncological cases are usually considered semi-emergency due to the risk of lowering overall survival with delaying surgery (9). Perez Lara et al. discussed the modified protocols used in a Spanish district hospital to prioritize surgeries on case-to-case basis to determine the appropriate time for operation (13). Similarly, Nagarkar et al. also reviewed the modified protocols for surgical teams in an Indian hospital which can allow safe surgical management (14). Since breast cancer is already reported to be aggressive type in Pakistan and time lapsed between the appearance of first symptom and the start of the treatment adversely influence survival outcome. Thus reduction in tru-cut biopsies probably has multifaceted causes and long term sequelae in terms of rising breast cancer mortality in these patients.

We observed that following alleviation of the COVID-19 cases, the surgical procedures performed increased higher than expected to compensate for the postponed cases during the wave. As a result, the annual analysis revealed no significant difference in total number of common procedures performed by the general surgical unit in 2019 and 2020. Though, the significant difference was not observed for five of the enrolled six procedures for the two years but this could be due to a small sample size. The study also allowed us to determine the COVID-19 associated primary factors influencing the general surgical practices at our institution. Monthly mortality due to COVID-19 was found to be the influential factor for change in frequency of the general surgical procedures collectively. The post-COVID year observed more procedures compared to pre-COVID year during the periods of lower pandemic mortality. Minimizing the decrease in surgical frequencies from pre-COVID times is commendable during the COVID-19 crisis. This may still not compensate for simultaneous increasing incidence of surgical diseases but may allow preparation of additional facilities around the country. The authors believe the lack of significant difference for total procedures between the two years, along with COVID-19 mortality influencing frequency of surgical procedures highlights a narrow window of opportunity for the surgical units during these pandemic times. During the lower mortality periods, the surgical departments should be encouraged to perform higher frequency of procedures to compensate for delayed elective cases during the pandemic waves. The strategy would allow us to adjust our operational performance with COVID-19 mortality to conserve resources during the periods of high demand, as well as avoiding the cost of significant reduction in annual surgical frequencies, which can lead to disease complications. There is another important aspect of looking at the long term sequelae of the delayed procedures such as advanced stages of breast cancers and number of strangulated and obstructed inguinal hernias need to be explored.

CONCLUSION

The study showed a considerable reduction in the surgical procedures performed before and during COVID-19. The deferral policies of elective general surgical cases can be strategically used to reduce transmission and conserve resources during the pandemic waves, and then be compensated during periods of low COVID-19 prevalence. In this way health care providers would be able to continue treatment for surgical diseases along with managing COVID-19 pandemic.

Ethical Consideration: The study was retrospective review of the hospital record, no patient's identity displayed at any time.
Conflict of Interest: There is no conflict of interest.
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Research article

BOTTLE-FEED VERSUS MOTHER FEED CHILDREN – LONG TERM EFFECTS OF INFANT FEEDING ON COGNITIVE DEVELOPMENT AND SCHOOL PERFORMANCE

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ABSTRACT

Mother feed (i.e. Breast feeding) provides essential nutrients, antibodies and immune cells to allow infant growth and protect them from infections. Mother feed not only have short term effects but it influences brain development as well as life time effects in many organ systems. This study was conducted to compare mother feed and bottle feed children at school going age. The self-administrated questionnaire survey was conducted including parents of children between 5 to 10 years of age (n=300). There was no significant difference found in the median age of children reported for, neither there was any significant difference in the weight of the two groups. However, bottle feed children significantly showed better performance in mathematics while mother feed children were significantly better in general science and physical activities at school. The study concluded that bottle feed or breast feed both provides nutrition and overall children were doing good.

Key Words: bottle feed, mother feed, school performance

INTRODUCTION

Breastfeeding is widely considered to be the optimal method of infant feeding due to its numerous benefits for both the mother and the child. Breast milk contains a range of nutrients, hormones, immune cells and antibodies that support the infant's growth and development, as well as protecting them from infections and diseases. However, not all mothers are able to or choose to breastfeed. As a result, infant formula has been developed as an alternative method of infant feeding(1). While formula can provide adequate nutrition for infants, there is evidence to suggest that breastfed babies may have some advantages over those who are bottle-fed. This may include differences in immune function, gut microbiota, and long-term health outcomes(2,3). There have been numerous studies on the relationship between infant feeding and school performance, but the results are often conflicting or inconclusive. Some studies have suggested that breastfeeding may be associated with higher academic achievements, while others have found no significant difference between breast-fed and formula-fed children. Though there is strong evidence suggesting lower number of infectious diseases and number of hospitalizations in breast feed infants as compared to bottle feed(4,5).

Overall, there are contradicting literature regarding the impact of bottle feeding versus mother feeding on school performance, as the relationship may be complex and multifaceted. Previously published studies have found that children who were breastfed for at least 6 months had significantly higher scores on standardized tests of verbal and nonverbal intelligence at the school going age as compared to those who were never breastfed (6,7). A meta-analysis of 18 studies concluded that breastfeeding was associated with higher cognitive performance in children,

particularly in language and reading skills. The effect was stronger in children who were breastfed for longer durations and received more exclusive breast milk(8).

Another study found that children who were exclusively breastfed for the first 6 months of life had lower odds of being diagnosed with attention-deficit/hyperactivity disorder (ADHD) at age 3 as compared to those who were never breastfed or received formula feed straight away(9). In another study investigators followed a group of children from birth to age 7 and found that those who were breastfed for at least 6 months had higher scores on tests of math, reading, and writing than those who were never breastfed or received formula(10). However, the effect was modest and disappeared after adjusting for other factors such as maternal education and socio-economic status. The study found that children who were breastfed for at least 6 months had higher scores on a standardized test of school readiness at age 4 than those who were never breastfed or received formula(11). The effect was partially mediated by language skills and behavior problems. While these studies provide some evidence for the benefits of breastfeeding on school performance, it's important to note that the findings are not always consistent. There was limited literature available from Pakistan. Therefore, this study was conducted to evaluate impact of the mode of infant feeding on their performance in school, in children between 5 to 10 years of age.

METHODOLOGY

The study was a population based survey from two large cities of Sindh including Hyderabad and Karachi, Pakistan. The parents of the school going children between 5 to 10 years of age were selected. The children whose parents were available to respond and those who were on mother feed or on bottle feed after three months of their life and exclusively continued the feeding for at least one year of their life regardless of weaning after six months. Their parents were requested to fill a self-administrated questionnaire. The sampling was done by using non probability snowball technique, where four children were recruited through a non-probability purposive sampling initially, then their friends were traced and request sent to their parents. Finally, the sample size of 300 parents was achieved. Figure 1 presents the method of sampling technique adopted in this study. The questionnaire in the first part confirmed that eligibility criteria that the child has mother or bottle feed after three months (regardless of the feeding pattern during initial three months) and continued feeding for at least one year. The information of the age, weight, performance in mathematics, Sciences and physical activities was asked. The information was gathered in categorical manner where average, below average and above average was considered.

Statistical methods

Data was entered in Statistical package for social sciences (SPSS version 23.0). Categorical variables were analyzed initially for frequency distribution then comparison was made between the groups by using cross-tabs and application of Chi-squared test. A p-value of <0.05 was considered significant. Bar charts were used for presentation of data.

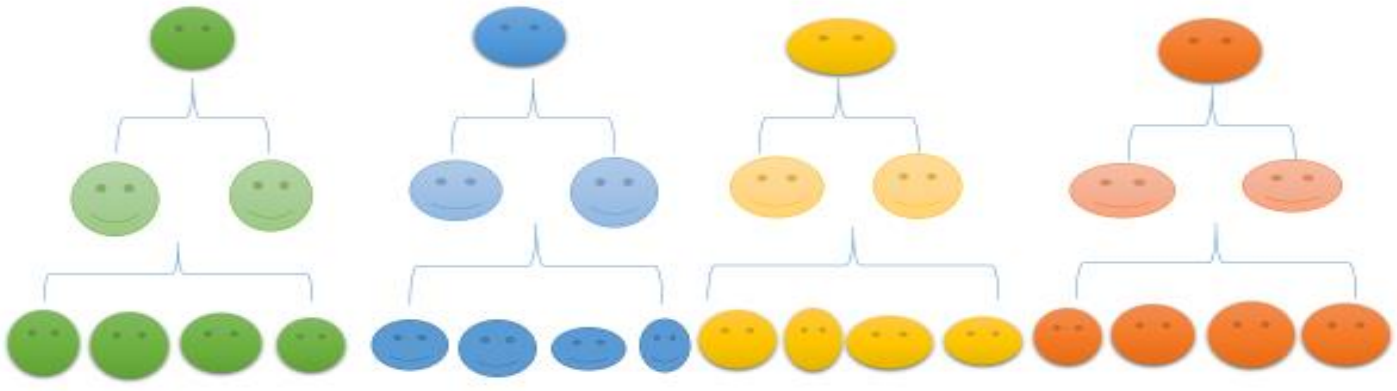

Figure 1. A summary of Snowball sampling method for the study

RESULTS

A total of 251 parents responded to the questionnaires regarding 300 children. Median age of the children was 7 (±SD 1.625) years. Age distribution of participants is given in Figure 2. A summary of the children characteristics is given in Table 1.

Comparison of Bottle feed and mother feed children

Both groups were comparable in age (Figure 3) and there was no significant difference in the weight of the children in both groups (Figure 4). The bottle feed children showed significantly high performance in mathematics (Figure 5), while mother feed children were ahead in their performance in general science subject (Figure 6). The children who were on mother feed were also significantly more physically active as compared to bottle feed children (Figure 7).

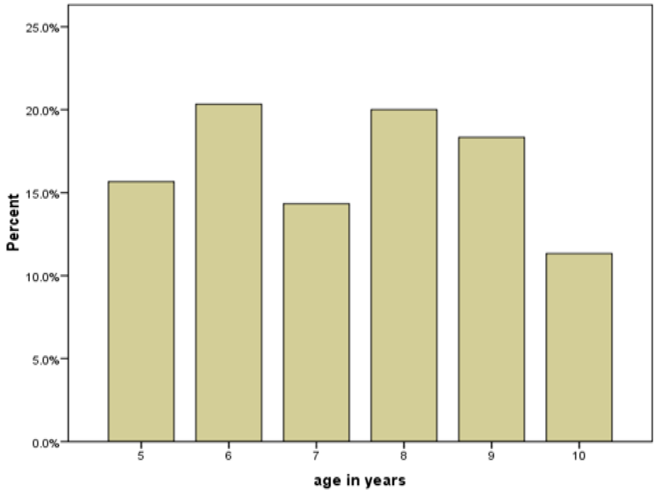

Figure 2. Age distribution of the children included in this study

Table 1. Sumary of weight and school performance in school going children

Parameter	Average N(%)	Below average N(%)	Above average N(%)
Weight	174 (58)	54(18)	72(24)
Performance in Maths	199(66.3)	53(17.7)	48(16.0)
Performance in Sciences	190(63.3)	77(25.7)	33(11.0)
Physical activity	185(61.7)	100(33.3)	15(5.0)

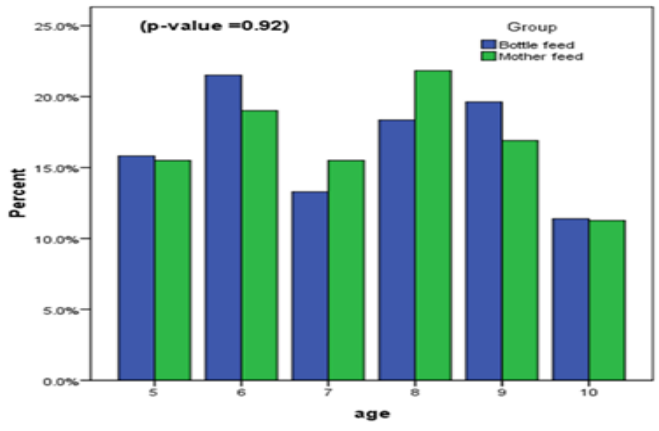

Figure 3. Age distribution of the groups- Mother feed versus Bottle Feed

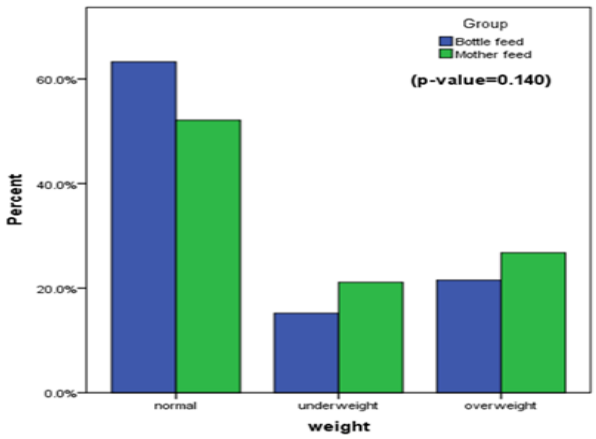

Figure 4. Comparison of weight of the groups- Mother feed versus Bottle Feed

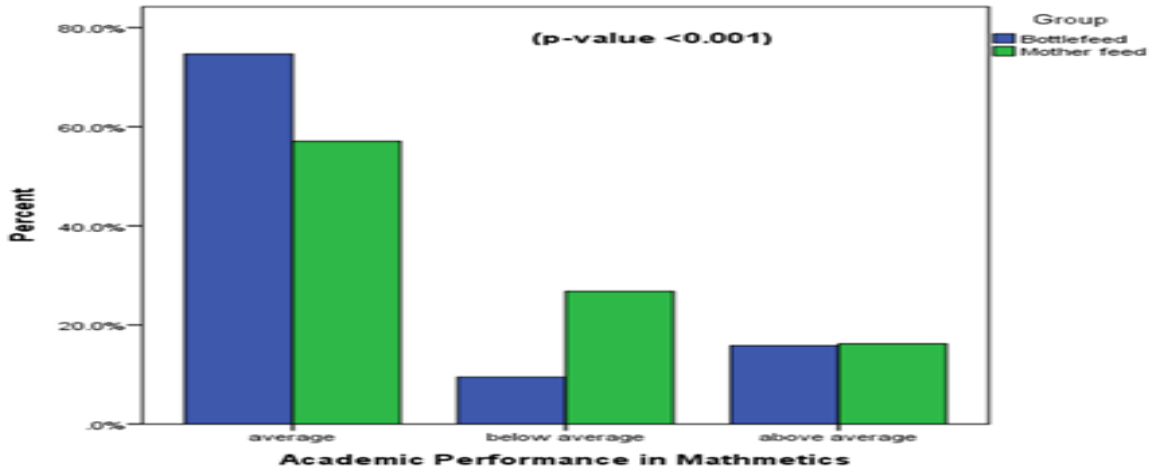

Figure 5. Comparison of Academic performance in Mathmetics- Mother feed versus Bottle feed

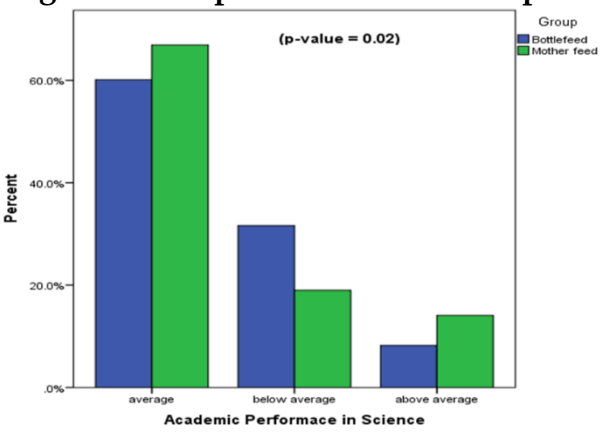

Figure 6. Comparison of Academic performance in Science- Mother feed versus Bottle feed

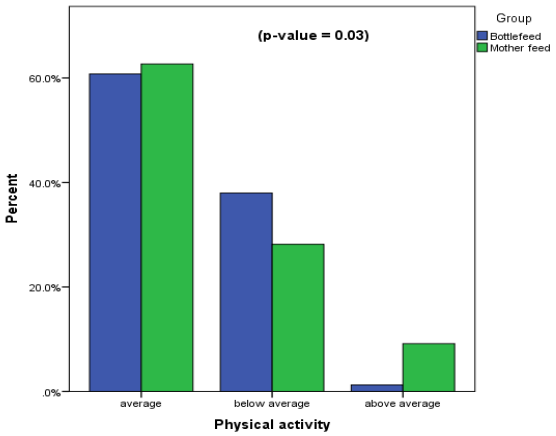

Figure 7. Comparison of physical activity- Mother feed versus Bottle feed

DISCUSSION

The study raises interesting points about the potential impact of feeding methods on academic performance and physical activity in children. Infant feeding is a crucial factor in the child's development, especially in terms of cognitive development and school performance. The nutritional content and the feeding method play a significant role in the cognitive development of the child. The two primary modes of infant feeding are bottle feeding and mother feeding. The debate over which method is better for cognitive development and school performance has been ongoing for many years.

Overall, this study provides important insights into the potential long term impact of feeding methods on child development. It is important to note, however, that every child is unique and may respond differently to different feeding methods. There have been several studies conducted in recent years that have examined the potential relationship between infant feeding and child development. One such study published in the Journal of Pediatrics in 2016 found that breastfed infants showed better cognitive development at 12 months of age, as measured by the Bayley Scales of Infant and Toddler Development(12). The study also found that longer duration of breastfeeding was associated with better scores on cognitive and language development tests. In terms of physical activity, a study published in the Journal Pediatrics in 2019 found that breastfed infants were more physically active at 3 months of age compared to formula-fed infants. The study also found that the duration of breastfeeding was positively associated with physical activity levels(13). It is important to note that while these studies provide important insights into the potential impact of infant feeding on child development, more research is needed to fully understand the complex relationship between these factors. Additionally, every child is unique and may respond differently to different feeding methods.

Additional studies have explored the potential relationship between infant feeding and child development. Another study found that breastfed infants had better mental and psychomotor development scores at 6- and 12-months of age, as measured by the Griffiths Mental Development Scales(14). The study also found that longer duration of breastfeeding was associated with better developmental outcomes.

Another study published in the European Journal of Pediatrics in 2018 found that breastfed infants had better visual and auditory attention compared to formula-fed infants at 6 and 12 months of age(15). The study also found that the duration of breastfeeding was positively associated with attention scores.

Our study is also consistent with existing literature, it is important to note that while the groups were comparable in age and weight, there may have been other factors that influenced the results. For example, socioeconomic status, parental education, and other environmental factors may have played a role in the children's academic performance and physical activity.

That being said, the study found that children who were bottle-fed showed significantly higher performance in mathematics, while those who were breastfed had an advantage in general science subjects. This may be due to the differences in the nutritional composition of breast milk and formula, as breast milk contains important nutrients and antibodies that are not found in formula.

Additionally, the study found that children who were breastfed were significantly more physically active than bottle-fed children. This may be because breastfed infants experience more skin-to-skin contact with their mothers and are more likely to be held and carried, which can promote physical activity and motor development.

It is known that breast milk contains essential nutrients and vitamins that help develop a strong immune system and cognitive abilities in infants(16). Breast milk also helps in the overall development of the child's cognitive, emotional, and social skills(17). Breastfeeding has also been linked to improved cognitive development in areas such as memory, language, and problem-solving.

The study has small sample size and parents were questioned about the past, therefore, there is a little risk of recall bias. The parents were not asked about the type of the formula they gave to their infant this might also influence the results and considered as a limitation of the study. However, this study provides an important insight about long term impact of formula milk.

CONCLUSION

The results of the study suggest that there is long term impact of the type of milk an infant is receiving. The children fed on formula milk showed significantly higher performance in mathmetics while breast fed children are more physically active and showing significantly higher performance in science subjects. Further studies to explore the type of thr formula milk used and its composition and correlation with long term outcome of the children is required.

Ethical Consideration: The study was approved by the local Research Ethics Committee

Conflict of Interest: There is no conflict of interest.

Funding: This study was not funded by any agency

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Research article

COMPARING MUSCLE ENERGY TECHNIQUE (MET) VERSUS CONVENTIONAL PHYSIOTHERAPY IN CASES OF ADHESIVE CAPSULITIS OF SHOULDER- A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT
This study was a randomized controlled trial conducted at Noor Hospital Rawalpindi, Pakistan to compare muscle energy technique (MET) and conventional physiotherapy techniques in patients with confirmed diagnosis of adhesive capsulitis. This study was, conducted between March 2021 to August 2021. A total of 30 participants regardless of gender, aged between 30 to 60 years, with confirmed diagnosis of idiopathic adhesive capsulitis were included. Participants with unstable shoulder fractures and dislocation, thoracic outlet syndrome, rotator cuff injuries, reflex sympathetic syndrome, rheumatoid arthritis, extreme shoulder pain not relieved by any medication or rest were excluded from study. The patients were assigned in experimental (n=15) and control group (n=15) using sealed envelope method. Participants in both groups were assessed at baseline and after 4 weeks. The outcome of the treatment was measured in terms of numeric pain rating scale (NPRS), Shoulder Pain & Disability Index (SPADI) and goniometer for measuring shoulder ROM. The overall mean age of participants was 51.64±5.31 years. The study included 12 (40%) males and 18 (60%) females. After 4 weeks of treatment a significant difference (p-value <0.05) was seen between groups in terms of pain, disability and shoulder ROM. The study concluded that MET is a non-invasive treatment for reducing pain. The MET was also shown to improve functional ability and ROM in patients with adhesive capsulitis in comparison to conventional physical therapy treatment.

Key Words: Adhesive capsulitis, Pain, Range of Motion, Frozen shoulder

INTRODUCTION

Adhesive capsulitis, commonly known as frozen shoulder is a common orthopedic practice complaint, with frequent referral for Physiotherapy. It presents with pain, and progressive reduction in shoulder range of motion, causing significant disability (1). Codman described the term 'frozen shoulder' for the first time in 1934, as a painful condition with progressive loss of mobility and pain when lying on effected side which is a key sign (2). There is no known cause of adhesive capsulitis but the radiographic findings of calcific tendonitis or osteopenia along with fibrosis and contracture of joint capsule are observed in patients (3). It commonly affects females of age between 40 to 60 years. Globally the rate of adhesive capsulitis is reported to be 2-5 % in general, however, the rate in diabetic patients is reported to be higher with a prevalence rate of 10-15% (4, 5). The two significant modifiable risk factors associated with frozen shoulder are diabetes and obesity (6). Adhesive capsulitis is categorized into three progressive patterns: freezing phase (severe diffuse pain), frozen phase (loss of ROM with reduction in pain) and thawing (recovery and gradual return of ROM). Primary adhesive capsulitis is idiopathic, while secondary adhesive capsulitis develops after any pathology like rotator cuff injury, diabetes and stroke (7).

Conservative management for frozen shoulder to relief pain and inflammation include NSAID, steroids given orally or intra-articular (8). Various physical therapy interventions are also used for pain management and to restore function which includes cold and hot packs, active and passive ROM exercises, Codman's exercises, mobilization, stretching and strengthening exercises, TENS, ultrasound and interferential therapy (9). Muscle energy technique (MET) is a non-invasive technique, introduced by Fred Mitchell, for the first time in 1948. The MET helps to stretch a muscle in a unique way, that patient initiates the movement while therapist facilitates the movement (10). The MET is combination of two muscular phenomena including Post Isometric Relaxation (PIR) and Reciprocal Inhibition (RI) (11). The PIR technique was introduced by Karel LeWitt et al in which submaximal isometric contraction of a stretched muscle is performed followed by relaxation and slight stretching of relaxed muscle (12). This technique uses the principle of autogenic inhibition (12). There are a number of different physiotherapy interventions being used to treat adhesive capsulitis. However, there is limited literature available on effects of muscle energy technique in this regard. Therefore, this study was designed to compare the effectiveness of MET with conventional physiotherapy techniques for adhesive capsulitis.

METHODOLOGY

This study was a randomized control trial, conducted at Noor hospital Rawalpindi between March 2021 to August 2021. The study protocol was approved from the ethics review committee of Ibadat International University, Islamabad, Pakistan. Sample size was calculated using online open epi tool. Those who fulfilled inclusion criteria were invited to participate in the study and a detailed treatment protocol was explained to the participants along with the risks and benefits. Those who agreed informed consent was taken. Both male and female gender of age 30 to 60 years, diagnosed with idiopathic adhesive capsulitis were included in this study. Participants with unstable shoulder fractures and dislocation, thoracic outlet syndrome, rotator cuff injuries, reflex sympathetic syndrome, rheumatoid arthritis, extreme shoulder pain not relieved by any medication or rest were excluded from study.

Those patients who agreed were randomized into two groups: experimental group and control group with 15 patients in each group, using sealed envelope method for randomization. Participants in experimental group received MET and conventional Physical therapy while the control group only received conventional physical therapy. The conventional physical therapy included hot pack for 5-8 minutes, passive stretching of muscles, manual therapy glides. The MET for shoulder abduction, flexion, extension, internal rotation and external rotation was done. Therapist provided resistance for 3-5 seconds and participants were asked to use muscle energy against resistance applied by therapist. Participants were then asked to relax for 3 seconds take up the slack and then repeat. MET were given for 6 reps per set and three sets in each session. The conventional physiotherapy for control group included hot pack 7-8 min, passive stretching of pectoralis major, pectoral minor, trapezius, serratus anterior for 20 second with 10 second rest with a repetition of five times in each session. Conventional manual therapy shoulder glides (anterior, posterior, inferior) were given as three sets of 10 reps in each session. The treatment was given to both groups as three sessions per week on alternate days for four weeks (a total of 12 sessions). Participants in both groups were assessed at baseline and after 4 weeks by an experienced physiotherapist. Figure 1 presents summary of study protocol.

The outcome measures used for this study were numeric pain rating scale (NPRS), Shoulder Pain & Disability Index (SPADI) and goniometer for measuring ROM.

Statistical analysis:

Statistical Package for Social Sciences (IBM SPSS, version 24) was used for data collection and analysis. For continuous variables normality test (i.e. Shapiro-Wilk) was applied. Given the normal distribution

of the data all parametric tests were applied to compare two groups. The difference of two groups was considered significant if the p-value was <0.05.

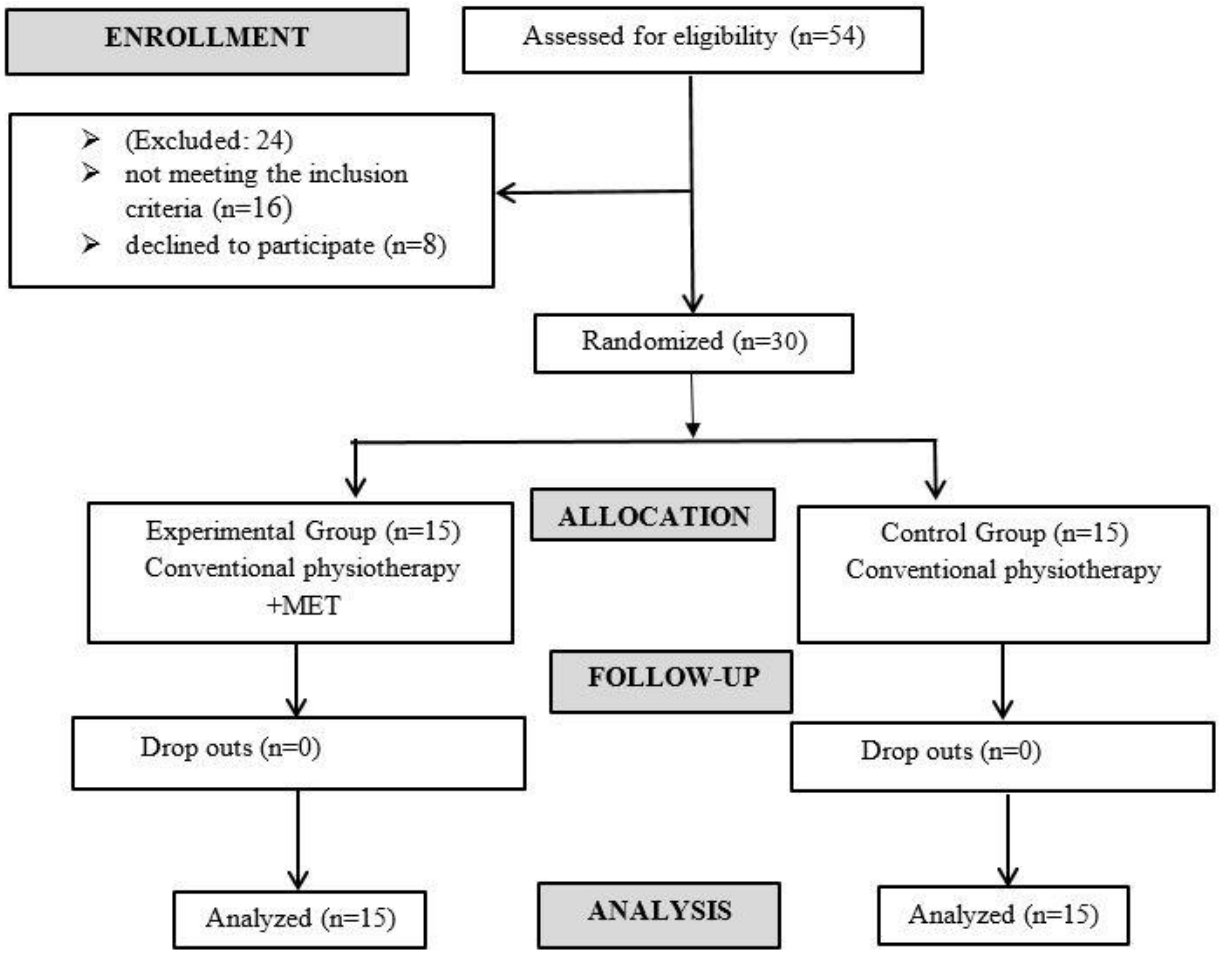

Figure 1: Consolidated Standards for Reporting of Trials (CONSORT) diagram.

RESULTS

Of the 54 participants assessed for eligibility, 24 (44.4%) were excluded and 30 (55.6%) were included in the study trial. There were 15 (50%) participants in each of the two groups (as shown in Figure 1).

The overall mean age of participants was 51.64±5.31 years. The mean age for experimental and control group was 51.13±7.21 years and 53.49±5.23 years respectively. The study included 12 (40%) males and 18 (60%) females. Majority of study participants 53.9% reported right shoulder affected and 46.1% with left shoulder affected.

At baseline all parameters including NPRS, SPDI and shoulder ROM were same in both groups (p-value >0.05). However, after 4 weeks of treatment significant difference (p-value <0.05) was seen between groups in terms of pain, disability and shoulder ROM. A summary of results is given in Table 1 and table 2.

DISCUSSION

The purpose of the current study was to evaluate the effects of muscle energy technique on shoulder pain, disability and ROM in cases of adhesive capsulitis. The study showed that pain, disability and

range of motion improved in both groups respectively. However, if we compare both groups then significant improvements were seen in patients who received MET. The main symptoms of adhesive capsulitis are pain and decrease in range of motion which results in difficulty performing ADLs.

Table 1: Inter-group comparison of shoulder pain and disability

Variables	Groups	At baseline Mean ± SD	P value	After 4weeks Mean ± SD	P value
NPRS	Experimental	7.13±2.14	0.28	2.28±1.43	0.04
	Control	7.41±4.68		4.39±1.57	
SPADI	Experimental	64.30±7.18	0.073	28.69±6.31	0.001
	Control	69.57±5.46		40.35±9.04	

Table 2: Inter-group comparison of shoulder range of motion (ROM)

Shoulder ROM	Groups	At baseline Mean ± SD	P value	After 4weeks Mean ± SD	P value
Flexion	Experimental	100.05±6.24	0.458	162.36±14.35	0.001
	Control	103.40±11.25		134.43±11.61	
Extension	Experimental	39.16±7.13	0.538	48.34±8.26	0.002
	Control	30.65±9.31		36.56±7.11	
Abduction	Experimental	55.73±10.60	0.341	93.37±11.48	0.001
	Control	54.89±13.87		75.34±6.13	
Internal Rotation	Experimental	43.51±6.47	0.312	69.64±10.36	0.001
	Control	40.46±9.33		51.49±13.64	
External Rotation	Experimental	38.37±6.48	0.044	66.54±5.08	0.001
	Control	34.13±7.36		49.71±13.15	

Literature supports the fact that Muscle energy technique improves extensibility of muscle and relaxing the affected muscles by crossing the restriction barriers. Moreover, MET helps in reducing stiffness, pain and provides greater functional gains. Viscoelastic properties and neural factors result in increased range of motion following muscle energy technique (13).

Narayana et al conducted a similar study in 2014 and found that group which was treated with MET showed better results considering scores of SPADI in comparison with group which was treated with conventional physical therapy. They reported that MET was very effective in patients with adhesive capsulitis for improving function of shoulder joint (14). Studies showed that improvement in pain and functional ability is a result of post isometric relaxation caused by application of MET. It is observed that exercises performed within pain free range causes stimulation of mechanoreceptors that modulates pain by activation circulatory pain biomarkers (11). Suri et al conducted a comparative study for effective treatment of shoulder adhesive capsulitis. They found MET to be more effective in comparison with Maitland technique for reducing pain, incorporating mobility and for improving range of motion of shoulder joint (15). Moore et al studied the immediate effects of MET, they concluded that significant

improvement was seen in range of motion of shoulder joint after treating with muscle energy technique (16). In another randomized control study, it seemed that muscle energy technique was more beneficial than mobilization in terms of pain and shoulder functions for patient with adhesive capsulitis (17). The sample size was small so study results cannot be generalized. Moreover, it was a short duration study and no long follow ups were taken are considered as limitations of the study. Thus large scale long term follow-up studies are recommended.

CONCLUSION

The study concluded that MET is a non-invasive effective treatment for reducing pain, improving functional ability and ROM in patients presenting with adhesive capsulitis in comparison to conventional physical therapy treatment.

Ethical Consideration: The study was approved by the local Research Ethics Committee
Conflict of Interest: There is no conflict of interest.
Funding: This study was not funded by any agency

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Research article

ASSESSMENT OF USAGE OF MOBILE APPLICATIONS FOR SELF-CARE IN DIABETIC PATIENTS ATTENDING DENTAL OPD A PRELIMINARY STUDY

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ABSTRACT

Pakistani population is ranked number 3rd in the prevalence of diabetes after India and China. Its self-management has been considered a keystone for the care of the disease. It is imperative to take measures that can help diabetic patients to maintain self-management. Recent advancements in the field of information technology, such as digital applications, might help to create a platform for delivering and managing self-care interventions that would be easily accessible. Thus, this study was designed to evaluate the frequency of utilization of smartphone technology for self-care. A multi-centric, cross-sectional study was conducted. The results of the study showed that most patients use smartphones but only a few users were aware of health applications for self-care of diabetes. Most patients were using health applications for their self-management only when they are in need. In conclusion, most patients in Pakistan use smart phone but they do not utilise health care mobile applications appropriately due to the lack of awareness. Given the increasing number of patients it is essential to provide public health awareness regarding use of these applications so that patients can manage their glycaemic control at home with convenience. This will also reduce burden on health care system.

Key Words: Self-management, Mobile health application, diabetes, awareness

INTRODUCTION

Diabetes has become a worldwide epidemic and a major public health concern (1). It is also considered the most challenging public health problem (2). About 10.5 percent of the global adult population was reported to be suffering from diabetes in 2021 (3). This number is predicted to rise to 643 million by 2030 and 783 million by 2045 (4). It's one of the most expensive diseases, moreover, 3 in 4 adults with diabetes live in low- and middle-income countries. Pakistan has surpassed the United States of America in the number of diabetics and now ranks third in the world in diabetes prevalence following China and India. According to the International Diabetes Federation (IDF), around 33 million people are living with diabetes in the country (5).

Diabetes management differs depending on the type and severity of diabetes (6). Diabetes self-management has been considered a cornerstone of diabetes care for decades, and it is thought to play an important role in preventing micro- and macro-vascular complications (7). Diabetes education, healthy eating, physical activity, medication, health care applications (apps), and device use, monitoring and using patient-generated data to adjust behavior and medication doses, preventing, detecting, and treating acute and chronic complications, coping with psychosocial

issues, and problem-solving are all components of self-management(8). It is imperative to take measures that can assist diabetic patients in maintaining self-management, and many health apps can assist patients in monitoring and tracking their glycemic control.

Information and communication technology (ICT) serves as a conduit for information when dealing with human health issues. Furthermore, advancements in digital technology allowed health applications to greatly assist healthcare professionals and patients. E-health applications used ICT technology for providing better tools for disease self-care and management. Smartphones are now able to run complete laboratory scanning for the diagnosis of diseases at the lowest possible cost i.e. using fewer men power, energy, and less usage of resources(9). The goal of mobile health applications is to provide a preventive healthcare facility just by using smartphones or wireless digital technology to collect, managing it, and can process disease-related data. (10).

A study done by Demido et al. identified top five applications, which were used by diabetes patients, these were based on augmented and customized usability scores (11). A study in America identified 11 unique applications for diabetes. Common application features include tracking blood glucose, HbA1c, medications, physical activity, and weight. Since Pakistan is one of the countries with high prevalence and increasing incidence, but till date there is limited data available to identify the pattern of use of mobile phone applications in the management plan of diabetes. Thus, this study was conducted to identify the rate and pattern of use of health applications and examine their effectiveness in changing health-related behaviors and clinical health outcomes.

METHODOLOGY

This study was a multi-centric cross-sectional descriptive study, conducted at Dow university of Health Sciences and its constituent/affiliated institutions, and other governments and private sectors of Karachi. Samples were selected by using the non-probability convenience sampling technique (Figure 1). Consent was taken from each patient before distributing the questionnaire. The data was collected from patients coming to Out Patients Department (OPD) and online Google form was sent to all the participants.

In-person interview:

A closed-ended, self-administrated, structured questionnaire was distributed among the diabetic patients presenting in OPD. Most of the patients who walked in the Dental OPD were those who were suffering from a poor systemic condition, most of them present with a history of diabetes.

Virtual data:

Online Google forms were shared among diabetic patients through social media tools. The patients for online forms were identified through social media groups.

Survey Questionnaire:

The questionnaire was in the English language and consists of four sections, section 1: the basic demographics, and educational status. Section 2: Diabetic profile, section 3: Problems with diabetes self-care, and section 4: Usage of the app by diabetic patients. All of the responses were recorded on a Likert scale.

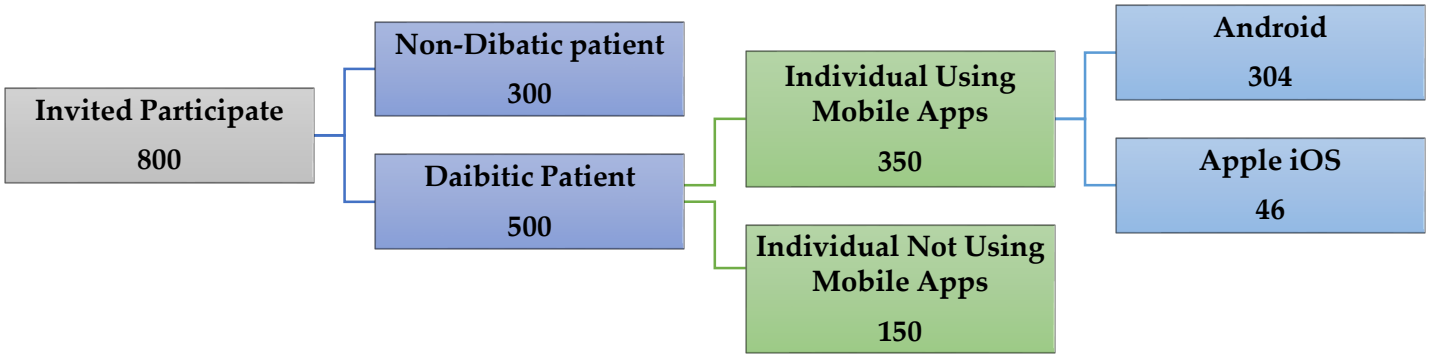

Figure 1. Summary of the patients selected for the study sample

Statistical Analysis:

Data was entered and analyzed using Statistical Package for Social Sciences (IBM-SPSS version 21.0). Mean and standard deviation (SD) were calculated for variables whereas frequency and percentage were calculated by descriptive analysis. Liner model indicates an association between the usage of health apps with educational status by using Chi square test, Results were considered statically significant when the p-value was <0.05.

RESULTS

A total of 800 individuals were invited to take part in this survey, out of which 500 people responded. All were known diabetics. There were 42% males and 58% females. Urban residents were 71% and the remaining 29% were from rural areas. 11% were uneducated, 14% were of below matriculation, 14% did matriculation / O levels, 15% did intermediate/A levels, 255 graduated and 21% were postgraduates (Table 1).

Of the participants, 70% were using smartphones, while 20% were well-skilled and the rest 10% were not very well-skilled. Of 500 diabetic patients, 350 people were using mobile apps to monitor their diabetes, 150 were non-users, 304 were android users, and 46 were apple iOS users as shown in Figure 1. Only 3% of patients had health apps to monitor insulin, and 97% did not have any health apps to monitor insulin. Whereas 13% had health apps that helped track progress on health-related goals, 17% had apps that help them in consultation with healthcare providers, besides this 53% were interested in using apps, and the remaining 47% were not interested, 50.4% recommended apps to the others, and 49.6% didnot recommend apps to others (Table 2).

Among the features of apps, most patients use apps for medication reminders. Other features like blood pressure, blood sugar, fitness, and calories were also used by patients but to a lesser extent. (Figure 2). Most patients are using health apps for their self-management only when they are in need (Figure 3). The number of educated people using health apps was significantly higher. In the multivariate model educational level of diabetic participants using health applications were more likely to be significant for the acceptance of health-related applications in comparison with those who were less educated mean 2.230 (± SD= 1.3894) times.

Table 1: Basic socio-demographic characteristics of the study population.

Gender	Male Female	208 292	42% 58%
Country	Pakistan Abroad	489 11	98% 2%
Living	Urban Rural	355 145	71% 29%
Education	Uneducated	56	11%
	Below matriculation	69	14%
	Matriculation / O levels	71	14%
	Intermediate / A levels	72	14%
	Graduation	127	25%
	Post-Graduation	105	21%

Table 2: Health applications by diabetic patients for their health-related goals

Skilled Using App	Yes, well skilled Not very well skilled Non-skilled	99 252 149	20% 50% 30%
Health App to Monitor Insulin	Yes No	14 486	3% 97%
Helped Track Progress on Health-Related Goals	Yes No	65 435	13% 87%
Helped in Discuss or consultations with Healthcare Provider	Yes No	84 416	17% 83%
Are you interested in using Apps?	Yes No	264 236	53% 47%
Do you recommend Apps to others?	Yes No	252 248	50.4% 49.6%

Table 3. Liner model indicates an association between the usage of health apps with educational status on diabetic patients

Educational status to self-care management by apps	Mean	Std. Deviation	P value
	2.230	1.3894	0.004*

*Denotes statistical significance Chi-square

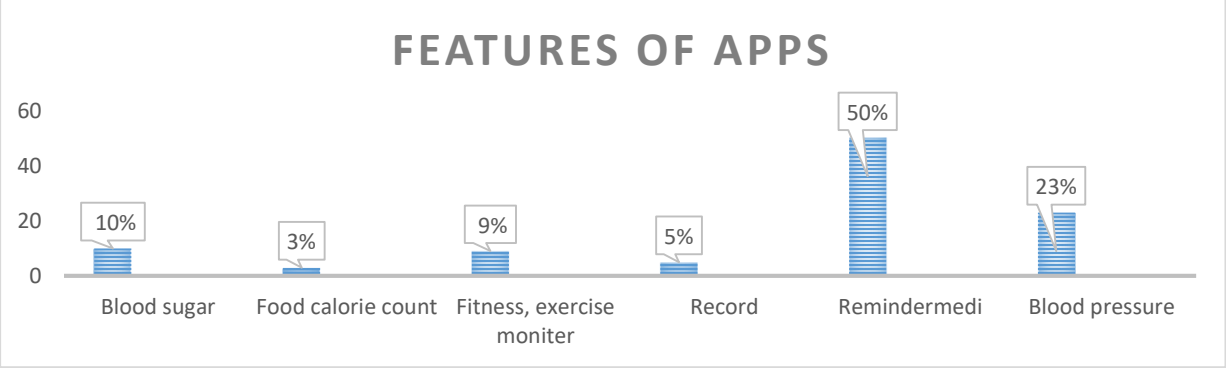

Figure 2: Most commonly used features used by the diabatic patients

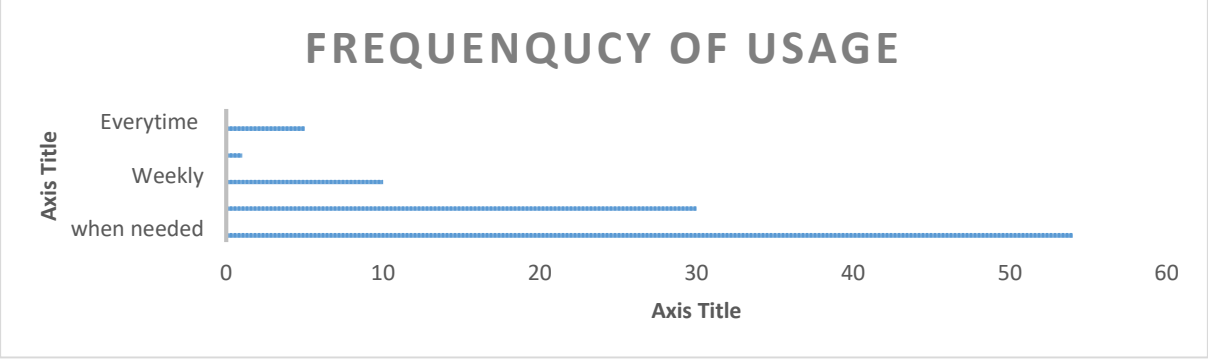

Figure 3: Frequency of usage of health applications by diabetic patients

DISCUSSION

This cross-sectional study observed cumulative and individual levels of self-care, overall, results indicate that most of the population in Pakistan is unaware of health apps that are useful for self-management/care in Diabetic patients. This might indicate less awareness of self-care or due to negligence toward preventive measures. Out of 500 participants in this research, 70% had access to smartphones where only 20% of those were good skilled and the rest of 10% were not skilled enough to the usage of health applications on their smartphones. These results revealed that the usage of health apps by diabetic patients to monitor their diabetes has not yet gained that popularity. Results also indicated that the majority, of the gap, was due to a lack of education. Those who are well-educated are using health apps for their self-management but poorly educated ones were not. As these findings were confirmed by the linear model which indicated a significant association between the usage of health apps for self-care with educational status. The negative usage was also due to the communication gap between doctors and patients. Lack of knowledge and limited access to healthcare facilities were also contributors to limited usage. Similar results were found in the previous study suggesting that the participants were more intrigued to use social media on their smartphones (12). The subjective evaluation shows that almost all of the participants of the study want to learn to use digital technology for health care, similar study done at the University of Malaysia showed that patients are interested in using the apps if they are trained, and facilities are available from healthcare providers (13). Another study also emphasizes the role of education as an integral part of diabetes self-care and management. If patients are educated enough and have access to healthcare facilities then they can use health apps for their self-management (13, 14).

A study reported from America on diabetic patients and showed clinically significant improvement in HbA1c as they used smartphone apps and statistically significant improvement using the app. Patients using apps for diabetes experienced improvements in hypoglycemic episodes. Earlier studies have recommended the top few health applications based on the extensibility of the application features (15, 16).

The limitation of the present study includes a small sample size, so, the results' generalizability is limited. Another limitation of this study was that the non-diabetic group was not compared with the diabetic one concerning the usage of health applications

CONCLUSION

Most patients in Pakistan are not using any health apps for the self-care/ management of diabetes. The lack of usage is mainly because of the absence of education, the gap between healthcare professionals and patients, and limited access to healthcare facilities. Clear policies should be defined in improving access to digital resources regarding the self-management of diabetes.

Ethical Consideration: Ethical considerations: The study was approved by the ethical and review committee of The Dow university of health sciences having an ethical review number (Ref: IRB-2578/DUSH/Approval/2022). Participants were asked to participate if they voluntarily participate, they were also allowed to skip any question if not comfortable answering.

Conflict of Interest: There is no conflict of interest.

Funding: This study was not funded by any agency

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Research article

EVALUATION OF PATTERN OF PRESCRIPTION FOR ASTHMA : A MULTICENTER PROSPECTIVE OBSERVATIONAL STUDY FROM PAKISTAN

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ABSTRACT

Asthma is a common allergic reaction and a number of drugs are available. This study was conducted to evaluate the prescribing pattern and usage of anti-asthma medications at different medical setups in Hyderabad. The study was conducted from August 2017 to July 2018. A total of 1000 patients from different medical setups diagnosed with asthma were recruited. A pre-designed, detailed questionnaire was used for their data collection. Their prescriptions were collected to evaluate and compare them with the standard guidelines of GINA. The prescribing pattern of anti-asthma was assessed regarding the type of therapy, route of administration, single or multiple treatments, class of drugs, doses, and frequency. Demographically, more asthmatics were found to be males (i.e 73.5%), 46.5% were adults, 58.3% from urban areas and 51.68% of the sample had outdoor jobs, while 41.5% of illiterate people were found to be asthmatic. A major type of asthma was persistent at 65.3%. A maximum prescription of 85.5% for asthma management was combined therapy. From long-term use, the monotherapy ICS group was reported in a considerable number (44.13%) (i.e. Beclomethasone in 70% and Budesonide in 7%). Prescriptions of multiple routes of administration were comparatively higher (79.5%). The study concluded that male, young, urban, illiterate and people with outdoor jobs were more likely to get asthma. Preventer drugs were prescribed more in combined therapy, in which Fluticasone + Salmeterol were preferred. The oral inhalational route was selected more. The treatment pattern was consistent with standard guidelines.

Key Words: Asthma, Rationality, Prescriptions, Practice, Pattern, Medications

INTRODUCTION

Asthma is an inflammatory disease of respiratory tract, which creates difficulty in breathing and causes wheezing during breathing (1-3). Asthma is considered a severe disorder with prevalence ranging from 1 to 21% in elders and more than 20 % in 6 to 7 years old children worldwide (4). Globally, one in every two fifty deaths has been accredited to asthma (5,6). Asthma is classified as intermittent and persistent asthma, further categorized as mild, moderate and severe persistent asthma. (7-10). Appropriate drug treatment can improve airway obstructions, thus reducing the severity of asthma (11). The rational management of asthma is considered to reduce the risk factors of asthma, i.e. to prevent recurrent exacerbations of asthma, prevent progressive failure of lung function, and provide appropriate pharmacotherapy with minimal adverse effects. As per the Global Initiative for Asthma (GINA) guidelines, different medications are advised to manage asthma. Therapy includes two categories of medicines. One is the long term used medications, also called control medications or preventers. The second

category is short-term used medications, quick-relief medications or relievers. These medicines include corticosteroids, prolonged and short-acting beta2 agonists, xanthenes derivatives, leukotriene receptor antagonists, mast cell stabilizers, and immunomodulators. These medicines can be used alone or in combination. Biological agents like Omalizumab, Mepolizumab and Dupilumab are also being used to manage severe asthma (2,12). Given the rise in the asthma attacks in cases with sub-optimal treatment asthma management guidelines recommended continuous preventive management as compared to the care done in crisis situation to relieve symptoms (10,13). Despite the availability of standard guidelines and the efficacious medicines through which asthma can be controlled optimally, the survey reports show less asthma control in many countries (14).

Prescription studies are done to evaluate the medication therapy designed by healthcare professionals for any patient suffering from any specific disease. These drug utilization studies have been done in the United States of America at institutions and local healthcare systems. Early studies were done to analyze the quality of prescribing patterns, especially in the case of antibiotics and Europe. These studies were quantitative in which, as per time and geography using, patterns of specific drug groups were compared and described. These studies showed significant variations in the utilization of many pharmaceutical drugs like anti-hypertensive, NSAIDs, Antidiabetics, antibiotics, psychotropic and lipid-lowering drugs (15).

However, there is limited literature available to study pattern of the prescriptions and how they meet the guidelines. Therefore, this study was designed to evaluate the pattern of prescription of anti-asthmatic medication and the medication usage. This study will also evaluate and compare the practice pattern of healthcare professionals of efficacious medications with the available standard guidelines.

METHODOLOGY

This was a prospective observational study conducted over 12 months, from August 2017 to July 2018 in different medical setups at Hyderabad, Sindh, Pakistan including 1000 patients. After getting consent from patients and their caretakers, the questionnaire was filled regarding their demographics, including age, gender, education, locality, occupation, and type of asthma. Non probability convenient sampling technique was adopted for this study where those who were diagnosed with asthma were invited to be part of the study. The patients of age over five years diagnosed with any asthma-like mild, moderate or severe asthma were selected and those of age less than five years and suffering from other chest problems like Chronic Obstructive Pulmonary Disease, Tuberculosis Bacillus, Pneumonia and Lung cancer were excluded from the study. Both indoor patients and outdoor patients were included. This study also included the patients who were on their routine follow up and even if they were hospitalized. The drug therapy was analyzed regarding the practice pattern like monotherapy or combined therapy, type of therapy, class of drugs, selection of molecules of each class and route of administration.

RESULTS

A total of 1000 patients were included in this study. There were 73.5 % males and 26.5% female patients. The younger population between 12 to 39 years were predominant (46.5%), followed by the children between 6 to11 years of age (33.7%) and 19.8% were older population (40+ years age). Urban population were represented more i.e. 58.3%. A 41.5% of asthmatic patients were illiterate followed by those having primary and basic education (34.5%) and university-level education (24%). Considerable number were 49.7% jobless, and those in indoor or outdoor job patients were 48.31% and 51.68%, respectively.

Pattern of prescriptions in asthma patients

A total of 25% of prescriptions came from public sector health care facility while 75% were from charity hospitals or private sector medical setups. More than 65.3% of patients were found with persistent type asthma compared to intermittent asthma found in 34.7% of patients (Figure 1). Prescriptions of monotherapy were less than 14.5% as compared to combined therapy at 85.5%. Among long-term use, mono therapy's maximum ratio of prescriptions was inhaled corticosteroids at 44.13% and a minimum usage was observed of oral corticosteroids at 2.7%. Other classes of drugs like long acting beta agonists (LABAs) 22.75%, Leukoterine inhibitors (LTIs) 17.24%

and xanthine derivatives at 4.13% were prescribed. Amongst the Inhaled corticosteroids (ICS) group, contained Beclomethasone, and budesonide. In the combined therapy, highest number of prescriptions were the combination of ICS+LABA's at 35.20%, and the lowest number was a combination of ICS+ LABA's+ LTI's at 2.10%. A summary of the drug prescription pattern is presented in Table 1. Subsequently, 79.5% of prescriptions contained multiple routes and 20.5% single routes. From multiple routes, the highest number (n=590) prescriptions were found with oral inhalation route of administration (Figure 2).

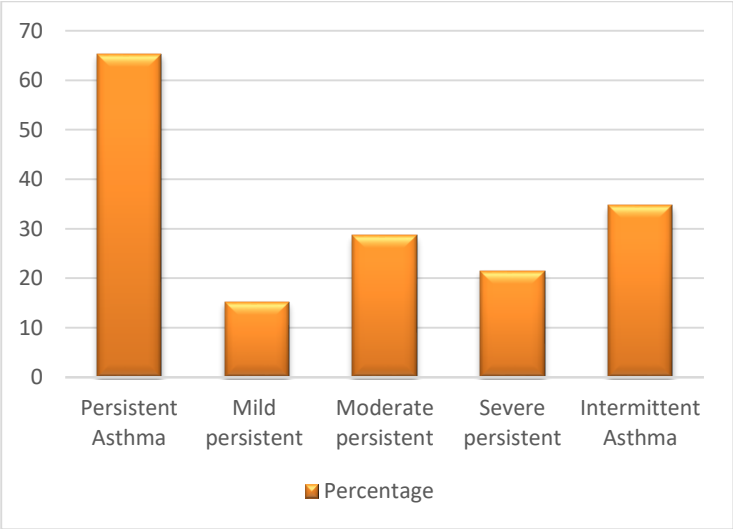

Figure 1. A summary of the types of Asthma found in Patients recruited in this study

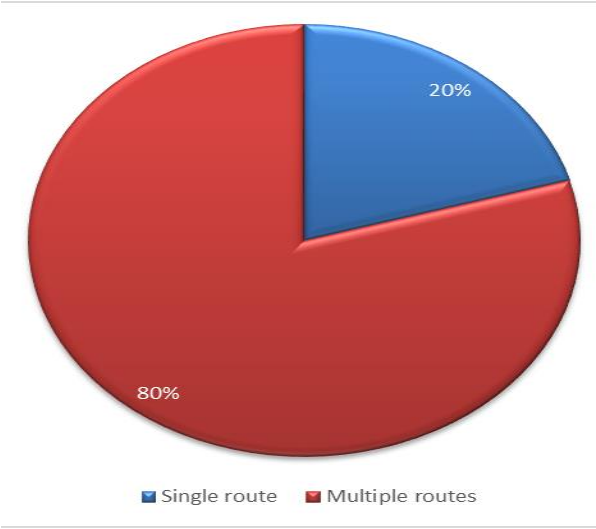

Figure 2. Pattern of route of administration of asthma patients

Table-1. A summary of the pattern of Different Classes of drugs prescribed for Asthma

Type Of Therapy		Monotherapy (Total 14.5%)		Combined Therapy (Total 85.5%)	
	Maximum Prescribed	Inhaled Corticosteroids (44.13%)		ICS+LABA's (35.20%)	
		Beclomethasone 70.31%	Budesonide 7.81%	Fluticasone + Salmeterol 56.47 %	Budesonide + Formoterol 18.27 %
	Minimum Prescribed	Oral corticosteroids (2.7%)		ICS+SABA's+LTI's (2.10%)	
		Prednisone 75% (Maximum)		Fluticasone+Albuterol+Montelukast 72.22%	
		Prednisolone 25% (Minimum)		Budesonide+Albuterol+Montelukast 5.55%	

ICS= Inhaled Corticosteroids, LABA's=Long Acting Beta Agonists, LTI's= Leukotriene Inhibitors

DISCUSSION

Prescription studies are done for many purposes, such as the evaluation of prescribing pattern or trend or attitude of physicians, drug utilization, knowing the implementation of recommended guidelines, evaluating the

rationality of prescriptions by comparing with the standard international policies like Global Initiative for Asthma (GINA) for anti-asthma medications (1, 4). A few studies, including a retrospective study on drug utilization in asthmatic patients in India conducted by Basavaraju, focused on the type of anti-asthma medications and the routes of administration and also report the frequent use of combined therapy in the management of asthma (16). Other related studies have also been reported from India and Turkey which presented the prescribing pattern and drug utilization in asthmatic patients (17, 18). The study by Shalini suggested improvement in current practice trends for rational and better drug utilization (18). On the other hand, Haluk's study showed that the prescription containing the steroids and short acting beta agonists (SABAs) group and an anticholinergic drugs were utilized as per guidelines (17). The selection of therapy was based on the type of asthma which was decided by the occurrence or the frequency of reported symptoms (1,5). Other factors related to patients such as age were also considered before deciding to start the treatment of asthma (11). The GINA guidelines for anti-asthma medications have recommended and classified the treatment plan of asthma into five steps; in each step, a specific class or classes of drugs can be prescribed as single or combined therapy that can be done based on the severity of asthma, frequency of symptoms, patient age and lung function condition (1, 6). From our study, the prescribing pattern of physicians shows that the use ICS class of drugs is preferably prescribed as monotherapy prescription. In guidelines, ICS are also preferred as a single therapy in step two of the treatment plan. Many prescriptions of combined therapy contain the ICS+LABA's which are also recommended in step two of the guidelines. Amongst these ICS+LABAs, the currently approved combination includes Budesonide + Formoterol; the results of our study are consistent with these guidelines. In our research, another variety of ICS+LABAs found was Fluticasone + Salmeterol, it is also mentioned in guidelines (1, 6). Triple therapy is also mentioned in the guidelines, which can be given in steps from three to five. In our study, drug classes prescribed as triple therapy were ICS+ LABA's+ LTI's. In guidelines like in step three, two controllers and one reliever can be given. Theophylline can also be given along with ICS and LTI's combination as stated in the guidelines. This study shows that in the majority of prescriptions, multiple routes of administration were selected for therapy. Both routes in combination were found in 59.2% of drugs for oral and inhalation. The parenteral route was also used in combination with the oral route. The findings of this study show that prescribing patterns or attitudes of prescribers are maximally matching with guidelines of GINA in selecting the type of drug class, types of therapy like monotherapy or polytherapy and also the routes of administration. Findings suggest that this attitude is somewhat the same as that of Turkish and Indian prescribers in treating asthma regarding a few aspects like type of therapy and routes of administration. This is the most critical finding of this study, which shows that GINA guidelines are being used and implemented here, which has a significant role in managing asthma and decreasing its load. But there are few other findings in prescribing patterns compared to related studies such that in this study, the choice of therapy to attack asthma is LABA seen more, and this is one of the appropriate selections of the drug. The study did not include clinical parameters of the clinical progress as response to therapy, the dose of the prescribed drugs and the duration were not included in this study, which is considered as a limitation.

CONCLUSION

The study concludes that more males patients, younger in age and dwelling in urban areas were presented with Asthma. Primary patients had intermittent asthma. Preferably combined therapy was found with most ICS+LABA groups of medications in which Fluticasone + Salmeterol were used more than Budesonide + Formoterol. Multiple routes like oral inhalational were used more frequently to manage asthma. Overall the management pattern followed the guidelines.

Declaration: This study is part of PhD Thesis of Syed Muhammad Mubashir Shah conducted at University of Sindh.

Ethical Consideration: The study was approved by the local Research Ethics Committee

Conflict of Interest: There is no conflict of interest.

Funding: This study was not funded by any agency

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Research article

INVOLUTION OF UNILATERAL MULTICYSTIC DYSPLASTIC KIDNEY: LONG TERM DATA FROM A SINGLE CENTER

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ABSTRACT

Unilateral multicystic dysplastic kidney (MCDK) is congenital anomaly which can be detected by ultrasound during antenatal period. The reported rate of MCDK ranges between 1 in 2,200 to 1 in 4,300 live births. This study was aimed to assess the determinants associated with the MCDK with follow-up until teens to evaluate the evolution of the disorder. This was an observational longitudinal study, involution degrees were observed following the baseline measurement of the size of the MCDK as documented on postnatal ultrasound, and long-term complications and renal function were also recorded. A total of 350 patients were identified, while 90 patients fulfilled the criteria of the study and completed the study duration of 10 years. Out of which 19 (21.1%) patients reported involution of MCDK size during follow-up as complete and partial, 7 (7.7%) within first year of age, 5 (5.5%) during first 2 years and 7 (7.7%) within 4 years of age. Large-sized MCDK at the time of diagnosis is less likely to involute through the first decade of life. However, conventional treatment is rational with the absence of complications.

Key Words: Multicystic Dysplastic Kidney, Solitary functioning Kidney, Involution of MCDK

INTRODUCTION

Multicystic dysplastic kidney (MCDK) is a congenital renal anomaly causing chronic renal failure in children (1). It is histologically characterized by abnormal and incomplete differentiation of metanephric mesenchymal tissue and ureteric buds, having fibromuscular tissue around the cysts (2). Unilateral Multicystic dysplastic kidney is commonly diagnosed during antenatal ultrasound. It's rate of occurrence ranging from 1 in 2,200 to 1 in 4,300 live births (3). The prevalence is higher in male fetuses, especially bilateral MCDK associated with oligohydramnios (4). Involution of MCDK with time has been reported in many studies, longer follow-up studies identified an increased risk of hypertension and renal malignancies in MCDK patients with time (5). The literature suggesting etiology of MCDK remains inconsistent, where some studies suggested positive relation with familial risk where there was a history of solitary kidney in first family members and MCDK incidents (6). However, associated disorders such as hypospadias, bladder diverticulum, Ehler-Danlos syndrome, and DiGeorge syndrome are known to be linked with MCDK (7).

The histopathological differences between polycystic kidney and MCDK are the presence of scanty and dysplastic abnormal cells between cysts and the absence of parenchyma in MCDK (8). Although conservative management

of MCDK has been acknowledged as an improved management route instead of nephrectomy but the literature is still not sufficient as the follow-up of an MCDK child till adulthood is limited (9). First identification of MCDK is usually through antenatal ultrasonography, or fetal abnormality scan performed in many established health care setups to identify any anatomical abnormality in the fetus before delivery. The number of antenatal MCDK documentation is not done in routine clinical practice as antenatal ultrasonography is not an established regulation in all obstetric setups. If not identified in antenatal scans, the child may present with palpable abdominal mass. Vesicoureteral reflux (VUR) is reported to be seen in 20% of MCDK cases, while pelvic ureter junction obstruction (PUJO) can also be seen on the contralateral side of MCDK as additional findings (10). The kidney with moderate to severe hydronephrosis may be identified as PUJO (11). The management choices include a conventional method of investigation of the kidney dimension based on ultrasonography as MCDK usually endure involution by the age of 10 years. This observation also aids in identifying malignant variations or obstructive features in the contralateral kidney (12, 13). Though the condition is not very rare in Pakistan but there is limited literature available. Therefore, this was conducted aimed is to assess the frequency of MCDK in children presented in our institute, and the determinants associated with the disease with follow-up to ten years to evaluate the progression of the disorder

METHODOLOGY

Study Design:

This was a longitudinal observational study conducted in the Pediatric urology department of Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan. Institutional approval from the ethical committee was obtained to conduct the study. The patients were enrolled via eligibility criteria of presented in the hospital within first month of life with unilateral MCDK. All the bilateral cases of MCDK were excluded from the study. Upon successful enrollment the demographic details were obtained from medical records starting 2012 till 2022, a total of 10 years of data was used to assess follow-up and involution of MCDK.

A total of 350 patients was brought in and 90 patients were deemed eligible to be recruited in this study and they were evaluated for involution frequency and determinants of MCDK.

Involution:

Involution suggests the reduction in the number or dimension of the multiple cysts present in kidneys. Whereas complete involution is the significant loss of cyst, and partial involution was taken as a reduction in the number or size of cysts. The baseline at the first encounter was considered as the initiation point while disease initiation was taken as the date of child birth, while the endpoint was the date when imaging showed no residual cysts or the last follow-up.

Complications:

An increase in Serum creatinine and blood pressure was monitored as complications along with radiological investigations, documented urinary tract infections, or any sign of lower urinary tract symptoms (LUTS) were also analyzed. Vesicoureteral reflux was identified as an associated complication on the contralateral side.

Statistical Methods

The data was entered and analyzed in Statistical package of social sciences (SPSS version 22.0), mean and standard deviation (±SD) were calculated for age, and years of MCDK diagnosis. The size on follow-up ultrasound were defined as Stasis of MCDK (Similar to the first measurement), Decrease in MCDK measurement (size reduction), and, growth in MCDK (increase in size). A p-value of <0.05 was considered significant.

RESULTS

A total of 90 children were enrolled in the study for 10 years, the mean age at presentation was 93.2 ± 137.3 days, with 70 (77.8%) males and 20 (22.2%) females. 06 (6.7%) of the children were diagnosed during antenatal radiological investigations while 84 (93.3%) were diagnosed post-delivery and referred to the urology department. Laterality of MCDK was 13 (14.5%) on the right side while 39 (43.3%) on the left side. The associated factors were

reported as twin pregnancy in 7 (7.8%) and intrauterine growth restriction in 3(3.3%) of patients. While in antenatal scans amniotic liquor quantity was adequate in 81 (90%) of the patients, only 9 (10%) reported inadequate liquor during pregnancy scan. A summary is presented in Table 01. The mean serum creatinine at the time of presentation was 0.4 ± 0.1 mg/dL. Upon follow-up 07 (7.8%) children indicated an increase in MCDK size within one year (in 1 patient), at 4 years of age (in 1 patient), and at 8 years (1 patient). A summary of the duration is given in Figure 01. The size increase in these subjects was measured between 3.1 – 4.0 cms to 6.1 – 7.0 cms, and 02 patients with maximum size improvements proceeded with nephrectomy to avoid the relevant risk of malignancy. The MCDK was reportedly decreased in the size in 19 (21.1%) patients after conservative management and in-depth evaluation during follow-up. Involution was identified in 7 (7.7%) patients within the first year of age, while 5 (5.5%) within 2 years and another 7 (7.7%) in 4 years of age. A summary is given in Figure 2. Involution was documented as complete, partial, and unchanged. With respective of laterality of MCDK, results indicated that right (n=13) sided MCDK showed partial involution in 5 (5.5%) patients while 2 (2.2%) patients were unchanged. The left (n=77) sided MCDK indicated complete involution in 2 (2.2%) patients, 12 (13.3%) showed particle involution and 33(36.6%) were unchanged. The contralateral side showed pelvic ureter junction obstruction in 3 (3.3%), while vesicoureteral reflux was diagnosed in 5 (5.5%) of patients.

Table I: Demographic details of Multicystic dysplastic kidney (MCDK) children presented in Out Patient Department

Details of study subjects		
Variables (n=90)		Frequency N(%)
Gender	Male	70 (77.8%)
	Female	20 (22.2%)
Presentation	Antenatal	6 (6.7%)
	Postnatal	84 (93.3%)
Referral	Primary	51 (56.7%)
	Secondary	39 (43.3%)
MCDK side	Right	13 (14.5)
	Left	77 (85.6%)
Associated factors	Twin pregnancy	7 (7.8%)
	IUGR	3 (3.3%)
	None	80 (88.9%)
Liquor quantity	Adequate	81 (90%)
	Not adequate	9 (10%)
Term on delivery	Full term	81 (90%)
	Preterm	9 (10%)

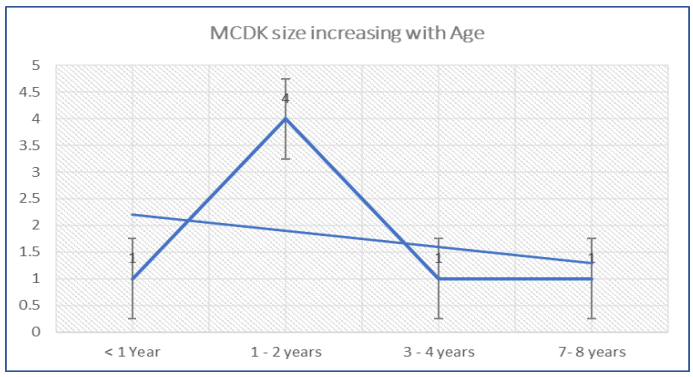

Figure 1. Frequency of MCDK size improvement with advancement in age of study subjects

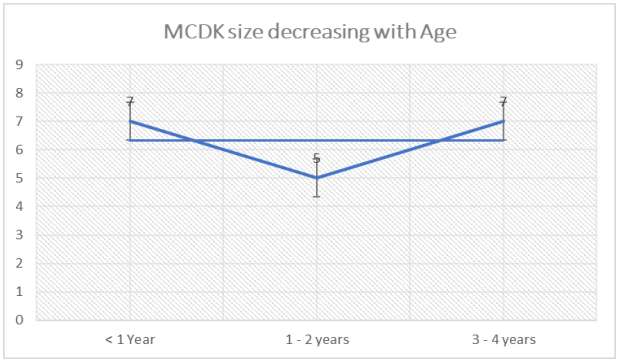

Figure 2. Frequency of MCDK size declines with advancement in age of study subjects

DISCUSSION

This study evaluated the involution of unilateral MCDK presented in single-center, our results indicated the maximum involution within first 10 years of age. Multicystic dysplastic kidney frequently seen congenital anomaly in children in urology practice, with a risk renal failure later in life. The renal abnormality developed during fetal development at gestational age with a higher prevalence in male infants as compared to females (14). The diagnosis during the antenatal scan is less frequent in developing countries, the reason for minimal antenatal diagnosis of renal anomalies including MCDK might be limited access to antenatal care and denial of radiological investigations during pregnancy by parents. This limitation of antenatal diagnosis has been reported in prior studies as well (15-16). Twin pregnancy was associated with congenital anatomical abnormalities in the fetus, in this study 7 (7.8%) of infants were twins, and intrauterine growth restriction was presented in 3 (3.3%) of infants indicating minimal risk of MCDK in IUGR children, this was also reported in previous studies (17). The literature supported our results as studies evaluated maximum positive involution, complete or partial before adulthood. MCDK size was reported as increased during the first 7 years of age with a maximum of 4.00 cms from the first reported size of MCDK, another study indicated a 15% MCDK increase requiring nephrectomy, while another study of 46 patients reported a 39.1% increase in MCDK size during the first year of age (13,18). While partial involution of MCDK was previously reported in 40.9% on the right side while 50% on the left side, however, in our study partial involution was reported as 5.5% and 13.3% on right and left sides respectively. While complete involution was reported in 27.2% of the same study, our study had 2.2% of complete involution of patients 19. The reason for the drastic difference in the involution rates between these studies is probably follow-up duration. We have evaluated patients for a longer period as compared to previously reported studies. Associated problems such as vesico ureter reflux, pelvic ureter junction obstruction, and hydronephrosis were identified in 5 (5.5%) and 3 (3.3%) respectively on the contralateral side of the affected kidney in our study. A previously reported study including 80 children diagnosed with MCDK reported VUR in 13 (16.3%) children while PUJO was in 2 (2.5%) only (20). Other congenital anatomical abnormalities of the renal system were not reported except for recurrent urinary tract symptoms in our study. Nephrectomy was performed in 2 (2.2%) of patients indicating a ≤ 4.0 cms increase in MCDK size, another study reported 7 (5.5%) nephrectomies due to improved MCDK size (21).

This study was reported from a single center with long term follow-up. However, the sample size was smaller, which is considered as the limitation of the study. The follow-up was also shorter, further long term follow-up and regular measurement of eGFR is also suggested to be evaluated to understand natural progression of the disorder.

CONCLUSION

The study concluded that a small number of patient cyst involute with passage of time, though large-sized MCDK at the time of diagnosis is less expected to involute through the first decade of life. However, conventional treatment is rational with absence of complications. Further long term follow-up studies are recommended to understand the disorder so that proper management guidelines can be designed.

Ethical Consideration: The study was approved by local Research Ethics Committee
Conflict of Interest: There is no conflict of interest.
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