ISSN-p: 2664-5734

ISSN-o:2709-5878

Liaquat Medical Research Journal

Quarterly

1 April – 31June2020

VOL. 2, No. 2, 2020

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Liaquat Medical Research Journal is the print, online, double blind, peer-reviewed, quarterly released journal devoted to publishing innovative biomedical research and scholastic / academic content from all fields of medical sciences, concentrating on innovative clinical, diagnostic and perspective preventive research.

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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Liaquat Medical Research Journal

is the official journal of the Liaquat University of Medical & Health Sciences, Jamshoro, Sindh, Pakistan.

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Research Articles

Research article

Bilateral axillary accessory Breasts with multiple fibroadenomas

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LMRJ.2020:2(2)
DOI: 10.3810/LMRJ.2020.2.2.01

Received: 2 Jan 2020
Revised:14 Feb 2020
Accepted for publication 19 Feb 2020

INTRODUCTION:

Developmental anomalies of the breasts are rare presenting complaints. They occur along the milk line of the mammary gland development, which extends from axilla to groin. These anomalies include accessory breasts (polymastia), absent breasts (amastia) and accessory nipples (polythelia). The development of accessory breasts is seen in 2- 6 % of normal population [1], the incidence in females being twice as higher as compared to males. The most common site of accessory breasts is in the axilla, where they are seen in about 70% of cases [2], comprising 23.2% of all axillary lumps, but they can occur at ectopic sites anywhere in the body. We report a clinical case of multiple fibroadenomas in bilateral axillary accessory breast tissues.

CASE REPORT

A 41 years old woman was referred to our breast unit with a lump in the right axilla for 4 weeks. The lump was painless without any history of discharge. There was no association with menstrual cycle and there was no known family history of breast cancer. She had two children.

On examination, she had bilateral accessory breasts with a 1 cm nodule in the right axillary accessory breast tissue. Ultrasound of both axillae confirmed accessory breasts on both sides and showed a 10 mm lump consistent with a lymph node in the right axilla. An ultrasound guided core biopsy was taken. Histopathology of the core biopsy, however, revealed it be a fibroadenoma. As per patient's wishes, bilateral accessory breast tissues were excised along with the aforementioned nodule in the right side. Histopathological examination of the tissues confirmed bilateral accessory breast tissues with multiple fibroadenomas.

DISCUSSION:

The breast development begins at about 6 weeks of intrauterine life as mammary ridge bilaterally on the ventral surface of embryo extending from axilla to groin and by the end of 6 months has multiple duct systems. This ridge then starts to regress and at birth a single fully developed duct system remains which is capable of lactation in both sexes. The accessory breast and nipple develop as a result of incomplete regression of the mammary ridge.

Accessory breasts contain normal breast parenchyma; hence they too can be the site of spectrum of diseases which affect normal breasts, including fibroadenoma and carcinoma. The incidence of the diseases in the accessory breasts is quite low resulting in delay in the diagnosis. The most common site of accessory breasts is the axilla (about 60- 70% of cases [4]), and they are usually bilateral. They can present anywhere from axilla to the groin. In females the mammary ridge extends to the vulva bilaterally, therefore accessory breast tissue can be found in the external genitalia. These accessory breast tissues become evident during pregnancy and lactation and also show some cyclical changes under the influence of the sex hormones.

Majority of the cases of the accessory breasts are asymptomatic and may be found incidentally on the imaging done for some other reason. Histopathological examination is mostly required to confirm the diagnosis. In the axilla, accessory breast tissue can be found separately from the axillary tail, and this confirms its independent entity.

The incidence of fibroadenoma in the accessory breast is extremely low and as reported by Alghamdi et al, it is only 1.51% [2]. To date only few cases of fibroadenomas in the ectopic breast have been reported. Most of the reported cases of fibroadenoma in the accessory breast are in the axilla although a case of fibroadenoma in accessory breast in pubic area has been reported [5] . In another case ectopic breast tissue in the perianal region was found to contain a fibroadenoma [6] .

Literature also comments on the presence of ectopic breast tissue on the face, neck, back, thigh and perianal region[7]. Therefore, any of these sites can be a possible presentation site for fibroadenoma or even carcinoma of the accessory or ectopic breast tissue.

Due to the low incidence of these cases and thus low suspicion rate, majority of these cases are mistakenly diagnosed as lymphadenopathy and lipomas or even sebaceous cysts. Fibroadenoma in the axillary accessory tissue is often misdiagnosed as lymph node even on ultrasound as in our case. The only reliable and confirmatory method of diagnosis is the histopathology.

Both the accessory breasts and the fibroadenomas do not usually require any treatment but on the wish of the patients these may be excised so as to reduce the anxiety of the patients due to apprehension of development of cancer; and also for cosmetic reasons and symptomatic accessory tissues. Alghamdi et al reported the reasons for excision of the accessory breasts as cosmetic, pain and discomfort, cyclical mastalgia, fear of malignancy and lactational abscess[2]. However, cosmetic disfigurement remains the reason in majority of cases.

The literature available is controversial regarding the association of congenital breast anomalies with the renal and cardiac malformations. Previously in some studies [8] it has been suggested that the breast anomalies might be a marker of the underlying anomalies of the urogenital system and cardiac system. Therefore, thorough examination of these systems is recommended in patients presenting with accessory nipples and breast, but other studies [8] on the subject did not show any association.

In the case of our patient there was no clinical history, symptoms or signs attributable to any of these systems so the patient was discharged from further follow-up.

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Review article

Metabolic Syndrome, telomere length and Aging- A review of literature

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This article may be sighted as: Devrajani.T. Metabolic Syndrome, telomere length and Aging-Review of literature. LMRJ.2020; 2(2) Doi:10.38106/LMRJ.2020.2.2-02

Abstract
Metabolic syndrome is reportedly one of the key health concerns worldwide. It is defined as a group of conditions including hypertension, dysglycemia, and abdominal obesity. The wear and tear of telomeres is known to be a major incident not only in mammalian aging, but also in distressed nutrient sensing, which may contribute to a number of metabolic dysfunctions. The metabolic syndrome was linked to the growing prevalence of obesity, which is at rise invariably in all age groups including elderly. The existing literature review focuses on the relationship of shorting of telomere and metabolic syndrome. As the shortening of telomeres influence cellular senescence and eventual stoppage of cell division. It is reviewed that the increasing number patients of the metabolic syndrome significantly affecting aging process by early diminishing the telomere lengthening.

Key words: Metabolic Syndrome, Telomere Length, Aging

Introduction

The metabolic syndrome (MetS) is a group of metabolic derangements resulting in acluster of clinical presentations including hypertension, diabetes mellitus and hypercholestrolemia. In 2005, a meeting planned by the International Diabetes Federation (IDF) put forward the first united agreement on the definition of Metabolic Syndrome. The IDF criteria for MetS was, central obesity with specific values according to ethnicity (ie waist circumference (WC) for European males must be greater than 94 cm and females must be greater than 80 cm; Japanese, Chinese and South Asian males must be greater than 90 cm and females must be greater than 80 cm. For Sub-Saharan Africans and Middle East and Eastern Mediterranean populace, European criteria is being used, for Central and South Americans, South Asian criteria is being used) with presence of any two from the following four characteristics:

1. HDL-cholesterol in males below 40 mg/dl and in females below 50 mg/dl,

2. Triglycerides equal to or greater than 150 mg/dl,

3. Fasting glucose equal to or greater than 100 mg/dl,

4. BP equal to or greater than 130/85 mmHg

Obesity is measured by using the Body Mass Index (BMI) and WC, which is stated as a key causative factor. Besides abdominal obesity, other factors are also required to be considered in the diagnosis of metabolic syndrome include the assessment of triglycerides, blood pressure, fasting blood glucose, or reduced lipoprotein cholesterol levels.(1) The pathophysiology of the metabolic syndrome is very complex and yet uncertain. A considerable number of patients have a sedentary life style, with advanced age, usually showing insulin resistance. The influencing factors include advancing age, genetics, increase weight, excess caloric intake and lifestyle.(2) Though, in spite of the significance of obesity people may not show signs of insulin resistance, occasionally others with normal weight can be resistant to insulin eventually ending up with metabolic syndrome.(3) The Adult Treatment Panel-III, according to the commonly inferred definition, is used to diagnose a metabolic syndrome when no less than 3 out of 5 of the following variants were found:

1. Visceral obesity (waist circumference of more than 102 cm in males or greater than 88 cm in females);

2. Dysglycemia (fasting blood glucose > 100 mg dL);

3. Elevated blood pressure (more than 130/85 mm Hg);

4. Elevated levels of blood lipids.(4,5)

It is established that metabolic syndrome accounts for a significant pathophysiological combinations to study metabolic process within animal models and humans. This results in an increased risk of cardiovascular disease as a peripheral or coronary atherosclerosis or heart dysfunction if metabolic syndrome is present. Furthermore, metabolic syndrome correlates with a few further systemic complications, which affect various systems and organs, for example osteoarticular disease, respiratory disease, fatty liver disease, and malignancy. Consequently, patients with metabolic syndrome have a reduced lifespan and raised all-cause mortality contrasted to the general people.(6, 7)Therefore, it is sequentially accepted that metabolic syndrome is associated with early ageing, which is of primary importance given the increasing global epidemic of metabolic syndrome. With this environment, it is very remarkable to understand biochemical processes associated with variations in metabolic syndrome with lifespan.(8)

Metabolic Syndrome in Pakistan Metabolic disorders resulting in chronic illness and end organ damage have remained research focus for a long time. Regardless of the nature of the

syndrome, the truth remains that all its constituent anomalies have been repeatedly and independently presented with an increased risk of both diabetes mellitus and cardiovascular disease.(9) For practitioners, metabolic syndrome can only act as an indicator of amplified cardio- metabolic risk, leading to any interventional endeavors, a function that can be offered most effectively by the easiest way to measure abnormality of the component alone. The prevalent elevation and availability of carbonated drinks and fast foods influence children in particular. This requires a deep understanding of people's health status with respect to cardio metabolic risks.(10)

Oxidative stress and Metabolic Syndrome Oxidative stress is a well-known mechanism that significantly contributes to several pathological conditions, and several human disorders have been strongly correlated with oxidative stress. Many cell functions seem to be controlled by free radical molecules, which can function as well as intracellular signals.(11, 12)Likewise, the protein redox state is associated with regulating a number of cellular activities, along with cell variation and stimulation of specific metabolic pathways.(13, 14)

Aging and Oxidative Stress

Aging is a biological process, characterized by a gradual wear and tear in metabolic functions and physiological activities resulting in morbidity and mortality. In line with the production of endogenous free radicals, reactive oxygen species and reactive nitrogen species as a result of different cellular mechanisms, which normally get neutralized, however with the ageing and obesity the production keep on rise while neutralization reduces. It is important to maintain A balance for proper physiological work between free radicals and antioxidants. In situations when free radicals production increases to override the body's capacity to neutralize them oxidative stress ensues. Free radicals adversely alter lipids, proteins, and DNA function and metabolism thus trigger a number of human diseases, causing cumulative and casual oxidative degradation of macromolecules stimulating loss with aging and ultimately cell death. Mitochondria tends to play pivotal role in the senescence process, as they are thought to be the primary intracellular source of anti-oxidants. Respiratory chain impairment causes reactive oxygen species (ROS) to induce mitochondrial components, including mitochondrial DNA, lipids, and proteins.(15) Progressive accumulations of oxidant- provoked somatic mutation in human mitochondrial DNA (mt DNA) resulting in wear and tear in the mitochondrial bioenergetics functions and play a part in aging process. Under physiological conditions, ROS low levels are produced in the course of mitochondrial respiration. Gradual oxidative impairment with age to mitochondrial (mt) DNA may cause DNA strand breaks and somatic mitochondrial DNA mutations.

The aggregation of these mt DNA variants result in disruption to the complexes of the respiratory chain contributing to a vicious cycle of decreased mitochondrial ROS synthesis

and consequent production of additional mitochondrial DNA mutations. This chain reaction was suggested to include increased oxidative impairment during ageing, which triggers a gradual decline in tissue and cellular functions due to insufficient energy supply and/or increased susceptibility to apoptosis.(16) Ageing induced oxidative impairment of proteins, lipids and DNA has been well reported, and thus provide an evidence to suggest mitochondrial dysfunction.(17) Pathophysiology Telomere length (18) is a fresh indicator of cellular aging, usually evaluated in leukocytes, and has been correlated with increased mortality and morbidity risks. Telomeres, consisting of mammalian DNA tandem repeats (TTAGGG) and associated proteins, are nucleoprotein complexes that are located at the ends of eukaryotic chromosomes. They contribute significantly to preserving the stability and integrity of the chromosome, forming an essential factor for cell survival. Telomeric DNA wears away whenever the cells divide, through partial "During DNA synthesis, replication of the lagging strand, referred to as the "end- replication problem." Through this method, each telomeric end reduces peripheral blood lymphocytes by about 20–60 base pairs (bp)/year. In vitro studies have shown that if telomeres turn out to be extremely small, cell division stops and encourages replicative senescence, leading to aging and consequent somatic cell death. Cellular impairment because of raised oxidative stress can additionally speed up the reduction process of TL. Thus, TL can be taken as an ageing biomarker, where elevated biological age could be seen by shorter TL. Certainly, metabolic disorders for example metabolic syndrome, which relates to aging, exhibit functional deterioration in tissues and major organs where pancreas and heart are particularly affected by ageing. A few studies have exhibited considerable correlations between central adiposity and shorter TL. Likewise, the TL was shorter as per the worsening of the metabolic conditions in demonstrative specimen of females. It is evident that a complex relation is present between metabolic syndrome components and TL with obesity. However, it is not yet known that the effect of TL in specific obesity groups such as metabolically healthy obesity (MHO). In this setting, the main objective of the current literature review was to explore the scientific evidence regarding absolute telomere length (aTL) in MHO people who were contrasted with a control group consisting of non-obese people with no metabolic syndrome and a cohort of obesity and metabolic syndrome patients.

Metabolic Syndrome and Correlation with Ageing

Metabolic syndrome directly correlated with raised mortality & atherogenesis due to MI as well as visceral adiposity accumulation during middle age correlated to exercise reduction & overeating. Moreover, there seems to be a genomic tendency to acquire metabolic syndrome.(19) Aging is taken into account as biological course of action typified by a gradual decline in metabolic course of actions as well as decline in physiological functions which results in mortality & morbidity.(20) Consistent with the aging theory “free radical”, reactive oxygen species, produced as biological oxidations byproducts, stimulate cumulative

& unintentional oxidative impairment to large molecules provoking the cellular abnormality with age then finally the cell dies.(20) Metabolic syndrome is usually reflected to stimulate precocious aging even though the system which is responsible for it is not fully recognized. It is turning out to be evident that involvement of longevity genes can possibly be there. Trials in over stimulation or disturbance of major lifecycle factor routes, for example mTOR, p66Shc, and Sirtuins result in expression of MS features in mice. Further routes are concerned in relating longevity and accessibility of nutrients, together with IGF-1 signaling and insulin, in addition to factors of FOXO transcription.(21) Free radicals are continuous produced during metabolic disorder which is thus believed to generate stipulations in which oxidative variations of cellular components increase, which consecutively results in dysfunction of mitochondria and finally loss of homeostasis of the cell. This motive has been convincingly applied as a factor of age- related decline in physiological processes, thus resulting in mitochondrial sense of "biological clock" for aging of the cell.(22) According to this concept a survey by Passos et al.(23) exhibited that the cellular senescence had greater ROS levels, mitochondrial dysfunction, further double-strand breakdowns of DNA as well as shorter telomeres, moreover it was exhibited that ROS of mitochondria increased telomere- reliant senescence. Lately, a few authors exhibited the association amid metabolic disorder & TL proposing raised cellular regeneration rate and thus speeding cellular aging.(24)

Telomere shortening is mostly the result of "end-replication" issue, caused by DNA polymerase inability to completely replicate the lagging strand's identical end.(25) One more factor taking part in telomere shortening encompasses the telomere ends processing to reconstruct projections of 3′ single-strand, and telomere shortening because of the DNA restoration system, especially for lone-stranded DNA impairment, are fewer effective within telomeric DNA as compared to other places within genome. The subsequent growth of single-strand breakdowns besides telomeres results in DNA impairment-reliant shortening while copying.(25) Therefore, shortening of telomere can possibly function as a marker of history of replication and cumulative genetic impairment of somatic cells.

These shorter telomeres can either accredited to shorter length at childbirth liable to diabetes or to augmented telomere loss in the course of cell division due to raised oxidative stress within prediabetes conditions, or both. It has been noticed that shorter telomeres are present in circulating epithelial originator cells in cases suffering from metabolic syndrome and in other conditions of high oxidative stress.(26) Several studies stated significant link between shorter TL and metabolic syndrome components, while other studies did not manage to confirm this.(27) Whether TL predicts a wide range of metabolic disorder such as lipid profile derangements, glucose, or hypertension ranges over a wide period is unknown.

Table 1 shows findings of several researches for association of telomere shortening with aging, organ damage and metabolic syndrome

Table 1: Findings from different researches

Association of metabolic syndrome with telomere length				
S.no.	**Author**	**Year**	**Study sample**	**Findings**
1	Yang Z et al.[28]	2009	767 subjects; Cases: 388 essential hypertension patients, 379 healthy controls	Hypertensive subjects have shortened telomeres, and the occurrence of coronary artery disease was linked with shorter telomeres in hypertensive subjects (P<0.05)
2	Demanelis K et al.(30)	2019	337522 subjects	Longer telomere length increases blood pressure and pulmonary function traits among middle-aged U.K. Biobank participants (p<0.05).
3	Nettleton JA et al.(31)	2008	840 subjects	After adjustment for demographic factors, age, lifestyle factors, other food or beverage consumption; the intake of processed meat was negatively influenced by telomere length (p<0.05)
4	Ornish D et al.(32)	2008	30 males	Higher telomerase activity was significantly associated with decline in LDL cholesterol (r=-0.36, p=0.041) and reduced psychological distress (r=-0.35, p=0.047).
5	Nordfjäll K et al.(33)	2008	989 individuals	Borderline or significant relation was found between telomere length and obesity parameters (BMI, weight, waist circumference and hip circumference) in women after adjusting for age and center. Whereas, a positive association to HDL was observed in males (p<0.05).
6	Cassidy A et al.(34)	2010	2284 females	Waist circumference was negatively influenced by telomere length (p<0.05)
7	Broer L et al.(35)	2014	11,448 participants	Raised leptin levels are associated with short relative telomere length (p<0.05).
8	Njajou OT et al.(36)	2012	2721 elderly subjects	Shorter telomere length is significantly correlated with increased adiposity (p<0.05)
9	Révész D et al.(27)	2014	2848 participants	The shorter baseline telomere length was associated with HDL, waist circumference, triglycerides, and fasting glucose, as well as the presence of metabolic syndrome and the total number of components (p<0.05). Though baseline differences gradually decreased

				over time, at the two-or six-year follow-up, shorter baseline telomere length was significantly associated with poorer scores of majority of metabolic syndrome components.
10	Zhang WG et al.[38]	2015	139 healthy subjects	Telomere restriction fragment length is associated with kidney function ($p<0.05$) and may serve as a marker of aging ($r=-0.314$, $P<0.001$)
11	Eunkyong K et al.(42)	2017	130 surgically resected paraffin-embedded hepatocellular carcinoma tumor tissue samples	H_2O_2 contributes to telomere elongation in advanced hepatocellular carcinoma through protein kinase B (AKT) activation
No association of metabolic syndrome with telomere length				
12	Khalangot MD et al.(37)	2019	115 adults	A high risk of shorter telomeres, which remained important after adjustment for gender, age and 2hPG rates, was associated with metabolic syndrome. Other components of metabolic syndrome and fasting plasma glucose levels did not influence the magnitude of the correlation, and the independent effect of these factors was not disclosed ($p>0.05$).
Controversial results				
13	Bhupatiraju C et al. (29)	2012	194 subjects; 96 hypertensive and 98 normal subjects	A significant negative correlation was found in both the hypertensive and normal individuals ($p<0.05$) between age and telomere length. Although insignificant ($p>0.05$), the diastolic and systolic blood pressure were negatively correlated with relative telomere length.
14	Verhulst S et al.(41)	2016	684 participants	Baseline insulin resistance during the follow-up period was not related with age-dependent changes in leucocyte telomere length (attrition), whereas baseline leucocyte telomere length was linked with increases in insulin resistance during this time.
15	Kim NW et al.[43]	2015	101 biopsies	Telomerase become less active in somatic cells however their activity appears to be increased in cancer cells which help them in growing exponentially and make them immortal.

Conclusion

This review concluded that there are two ways to decrease the important role of telomeric length as the well-known event in age. One reflects the impact of various chronic diseases such as insulin resistance and diabetes by attrition of telomeres, an effect most likely due to mitochondrial dysfunction and pro- inflammatory state. Second, shortening the telomere causes damage to DNA, cellular senescence and apoptosis, and triggers associated metabolic syndrome-related ageing disorders. In contrast, telomer length maintenance or elongation is associated with cell immortality and ultimately tumor growth. Future Directions

There is still an unresolved and puzzling relationship between obesity and telomere morphology. Interesting work on this relationship is therefore needed in order to cure life and prolong survival. Future well- designed multi-faceted intervention studies must take this bidirectional relationship into account and examine whether targeting obesity can minimize, interrupt, or even reverse telomere attrition to avoid further deterioration to cardiovascular and aging- related complications.

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Research article

Factors Contributing To Phlebitis Among Patients Admitted In Medical-Surgical Units At Tertiary Care

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LMRJ.2020:2(2)
DOI: 10.3810/LMRJ.2020.2.2.03
Received: 2 April 2020,
Revised:14 May 2020,
Accepted for publication 19 May 2020

Abstract

In the health care settings, there is a constant use of peripheral venous catheters for different purposes, however, its use is not risk-free. This study aimed to assess the risk factors and identify prevalence of phlebitis amongst adult patients admitted in the Medical-Surgical units at Liaquat University Hospital Hyderabad. A descriptive cross sectional study was conducted. Data was collected from Medical-Surgical units at Liaquat University Hospital Hyderabad in three months. Questionnaire was used as a data collection tool consisting of 25 questions for the different categories. A total of 246 subjects, having 59.8% male and 40.2% females with the average age of 75.77 years, participated in study. Phlebitis grade 2 & 3 appeared to be more common in age between 18 to 70 years with average percentage of 41.1and 40.2 respectively. Statistically, Hepatitis C virus and pyrexia found significantly associated with development of phlebitis. The study concluded that high rate of phlebitis grade II & III in the study population.

Keywords: Infusion, Risk Factors, Phlebitis, Short Peripheral Catheter

Introduction

Phlebitis is an intravenous infection and a significant public health issue with prevalence rate of 20% in Pakistan, 27.7% in India and 4% in United States of America. The use of peripheral venous catheters for various purposes is constant in health care settings. However, its use is not risk-free. Most common local complication reportedly include phlebitis, and its occurrence ranges from 4.5% to 60% depending on the different settings.[1] In patients with intravenous treatment, Phlebitis ranks third among in-hospital complications. This complication also causes functional impairment of the affected part presenting with pain, swelling, heat, flushing of the venous canal and adjacent tissues.2

The pathophysiology of phlebitis has had many hypotheses. The theory widely accepted is catheterization leading to vein pain, inflammation of tunica intima, and possible development of thrombus.3 A major role in developing phlebitis would be the catheter type, the insertion site, skin preparation method, site dressing, the method of fixing catheter, length of the catheter, frequency of exchange, irritating drugs, infusion rates, catheter fixation dressings, catheter placement procedures, and staff skills. Phlebitis clinical manifestations are pain, swelling, erythema and palpable catheterized vein thrombosis.4,5 Replacement of intravenous peripheral cannulas to reduce the phlebitis development in adult patients every 72 to 96 hours.6,7 A possible risk of infection includes manual dexterity, technical skills, expertise of pharmaceutical therapies, and familiarization with vascular system intravenous anatomy and physiology.8 The frequently catheter use puts patients at risk and expose to a series of complications. These intravenous catheterization risks and complications can affect the clinical condition, well-being and potential result of a patient who needs to have a peripheral catheter inserted in another location.9 Intravenous catheter replacement causes patient discomfort and can lead to permanent damage of affected veins, longer hospitalization, increased cost and treatment, and possible death if complications occur.10

The Visual Infusion Phlebitis Score (VIPS), which assesses presence, severity and location of phlebitis. A value of 0 means there are no phlebitis signs; 1, first probable sign of phlebitis; 2, early phlebitis stage; Scales 3, 4 and 5 show moderate phlebitis, advanced phlebitis/ thrombophlebitis or advanced thrombophlebitis.4,11 Many institutions in the country may not be use a scale to assess phlebitis. It is important to determine the phlebitis rate and the risks to facilitate the measurement.12

There is a dearth of information on studies of phlebitis factors in Pakistan. The study may help to assess and inform healthcare professionals about the factors that contribute to phlebitis. This data will be useful for healthcare systems to improve patient outcome and to reduce the length of stay of patient, reducing the costs for healthcare and subsiding the discomfort among patients that will ultimately decrease burden of disease. The objectives of the study were to assess the risk factors for phlebitis and to identify the prevalence of phlebitis among adult patients admitted in Medical-Surgical units at Liaquat University Hospital Hyderabad.

Materials and methods

A descriptive cross-sectional study was carried out at medical-surgical units I, II, III & IV at Liaquat University Hospital Hyderabad during October 1st to December 31st 2019. A total of 246 patients were selected by using a non-probability convenience sampling technique. Inclusion criteria was patients of both genders aged more than 18 years, being admitted within the medical and surgical units, undergoing any form of intravenous therapy, having catheter in situ in use or not. The exclusion criteria was medically compromised patients with no ability to give informed consent, being institutionalised (for example prisoners).

Data was collected following clearance approval from research ethics committee of LUMHS (DOC#LUMHS/REG/ACD/28274/75). Data was collected from the sample population receiving some form of intravenous therapy within the medical-surgical units of Liaquat University Hospital. The patients were presented with a data sheet and informed consent was obtained. Using the VIP scale, patients at catheter placement sites were examined from the bedside for any phlebitis signs and reported the presence and severity of phlebitis.

Using the patient notes and charts, patient- related characteristics leading to phlebitis, including demographic details, medical diagnosis and current medical history, were reported on the clinical audit form. On examination, catheter characteristics were noted, and the patient was asked to explain the dates

of catheter insertion and removal of the catheter. Using the patient's notes, drug chart and fluid balance sheets, infusion-related features leading to phlebitis were observed.
The data was analyzed in Statistical Package for social sciences (SPSS) version 23. Frequencies and percentages were calculated for qualitative variables and were presented in bar charts. Means and SD+ were calculated for continuous variables. The Chi-square test was used to analyze qualitative categorical data among risk factors association with phlebitis. P-value <0.05 was set as significance.

Results

Phlebitis was often found to be elevated in medical units relative to surgical units. 26% (n=64) of those admitted to the Medical Ward # III developed phlebitis in the participants, 15.4% (n=38) were in Medical-IV, 14.6% (n=36) were in Medical-I and 9.8% (n=24) were in Medical-II. The percentages of phlebitis in all surgical units were significantly different, with 10.2% (n=25) in Surgical-IV, 9.3% (n=23) in Surgical-I and 7.3% (n=18) in each Surgical II & III unit being observed as indicated in Figure 1.
Figure 2 shows that in 41.1% and 40.2% of cases, the majority of participants had Level II & III phlebitis, while 10.6% had Level IV, 6.5% had Level I and 1.6% had Level V. The Mean= 2.60, SD= 0.826, Min: = 1, Max: = 5, Mode = 2. Grade II and III were the most severe grades observed. Phlebitis stages II & III and IV & V that require catheter re-setting and possible treatment.

Ninety-nine (37.8%) participants had infection and 124 (81.7%) participants of those without infection had phlebitis stage II & III, while 75 (80.7%) of those infections had phlebitis stage II and III, but there was no significance (p = 0.916). Table 1 shows. There were no comorbidities in 5 (10.9 percent) participants, while 41 (89.1%) participants had 1 or more comorbidities. There were II, III & IV phlebitis stages in 200 out of 219 participants without comorbidities, while 26 (96.2%) of those with 1 or more comorbidities had II, III & IV phlebitis stages. The co-morbidity is not significant (p = 0.615) associated with the development of phlebitis, similar to medical diagnosis.

Only 7.3% of participants were unknown about their HBV status, 85.8% of participants were HBV negative but 82.0% of participants developed stage II & III phlebitis, while 6.9% of participants were HBV positive and 82.4% developed stage II & III phlebitis. The frequent development of phlebitis is not significant (p = 0.675). 66.7% of participants were HCV negative, but 82.4% of participants developed phlebitis in stage II & III, while 26.4% of participants were HBV positive and 80.0 percent developed phlebitis in stage II & III and 7.3 percent of participants were unaware of their HBV status. 76.50% developed phlebitis in stage II & III. HCV is a significant difference that leads to phlebitis (p = 0.015). Of the 48 (19.5%) who had diabetes mellitus, all had phlebitis, but 79.3% had phlebitis in stages II & III. 55.7% of participants had pyrexia, 82.5% of them had phlebitis in stage II & III; 44.3% of participants had no pyrexia, but 79.8% of participants developed phlebitis in stage II & III. Pyrexia leads to the statistically significant development of phlebitis (p= 0.044) as shown in Table 2.

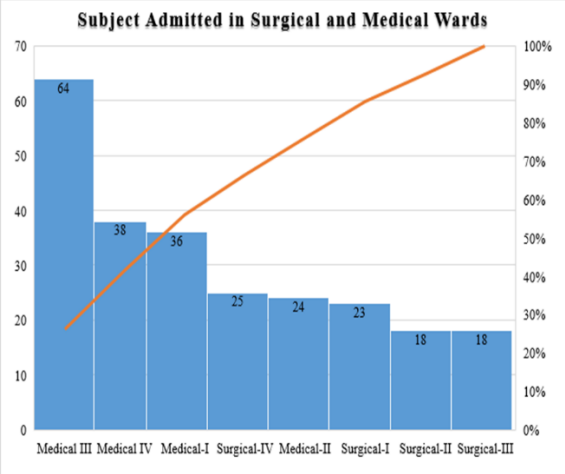

Figure 1: Distribution of Subjects Admitted in Surgical and Medical Units

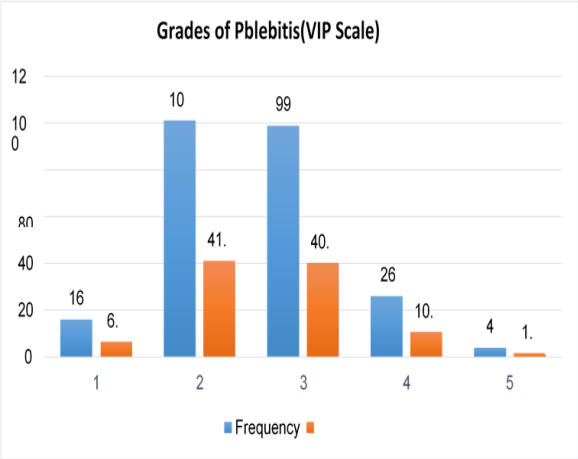

Figure 2: Grades of Phlebitis (VIP Scale) of the Subjects

Table 1: Distribution of diagnosis and Co- morbid medical conditions of the Subjects

	n	%	Grades of phlebitis Frequency					P Value
			1 n (%)	2 n (%)	3 n (%)	4 n (%)	5 n (%)	
Medical/Surgical diagnosis of the subjects								
Infectious diseases	93	37.8	7 7.5%	38 40.9%	37 39.8%	9 9.7%	2 2.2%	0.961
Non-infectious diseases	153	62.2	9 5.9%	63 41.2%	62 40.5%	17 11.1%	2 1.3%	
Total	246	100						
Co-morbid medical conditions of the subjects								
None	219	89.02	15 6.8%	93 42.5%	88 40.2%	19 8.7%	4 1.8%	0.615
1 or more	27	10.98	1 3.7%	8 29.6%	11 40.7%	7 25.9%	0 0.0%	
Total	246	100						

Table 2: Distribution of HBV, HCV, DM

	n	%	Grades of phlebitis Frequency					P value
			1 n (%)	2 n (%)	3 n (%)	4 n (%)	5 n (%)	
HBV status								
Unknown	18	7.3	3 16.67%	7 38.9%	6 33.3%	2 11.1%	0 0.0%	0.675
Negative	211	85.8	11 5.2%	88 41.7%	85 40.3%	23 10.9%	4 1.9%	
Positive	17	6.9	2 11.8%	6 35.3%	8 47.1%	1 5.9%	0 0.0%	
Total	246	100						
HCV Status								
Unknown	17	6.9	3 17.6%	7 41.2%	6 35.3%	1 5.9%	0 0.0%	0.015
Negative	164	66.7	12 7.3%	68 41.5%	67 40.9%	16 9.8%	1 0.6%	
Positive	65	26.4	1 1.5%	26 40.0%	26 40.0%	9 13.8%	3 4.6%	
Total	246	100						
Diabetes Mellitus								
No	198	80.5	14 7.1%	80 40.4%	82 41.4%	20 10.1%	2 1.0%	0.473
Yes	48	19.5	2 4.2%	21 43.8%	17 35.4%	6 12.5%	2 4.2%	
Total	246	100						
Pyrexia (> 38.5 C)								
No	109	44.3	9 8.3%	52 47.7%	35 32.1%	13 11.9%	0 0.0%	0.044
Yes	137	55.7	7 5.1%	49 35.8%	64 46.7%	13 9.5%	4 2.9%	
Total	246	100						

Discussion

The present study represented the incidence of phlebitis, with 41.1% grade II phlebitis and 40.2% grade III phlebitis, followed by 10.6% grade IV phlebitis, 6.5% grade I phlebitis, and 1.6% grade V phlebitis, the highest percentage. The rates of phlebitis grade II in studies were 35.1% and higher rates were 53.6%, while the grade III rate (23.7%) was contrary to this research in another study.[13–15]

In current Study, the average number of catheters was 1.30±0.49. There was a higher percentage of grade II & III phlebitis 86.3% and Pyrexia status of the Subjects in patients who had one catheter in situ compared to those who had two simulation catheters 68.7%; however, there were phlebitis grade IV & V (22.4%) in patients who had 2 simulation catheters. Similarly to this study results, a study indicated the chances of phlebitis chances of developing phlebitis with more than one coexisting SPC were significantly higher. The frequency also rises when inserting the catheters into the same arm is repeated.16,17

In the present study, HBV was not found significant (p = 0.615), while HCV and Pyrexia (>38C) were found significant (p = 0.015) and (p = 0.044), respectively to develop phlebitis. However, the results were not found to compare the results with this study findings, though in a study chronic diseases (p = 0.005) and infections (p = 0.007) found significant to develop phlebitis.15

As observed in this study, placement of the catheter at the joint sites of the wrist's dorsal aspect had a higher proportion of phlebitis grade II 51.9% right wrist dorsal aspect, 44.6% right forearm, 50.0% left forearm, 30.2% left wrist dorsal aspect and III 36.5% right wrist dorsal aspect, 39.3% right forearm, 30.0% left forearm, 45.3% left wrist dorsal aspect. One study showed only the forearm's threat.16 Another study indicated that phlebitis grade I, 46.1% was related to the hand veins and grade II, III and IV with the forearm veins 85.0%, 81.8% and 69.2%, respectively, these findings were higher than this present study.13

The current study reported that the most frequently catheter gauge 22 was used with incidence of phlebitis grade II 43.7%, which was higher than a study findings 29.3%, whereas grade III was 38.0% as compared to other study findings 52.1% which were higher. The phlebitis grade II and III was reported 38.5% each as compared to a study results 18.9% and 54.2%, respectively, the grade III reported findings were higher than the current study.18 Many other authors stressed that using smaller size catheters allows the circulation of blood in adjacent tissue, thus avoiding vein injuries.7,19,20

The present study showed that 80.5% catheters were in current use and developed phlebitis grade II (44.4%) and III (37.9%), while 14.6% catheters were in situ with regular flushing. Catheter flushing found significant (p= 0.022) as a risk factor to develop phlebitis and no similarly result found in other studies. A study presented that the saline were not flushed in patients, they developed more than 10 times higher risk of incidence of phlebitis.1 In this study, the phlebitis grade II (41.7%) and grade III (39.1%) developed in patients who received antibiotics IV therapy. The similar results found in other studies, grade II and III of phlebitis were the most common in patients receiving intravenous antibiotics.8,21

This study showed that 51.2% and 26.4% of subjects received continuous infusion and reported most common phlebitis grade II and III. It is evident that there is a strong link (p = 0.015) between phlebitis development and the form of infusion and similarly a study highlighted continuous infusion to be a predictor of phlebitis and found more statistically significant (p = 0.006), while another study reported a higher risk of phlebitis in SPCs with intermittent infusions .22–24

Conclusion

The catheter flushing, infusion system, HCV and pyrexia variables were statistically significantly linked to the development of phlebitis, while the catheter gauge was the least significant. This study concluded that there was a high prevalence of phlebitis and the highest percentage of grade II & III phlebitis was found, followed by grade I, grade IV, and grade V phlebitis.

Conflict of Interest

Authors declare no conflict of interest related to publication of this article.

Grant Support Financial Disclosure: None

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Mini review

Intralesional steroid injection and dilatation for subglottic stenosis in patients with Wegener's granulomatosis- a review of literature

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LMRJ.2020; 2(2)
Doi: 10.38106/LMRJ.2020.2.2-04

Abstract

Subglottic stenosis is one of the major complications of the Wegener's granulomatosis. There are no set guidelines available for management. Intralesional steroid injection and dilatation seems to be a safe and successful method of treatment. We report a review of available literature on intralesional steroid injection and dilatation for subglottic stenosis in patients with Wegener's granulomatosis.

Introduction

Wegener's granulomatosis is a rare autoimmune disease, predominantly affects middle aged males. Subglottic stenosis is one of the complications seen in the patients with upper airway involvement (10-20% of all cases) [1] even when the disease is in the remission. As a result of better systemic control and improved life span of the patients suffering from Wegener's disease increasing number of the patients are expected to present with subglottic stenosis[2]. Despite being a major issue for the consultants dealing with these cases and troublesome for the patients who are in remission, there are no set guidelines for the management of this condition.

It is suggested that the stenosis of the subglottic region results from scarring of the inflamed upper airway, however in some cases localised inflammation in the region leading to stenosis was the only symptom of the Wegener's disease. It is also thought that extensive surgery would lead to more scarring and worsening of the condition but recently a number of surgical options have been tried including reconstruction of the region, in the patients with remission, however there was associated interference with phonation and/or long term morbidity. The most attractive results from the author's point of view were of the intralesional steroid injection and dilatation. The studies presented have a very small number of patients or were case reports; hence we now report review of these studies.

Literature search was done using PubMed database with key words "Wegener's granulomatosis/ disease / Subglottic stenosis/ Intralesional steroid injection" Final search was done on 24th January 2021. All the studies reporting results of intralesional steroid injection in the subglottic stenosis in patients with Wegener's Granulomatosis were included. There was no restriction of sample size; even case reports

were considered given the fact of rare condition and comparatively new approach of management.

A total of 5 publications were found including 2 case reports and 3 case series. A total of 46 patients had intralesional steroid injection with dilatation. None of the patients required tracheostomy and 47% of the patients required more than one session. There was no major adverse effect of the procedure reported in any of the studies. An additional relatively recent study has been reported in children with compromised air way due to wegener's, the study suggested that children require surgical management for correction of their airway eventually even after intralesional injection therapy with cortisteroids[3] The same study has reported extensive review of literature which also reported only a few cases.

The review of the studies showed promising results of intralesional injection and dilatation in patients with subglottic stenosis developed as a complication of Wagener's granulomatosis. There was 100% success rate of the procedure in all studies and none of the patients required tracheostomy[4, 5].

The surgical procedures in the Wegener's Granulomatosis have a higher rate of recurrence as well as long term morbidities. Most of the procedures e.g. partial cordectomy or tracheostomy, and even reconstruction have higher morbidities and undue stress to the patients affecting their quality of life[6, 7].

For the patients who are in the remission and responded well to steroid therapy, and given the suspicion of more scarring following their surgery, intralesional injection is an attractive option. Most of the studies reported on the subject have a day care procedure, minimal

stay to the hospital and with long term good results in association with prevention of unnecessary surgical trauma [1, 2, 8]. There is no standard treatment for this condition in patients with Wegener's Granulomatosis available at this stage to compare with, but it is strongly recommended to opt this option as first line management in patients with troublesome stenosis.

The study has limited importance as there was a small number of studies with a small sample size and some were merely case reports, hence prospective studies with long term follow-up and acceptable sample size are required to set guidelines for recommendations for management of this condition.

We conclude that from the evidence given, it is suggested that the intralesional steroid injection with dilatation of the stenosis is safe and successful method in most cases and should be used as the first line of management in these cases. Larger prospective studies are required to set the guidelines.

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