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Editorial

E-journals; merits and demerits

Electronic journal (e-journals) is a periodic publication in electronic format made available on the internet or in a CD-ROM. Introduced initially as complementary to paper-based journals (p-journals), e-journals have expanded, exponentially, during the recent past. Some journals are published only in the electronic format while some are published in print form in addition to the electronic form. Despite numerous advantages associated with e-journals, there is a growing concern among academics regarding the quality of the content in some e-journals although this has not been proven adequately.

E-journals are popular due to several reasons. They allow remote and easy access and provide access to multiple users simultaneously. In addition, e-journals can accommodate multimedia information, sounds, original data of the study and supporting documents. They require no physical storage space and can be saved digitally and hence environment friendly. In addition, they can be shared with others easily and some e-journals are interactive.

E-journals are not without limitations. Not all e-journals are of high quality and the review process of some e-journals is questionable. Further, they are not accessible without an internet access. Libraries find it difficult to retrieve them rapidly when required. This may take more time and more working hours.

In a complex situation, it is difficult to make predictions. It is certain that the number of e-journals will expand further. In order to retain the credibility, it is essential for the e-journals to adhere to the accepted principles of review process. Despite these limitations e-journals, however, will survive as they target readers and directly deliver to them bypassing libraries.

Sarath Lekamwasam
Eisha Waidyarathne
Editors / GMJ

GALLE MEDICAL JOURNAL; INSTRUCTIONS TO AUTHORS

The Galle Medical Journal is published by the Galle Medical Association. The *journal* is published biannually, March and September and the submissions are accepted throughout the year. The aims of the Journal are to foster co-operation among the medical fraternity and to be a forum to make literary contributions, share experiences encountered in medical practice, update their knowledge and have debates on topics related to all aspects of medicine. Also, we attempt to cater to the educational needs especially of the postgraduate trainees. The *Journal* publishes original articles, reviews, leading articles and case reports. When an article is reviewed for publication we expect that the work it reports has not been published, submitted simultaneously to another journal or accepted for publication elsewhere. All manuscripts will be reviewed anonymously before acceptance.

Manuscripts must be submitted with the text type written in 12-point Times New Roman font double spaced. Text and all illustrative material should be submitted in two hard copies and the electronic version in Microsoft Word document format. In order to avoid delay we require authors to comply with the following requirements. **All manuscripts should accompany a covering letter indicating the number of words in the manuscript, institution where ethical clearance was granted, conflict of interests and contact details of the corresponding author.**

Types of contributions:

Review articles and Leading articles: We encourage submission of review or leading articles which are less than 3000 words in length and address topics of current interest. They should be supported by no more than 20 references. Submissions may be subjected to external review before acceptance.

Original articles: Should normally be in the format of introduction, methods, results and discussion. Each manuscript must have a structured abstract of 200 words. The text should be limited to 3000 words and maximum of 5 tables/figures taken together with no more than 15 references. Lengthy manuscripts are likely to be returned for shortening. The discussion in particular should be clear, concise and should be limited to matters arising directly from the results. Avoid discursive speculation.

Case Reports: These should not exceed 750 words and 5 references; no abstract is required. Case report should be informative and devoid of irrelevant details.

References:

These should conform to the Vancouver style. The reference in the text should be numbered consecutively in Arabic numerals in parentheses in the same line of the text in the order in which they appear. The first five authors should be listed and if there are more than five, then the first three should be listed followed by et al. Examples are given below:

1. Kumar A, Patton DJ, Friedrich MG. The emerging clinical role of cardiovascular magnetic resonance imaging. *Canadian Journal of Cardiology* 2010; **26**(6): 313-22.

2. Calenoff L, Rogers L. Esophageal complication of surgery and lifesaving procedures. In: Meyers M, Ghahremani G, eds. Iatrogenic Gastrointestinal Complications. New York: Springer, 1981: 23-63.

Units / Abbreviations

Authors should follow the SI system of units (except for blood pressure which is expressed in mmHg). Authors should use abbreviations sparingly and they should be used consistently throughout the text.

Manuscripts that do not conform to these requirements will be returned for necessary modifications.

Manuscripts should be addressed to Chief Editors, Galle Medical Association, Teaching Hospital, Karapitiya and all soft copies should be sent to *gmathk@gmail.com*

Psychological distress in cancer patients in Southern province of Sri Lanka

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ABSTRACT

Introduction: Stress in cancer patients directly affects the outcome of treatment. Aim of the study was to assess stress levels in cancer patients.

Methods*:* A sample of cancer patients (N=210) were assessed using an interviewer administered questionnaire and the General Health Questionnaire - 12 item version (GHQ-12).

Results*:* Whole sample had reported some level of distress; a large majority (65%) had reported severe levels of distress (GHQ>20). The overall mean GHQ score (mGHQs) was 22.50 (SD=3.8). Severe distress level indicated by participants with different cancer types ranged from 57% of those with breast cancer to 84% with lung cancer. No significant differences were found in mGHQs of five cancer types (p=0.056). Half of the participants (51%) had reported disabilities and their mGHQs (±SD) was 23.79 (±4.30), while mGHQs (±SD) of those without disability was 21.17 (±2.70) (p<0.001). Among them, 49% had two disabilities (mGHQs - 21.16±2.69), 27% had more than three disabilities (mGHQs - 24.82±4.62). Majority (64%) earned monthly income of <Rs. 10,000/- and their mGHQs was 23.19 while that of those who earned > Rs. 10,000/- was 21.28 (p<0.001).

Conclusions: Lung cancer patients were severely distressed. Cancer patients with lower income and disabilities were reported to have higher distress. Psychosocial support services should prioritize patients experiencing disabilities and those who are from lower economic background.

Key Words*:* Cancer, psychological distress, disabilities, GHQ

Introduction

Worldwide, one in eight deaths are due to cancer; cancer causes more deaths than AIDS, Tuberculosis and Malaria combined (1). Cancer is the second leading cause of death in developed countries as well as in developing countries (1). An estimated 14.1 million new cancer cases and 8.2 million cancer-related deaths occurred in 2012 worldwide, and incidence is higher among male gender (2). Risk of developing cancer is increased with increasing age (3). Cancer competes with heart diseases to become the leading cause of death in Sri Lanka (3, 4).

The patterns of diseases in Sri Lanka are somewhat similar to those in the developed countries. According to the National Cancer Control Programme (NCCP) in Sri Lanka, incidence and mortality rates of cancer patients have been increasing. In years1985 and 2008, cancer incidence was 31.6 and 81.6(crude rate per 100,000 populations) respectively (5).

When patients are diagnosed and living with a life-threatening illness such as cancer, it causes high levels of stress. Stress is a common psychological problem among cancer patients and plays a major role in their lives. Distress develops during any

phase of cancer, directly affects the outcome of the treatments (6). High incidence and prevalence of distress are common among cancer patients worldwide. One study reported higher levels of distress varying from 41% in patient with breast cancer to 23% in those with upper gastro-intestinal tract cancer (7). Overall prevalence of distress in cancer patients has been reported in the range of 35% -38% (8). Lung, pancreatic, head and neck, Hodgkin's disease, and brain cancer patients were the most distressed (9).

International Classification of Functioning, Disability and Health (ICF) of World Health Organization (WHO) have defined the term 'disability' as impairments, activity limitation or participation restriction in daily activities (10). Physical disabilities/ functional limitations in daily activities, cancer related fatigue (CRF) are more common among cancer patients; and such conditions would severely affect the psychological well-being of terminally ill cancer patients, causing higher level of psychological distress (6,11). As the best predictors of psychological distress, fatigue, metastasis, functional limitations (11) and fear of disease progression (7) were considered in the previous studies.

Impact of psychological distress on heterogeneous cancer patients in Sri Lanka is largely unknown. Although cancer victims a severe burden to the health system of the country, little attention has been paid. It was found that only a few studies have been done on stress in cancer patients (12). A study of a sample of 75 Breast Cancer (BC) patients reported that nearly 50% of the patients had experienced psychological distress during the period following their diagnosis (12).

There is a severe shortage of data pertaining to psychological profile of cancer patients in Sri Lanka. Such data are important to design effective strategies and psychosocial intervention to reduce stress and to improve psychological well-being of these patients who are the recipients of services from under-resourced health system in Sri Lanka.

The aim of the present study was to assess the psychological distress in cancer patients treated at a tertiary care hospital in the Southern province of Sri Lanka. In addition, it was expected to identify the factors which influence the stress levels among cancer patients.

Methods

Two hundred and ten (210) randomly selected cancer patients who obtained the services from cancer unit in Teaching Hospital, Galle from May, 2013 to January, 2014 were studied using an interviewer administered questionnaire, bed head tickets and the diagnosis cards of the patients. Sinhala version of General Health Questionnaire- 12 item version (GHQ-12) (13, 14) was applied to measure short term psychological distress during previous few weeks.

First part of the questionnaire consisted of demographic data (age, sex, marital status, education, occupation, income levels, etc.) and clinical characteristics (cancer types, stage, time since diagnosis, disabilities, etc.) of the patients. Disabilities in daily functioning were assessed in 7 areas; walking, attending self-care, eating/drinking, talking, hearing, vision and involvement in household work. Subjects were asked to respond questions using Likert- type scale. In the second part, GHQ-12 scale was included and used to measure the stress levels among study population. GHQ, score of more than 15 was taken as evidence of distress while a score of more than 20 suggested severe problems and psychological distress.

Inclusion criteria of subjects included confirmed diagnoses as any type of cancer by the Consultant Oncologist, admitted to oncology wards in the above hospital, continuous treatment taken from oncology wards or oncology clinic for 6 month period. Patients aged 25 years or older who were able to understand Sinhala language were invited for the study. Those who provided informed consent with sufficient physical and mental stability were included. Patients who had surgical or medical complications or in critical state or end stage of cancer were excluded.

Ethical approval was granted from the Ethics Review Committee of the Faculty of Medicine, University of Ruhuna, Sri Lanka. Permission was obtained from the Director, relevant Consultants and Sisters In-Charges of the Teaching Hospital, Karapitiya, Sri Lanka. Patients were interviewed by the author in relevant oncology wards or follow-up clinics. Basic demographic details and other data were collected.

All data were coded and entered into a database, analyzed using the Statistical Package of Social Science (SPSS) version 17.0. Basic descriptive statistics were calculated to describe the study sample and expressed as means and standard deviations. Bivariate statistical tests were used to identify associations between GHQ scores with demographic data and clinical characteristics. Independent samples t-test and one-way analysis of variance (ANOVA) were used to compare means of variables in two groups and three or more groups respectively. Pearson correlation coefficient was used to compare the relation between distress levels, cancer types, and socio-demographic parameters. All results were regarded as statically significant at $p < 0.05$.

Results

Sample consisted of 97 breast (46%), 32 oral (15%), 32 colon (15%), 25 lung (12%) and 24 uterine cancer (11%) patients. The mean age was 55 years (SD =10.2). Different types of disabilities affecting daily life such as eating/drinking (25%), home activities (20%), walking (19%) were reported by the participants. Summary of socio-demographic details is given in **Table 1**.

Overall mean score of the GHQ scale was 22.50 (SD =3.8) and scores ranged from 16-35. The whole sample had reported some level of distress; a large majority (65%) had reported severe levels of distress (GHQ>20).

Considering five cancer types, severe distress levels (GHQ>20) were found in 84% of lung cancer patients followed by 79% of uterine cancer patients, 69% of oral cancer, 59% of colon cancer and 57% of breast cancer patients.

The mean GHQ scores of patients with different cancer types were given in **Table 2.** No significant differences were found in mGHQs of the five cancer types (p=0.056).

ut of studied socio-demographics and clinical characteristics of the participants, level of income and disabilities contributed to the stress level (p<0.001) (**Table 3**).

Table 1: Socio-demographic details of cancer patients

Categories/ variables	N (%)
Age	
<55years	113(54)
>55years	97(46)
Sex	
Female	149(70)
Male	61(30)
Marital status	
Married	176(84)
Unmarried / Single	34(16)
Educational status	
Up to 10 years	65(31)
More than 10 years	145(69)
Employment status	
Employed	115(55)
Unemployed (never worked/retired)	95(45)
Time since diagnosis	
<12 months	137(65)
>12 months	73(35)
Self-reported disabilities	
No	103(49)
Yes	107(51)
House hold income level	
< Rs. 10,000 per month	134(64)
> Rs. 10,000 per month	76(36)

N- Number of patients, %- percentage of patients

Table 2: Mean GHQ scores by cancer types

Cancer type	mGHQ score	SD	p value
Lung	23.96	4.1	0.056
Oral	23.28	4.4	
Uterine	23.21	3.3	
Breast	21.95	3.7	
Colon	21.72	3.0	

mGHQs - mean GHQ scores, SD - standard deviation, p value < 0.05

Table 3: Influencing factors on stress levels of the study population

Variable	N	%	mGHQs	SD	p value
Income					
< Rs. 10,000	134	64	23.19	4.1	< 0.001
> Rs. 10,000	76	36	21.28	2.7	
Disabilities					
Yes	107	51	23.79	4.3	< 0.001
No	103	49	21.27	2.7	

N- Number of patients, %- percentage of patients, mGHQs- mean GHQ scores, SD- standard deviation, p value< 0.001

Considering studied cancer patients who had disabilities, statistically significant differences in having disabilities were found among five cancer types ($p<0.001$); oral, breast and uterine cancer patients had indicated significant differences in disabilities in multiple comparison (post hoc test).

Disabilities studied in this study were related to the type of cancer. Out of all oral cancer patients, 69% had reported disabilities in eating/drinking and 41% had reported disabilities in talking; 36% of lung cancer patients had reported disabilities in walking and 28% of them had reported disabilities in eating/ drinking and difficulties in doing home activities.

Among subjects with different cancer types, higher number of breast cancer patients had reported disabilities (n=38, 35%), followed by oral (25%), colon (16%), lung (16%), and uterine (8%) cancer patients (table 4). Irrespective of cancer type, all patients who reported disabilities had significantly high mGHQs compared to their counterparts who had not reported any disability except colon cancer patients (**Table 4**).

Further, mean stress scores were significantly related to the types of disabilities, number of disabilities and the different combinations of the disabilities. **Table 5** illustrates mGHQs of patients with different types of disabilities.

Table 4: Comparison of mean GHQs of subjects with/without disabilities

Cancer type	Disability	Number	mGHQs	SD	p value
Breast					
	Yes	38	23.39	4.6	0.006*
	No	59	21.02	2.7	
Oral					
	Yes	27	24.00	4.4	0.03*
	No	05	19.40	1.9	
Colon					
	Yes	17	22.12	3.4	0.43
	No	15	21.17	2.5	
Lung					
	Yes	17	25.24	3.8	0.02*
	No	08	21.25	3.4	
Uterine					
	Yes	08	25.38	4.1	0.02*
	No	16	22.13	2.3	

mGHQs- mean GHQ scores, SD- standard deviation, p value < 0.05, * significant differences among mGHQs of disabilities among cancer types

Table 5: Mean GHQ score for different types of disabilities

Type	Disability	mGHQs	SD	p value
Attending self-care				
	Yes	27.82	3.4	< 0.001
	No	22.21	6.2	
Walking				
	Yes	25.46	4.4	< 0.001
	No	21.82	3.3	
Home activities				
	Yes	24.64	5.0	< 0.001
	No	21.96	3.2	
Eating/ drinking				
	Yes	24.60	4.3	< 0.001
	No	21.81	3.3	

%- frequency of disability, mGHQs- mean GHQ scores, SD- standard deviation, p value < 0.001

Comparing patients who had different numbers of disabilities (eg: two, three or more), 49% of the sample had reported two disabilities and 27% had reported more than three disabilities ($p<0.001$). A higher mGHQ score was reported by patients who had more than three disabilities (24.82±4.62).

Stress levels were significantly associated with different combination of disabilities they have experienced. Among various combinations like walking - attending self-care, eating - attending self-care etc., combination of talking - attending self-care had scored the highest mGHQ (32.00±1.4) than other studied disabilities in this group of patients.

Discussion

All cancer patients in this study reported some level of distress; 65% found to have severe stress. Some western studies report the prevalence rate of stress in cancer patients in the range of 35% -38% (8, 9). Compared to western samples, our study sample reported higher stress levels. Community study of cancer outpatients reported lower prevalence rate of stress (24.5%) (15), compared to that of patients who were in large tertiary cancer center (37.8%) (9). Another study has found prevalence of cancer-related distress in a range of 24% –59% depending on the type of cancer, and higher levels of distress varied from 41% in breast cancer (BC) to 23% in upper gastro-intestinal (GI) tract cancer patients (7). In addition Gao *et al.* , (15) suggested that cancer type/site was the best predictor for psychological distress in various treatment settings.

Among five cancer types which we studied, severe psychological distress (GHQ score $\geqslant$ 20) was found in 84% of lung cancer patients. Zabora *et al.* (8) had compared 14 cancer types and stress levels; indicating that lung cancer (LC) patients had scored the highest stress level (43.4%) while gynecological cancer patients experienced lowest stress level (29.6%). In the current study, the highest mean GHQ score was reported by lung cancer patients (23.96±4.1) and the lowest mean stress score was reported by colon cancer (21.72±3.0) patients. Other studies in the west also reported similar findings (8, 16). Among all cancer types of present study, BC patients had scored the lowest prevalence of stress (57%), and it was still higher than the levels found in BC patients in Herschbach's study (41%). In the same study prevalence of stress in GI cancer patients was lower (23%) while in our study, the prevalence of stress was higher in colon cancer patients (59%). Lung, pancreatic, head/ neck, Hodgkin's disease, and brain cancer patients were the most

distressed patients when considered the cancer sites (9).

Majority of our sample reported lower monthly income, and they scored higher mGHQ. In other words psychological distress was higher in cancer victims who had lower income (<Rs. 10,000/-). Psychological distress of cancer patients was reported to be decreased with increase in income levels (8,9,16). Unemployed BC women significantly had more stress; their stress can be lowered by employment (16). The reasons for having low stress in employed women might be related to the ability to overcome issues in a better manner as a result of having a wider social environment and self-confidence (16). However, there is evidence that most cancer survivors have suffered from significant work-related disabilities (17) which may affect work performance, resulting in low income or turn-out from the job, causing further increase in distress.

Different types of disabilities were reported by the participants of the present study. Irrespective of the cancer type, those experiencing disabilities have to depend on others to different extents. It may contribute to increase their stress levels further. Many western studies had reported similar findings on disabilities and stress levels in cancer patients; usually starting as discomfort or pain and severely affecting the psychological well-being of terminally ill cancer patients; due to worsening of physical functions and cancer-related fatigue (6, 11, 18). A high prevalence of limitations in daily activities and/or instrumental activities was reported by the elderly cancer patients (19). Considering LC patients in the present study, they had experienced various percentages of different types of disabilities and it may have led them to score the highest stress than others. Similarly in a study of women in USA who had lung cancer reported poor physical functioning, than women with breast cancer (20).

In Sri Lanka it is less known how cultural factors such as beliefs about cancer affect the patients psychologically. Discrepancies in accessibility of health care system to different sectors of population hinder early detection of cancer and also prevent getting proper treatment. As a result, cancer patients may develop higher levels of fear and anxiety when they are diagnosed with a cancer. In addition, socio-economic burden also contributes to psychological distress. Chandwani and colleagues had revealed that failure in early detection and interventions lead to elevated levels of distress with a negative impact on cancer outcomes, cancer therapies, survival and disease progression, resulting a decrease in patients' quality of life, and increase in care costs (19**).** However, further research is recommended to screen stress among cancer patients routinely in local setting.

Results of the current study may not be applicable to whole country due to the selected single study setting. It was a limitation of this study.

Conclusions

In our study, psychological distress affects all cancer patients, and is a significant health problem. Stress levels in cancer patients were influenced by some socio-economic factors, type of cancer, type of disability, number of disabilities, and combination of disabilities they have experienced. Those who had lower income and had disabilities were severely stressed.

Lung cancer patients were severely distressed compared to those with other types of cancers. Psychosocial factors contributing to psychological distress in cancer patients need to be studied further. Psychosocial support services should target more vulnerable patients experiencing disabilities and those who are from lower economic background. Studies in other countries emphasize the need for maintaining patients' daily activities and providing support to cope with cancer-related physical disabilities and emotional distresses (24). Therefore special attention must be paid to detect cancer patients with high level of stress and to address their psychosocial needs appropriately.

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An oral presentation based on this study was done on 02.02.2016 at International Multidisciplinary Research Conference 2016 in Colombo. Title of abstract was "Psychological distress in cancer patients in Southern province of Sri Lanka, (Multidisciplinary Research 2016- ISBN 978-0-9939889-8-1).

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Early clinical experience with the new Amplatzer Ductal Occluder II for closure of the Persistent Arterial Duct (PDA)

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ABSTRACT

Introduction: Transcatheter PDA closure has gained acceptance over surgery because of its cosmetic benefits, shorter hospital stay and absence of pain associated with a thoracotomy. The Amplatzer Ductal Occluder II (ADO II) device provides a solution for the closure of small to moderate-sized PDAs

Objective: To describe early single-centre clinical experience with ADO II.

Methods: Children with a haemodynamically significant patent ductus arteriosus (PDA) who underwent percutaneous trans-pulmonary closure with Amplatzer Ductal Occluder II (ADO II) were included. Data was collected from computer based patient records.

Results: Trans-pulmonary PDA closures using ADO II were undertaken in 65 children (46 females) with a mean age of 2years 3 months (range 5 months to 14 years) and a mean weight of 9.6kg (range 4.2-25kg).

Complete occlusion was noted pre-discharge in 64 (98.4%) patients. One (1.6%) had residual shunting after deployment followed by embolization to the left pulmonary artery on the third day of the procedure. Of the 65 children, five (7.7%) had mild flow acceleration in the left pulmonary artery and another one (1.6%) had mild aortic flow obstruction following the procedure.

At 7 and 30 days, echocardiography confirmed complete ductal occlusion without need for further intervention in all 64 (98.4%) successful cases.

Conclusions: ADO II is highly effective in rapid occlusion of morphologically varied small to moderate-sized PDAs.

Key words: Ductal occluder; patent ductus arteriosus; trans-pulmonary; residual shunting)

Introduction

The reported incidence of patent ductus arteriosus (PDA) in infants ranges from 0.138 to 0.8 per 1000 live births (1,2). Transcatheter PDA closure has gained acceptance over surgery because of its cosmetic benefits, shorter hospital stay and absence of pain associated with a thoracotomy. Since the initial description by Portsmann et al of nonsurgical closure of PDA the percutaneous approach has become standard clinical practice (1). Coils and devices have broadened the range of patients and anatomies treatable with percutaneous techniques (3-6). The ADOII device provides a solution for the closure of small to moderate-sized PDAs. The ADOII device is a modification of the ADOI device as produced by AGA Medical Corporation. It is one of the ranges of vascular occlusion devices based on nitinol wire meshes shaped in sequential lobes.

ADOII is characterized by two low-profile retention discs for placement in the aorta and pulmonary artery (PA). Connecting waist of variable diameter and length for positioning within the PDA itself is attached to the retaining discs by two articulations. This allows the positioned, relatively soft device to adapt to the patient's anatomy rather than distorting the anatomy to its shape. The aim of the study was to describe the early single-centre clinical experience with the Amplatzer Ductal Occluder II (ADO II)

Methods

Children presenting with a haemodynamically significant PDA to Teaching Hospital Karapitiya (THK), Galle, Sri Lanka, who underwent percutaneous closure with the ADOII were included in this study. In instances where the PDA was larger than 5.5 mm in diameter, use of the device was not considered. Patients with additional cardiac anomalies requiring surgical correction were referred for surgery as were patients <3 kg in weight. Data collected from computer based patients' records included demographic, clinical, and echocardiographic parameters.

The trans-pulmonary technique for device deployment was adopted. Initially an aortogram was performed using a pigtail catheter. The sizing of the device is based upon the waist diameter and length measured by angiography (**Figure 1**). The duct is crossed from the PA and the aortic retainer is then exposed in the main aorta and the delivery system withdrawn to allow for the waist to be deployed in the duct itself. The pulmonary retainer is then exposed against the pulmonary arterial wall. Device positioning and residual PDA leaks were confirmed by aortic angiogram (**Figure 2**). All patients were treated with pre-procedural intravenous cefuroxime (30 mg/kg) with additional three doses post-procedurally. Intravenous heparin (50 U/kg) was administered at the commencement of each procedure. All patients underwent echocardiography on the next day, after 7 days and at 30 day follow-up visits.

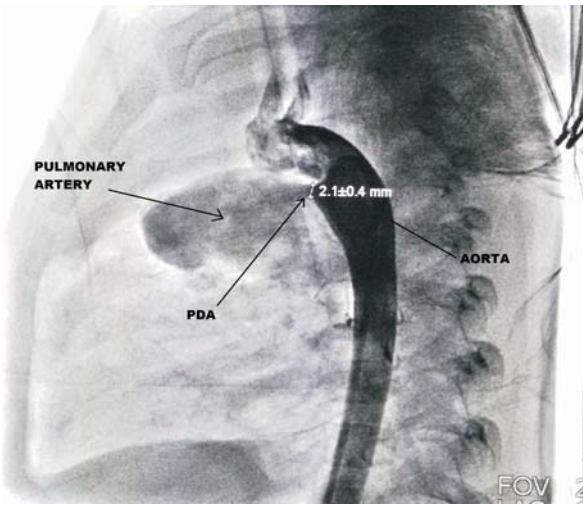

Figure 1: Angiogram to visualize the PDA

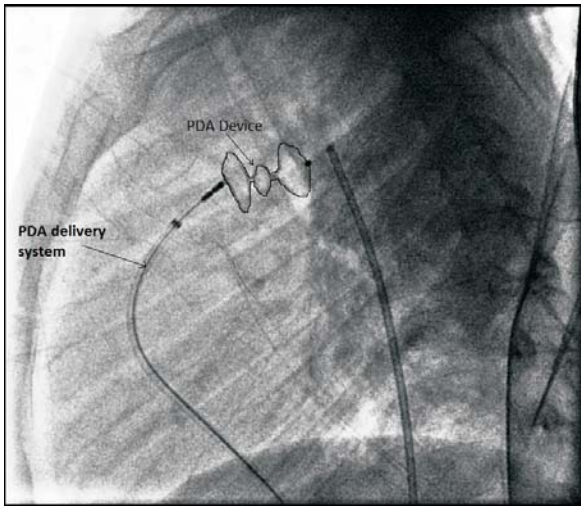

Figure 2: PDA device after deployment

Results

The frequency of age group distribution is given in **Table 1**.

Table 1: Frequency of age group distribution

Age group	No. of patients
≤ 1 year	26
1-2 years	17
2-5 years	17
5-10 years	04
Above 10	01

Of the 65 patients, 46 were females. Fifteen patients had weights from 3.1 - 6 kg, 31 had weights from 6.1 -10 kg, 13 had weights from 10.1 - 15 kg, 3 had weights from 15.1 - 20 kg and 3 patients had weights above 20 kg.

Angiographic measurement of the PDA size and the PDA device sizes are shown in **Table 2 and 3** respectively.

Table 2: Angiographic measurement of the PDA size

PDA size (mm)	No. of patients
1 - 2	26
2.1 - 3	24
3.1 - 4	11
4.1 - 5	3
> 5.1	1

Table 3: PDA device size

Device size (mm)	No. of patients
6 × 6	16
6 × 5	01
6 × 4	17
5 × 6	14
5 × 4	08
4 × 6	02
4 × 4	04
3 × 6	03

From May 2012 to January 2016 trans-venous PDA closures using ADOII were undertaken in 65 children. 6mmX4mm ADOII was the commonly used device in our series. Mean age was 2 years and 3 months (range 5 months to 14 years) with a mean weight of 9.6 kg (range 4.2-25 kg). The mean ductal diameter was 2.55 mm (range 1.1-5.1mm). ADO II was released in all 65 children.

One (1.6%) patient had residual shunting after deployment of ADO II followed by embolization to the left PA on the third day of the procedure. This child underwent surgical closure of the PDA after the surgical removal of the embolized device. Complete occlusion was noted pre-discharge in the remaining 64 (98.4%) children. Five of these 65 children had mild flow acceleration in the left pulmonary artery (LPA) and another had mild aortic flow obstruction following the procedure. These 6 children are doing well at present with good weight gain despite still having mild LPA origin narrowing and mild obstruction to the descending aortic flow due to the presence of the device. These are common complications following PDA device closure and are usually overcome with growth of the pulmonary artery. At 7 and 30 days, echocardiography confirmed complete ductal occlusion without need for further intervention in all 64(98.4%) successful cases.

Discussion

Transcatheter closure procedures have been performed with high success rates both in children and adults (3-6,8-18). Due to advances in diagnostic and therapeutic modalities diagnosis and treatment of PDA can be accomplished at a relatively early age (5-9). Thanopoulos et al (15) reported success rates of 95% and 98% soon after and one month after device implantation in patients with a mean age of 3.6 years.

The ADOII device provides a solution for the closure of small to moderate-sized PDAs in children (14,15). We have demonstrated that percutaneous treatment with ADOII can be realized with lower complication and residual shunt rates. The immediate and short term follow up success rates (complete occlusion) for duct occlusion by ADOII at 24 hours, 7 days and 1 month were 98.4% all in our series which compares favourably with data reported using Amplazter ADOII devices (8). The multiple layers of nitinol allow for rapid ductal occlusion which reduces residual shunt risks. The ability to position the ADOII such that each of the retention discs assumes its independent orientation significantly reduces the risk of protrusion, anatomical distortion and displacement which has resulted in a 98.4% (n=65) success rate of device deployment in our series with only one (1.6%) re-intervention due to device

dislodgement which compares favourably with reported data (8).

The ADOII device was designed by the manufacturers with the express intention that the retaining discs would be positioned in the aorta and PA. However, in the presence of a large ampulla, the aortic retaining disc will be positioned within the ampulla and not the aorta. This position makes the aortic disc to appear spherical while the pulmonary disc to be flattened giving a disfigured orientation after deployment although this is the accepted configuration in case of a PDA with a large ampulla. When approached transvenously which we practice coupled with the soft and flexible nature of the Amplazter ADO II devices, the aortic disc can be well positioned in the ampulla without protruding to the aorta, while still allowing the rest of the device to assume its intended position. This has resulted only 1.6% (n=1) of cases with mild obstruction to the aortic flow in our series.

In case of a short duct, the central waist may protrude into the PA, leaving the PA retaining disc redundant. This occurs even more so if the device is significantly oversized. As such, the shorter device will usually be applicable unless the duct is extremely long. In our experience, this positioning was problematic only in five cases (7.7%) with pressure gradients ranging from 10-22 mmHg noted across the left PA origin. Correct and high quality ductal imaging techniques available in our unit allowed us to accurately assess the ductal anatomy and the size which helped us to select the appropriate sized device thus preventing any unwanted pulmonary flow obstructions.

Embolization during release of the device is one of the important complications of the procedure (7-9). Embolization can occur in systemic and generally in pulmonary artery (7-9). In a published series of 27 cases, Forsey *et al.* (8) reported displacement of the device (n=1) and embolization (n=1).They attributed development of these complications to underestimation of ductal diameter secondary to spasm of the ductus arteriosus induced by catheterization. In our study, as a procedural complication only one (1.6%) device embolization to the PA was observed three days after the device deployment.Although the selected size of the device matched with the measurements of the acquired ductal images we assume this to be attributable to underestimation of ductal diameter secondary to spasm of the ductus arteriosus induced by catheterization.

Vascular injury to the femoral artery and the vein at the local access site, haematoma formation and damage to the local soft tissues have been reported in published data (5-8). In our series all cases had palpable popliteal pulses 6 hours following the procedure and intravenous heparin infusion was not required in any child.Infection of the local vascular access site was not reported and vascular surgical intervention was not needed in our series. Although this is mainly attributable to the operator experience the ADOII design and flexibility has also allowed delivery with 4 or 5 F delivery catheters with minimal local tissue and vascular injury as compared to ADO I which needs a minimum of 6F delivery system to deliver the smallest available device.

Conclusions and recommendations

- ADO II is highly effective at providing rapid occlusion of morphologically varied small to moderate-sized PDAs.
- Occluder design allows delivery with 4 or 5 F delivery catheters with minimal local tissue and vascular injury.
- Stable occluder position is dependent on accurate device sizing correct positioning of both aortic and pulmonary discs, good quality imaging to visualize device configuration and operator experience.
- Flexibility of the articulations allows this device to simplify the treatment in a range of patients and specific ductal anatomies that are more challenging.
- A larger range of sizes and configurations of this occluder may be required to successfully occlude all ductal sizes and morphologies.

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Prevalence and pattern of Dyslipidaemia among patients with newly diagnosed type 2 diabetes mellitus in Southern Sri Lanka; a cross sectional study

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ABSTRACT

Introduction: Dyslipidaemia is one of the major risk factors for cardiovascular disease (CVD) in diabetes mellitus. However, the magnitude and characteristic features of dyslipidaemia among Sri Lankans with newly diagnosed diabetes is not yet known. We aimed to study the prevalence and pattern of dyslipidaemia in a cohort of patients with newly diagnosed type 2 diabetes mellitus (T2DM).

Methods: This study was carried out in 403 newly diagnosed T2DM patients attending a specialist diabetic clinic in Southern Sri Lanka. Dyslipidaemia was diagnosed if patients had one or more parameters of lipid profile outside the target values recommended by the American Diabetes Association (ADA).

Results: Diabetic dyslipidaemia was observed in 90% of patients with females having higher prevalence (94.7%) than males (87.0%, P=0.04). The most prevalent type of dyslipidaemia was isolated elevation of low density lipoprotein (LDL) cholesterol (84.3%). Raised triglyceride (TG) and low high density lipoprotein (HDL) were comparatively less common and observed in less than 20% subjects. Factors such as obesity, waist circumference, age and degree of hyperglycaemia at presentation had no significant effect on the pattern and prevalence of dyslipidaemia.

Conclusions: This study revealed a higher prevalence and a different pattern of dyslipidaemia among newly diagnosed patients with T2DM. Finding of raised LDL with relatively low TG observed in this study was different to the pattern of diabetic Dyslipidaemia described in Caucasians.

Keywords*:* Prevalence and pattern, diabetic dyslipidaemia, newly diagnosed, type 2 diabetes mellitus, Asian ethnicity

Introduction

Patients with type 2 diabetes mellitus (T2DM) are at higher risk of developing coronary artery disease (CAD) and other vascular diseases such as ischemic stroke. The risk is primarily due to a greater burden of atherogenic risk factors among diabetics, including hypertension, obesity, and dyslipidaemia (1). A number of studies have shown the beneficial effect of treating dyslipidaemia on cardiovascular morbidity and mortality in patients with T2DM (2,3).

The American Diabetes Association (ADA) recommends screening for dyslipidaemia at the time of diabetes diagnosis and every 5 years thereafter, or more frequently if needed to achieve goals (4). ADA in 2016 update recommends moderate-intensity statin treatment for all patients with diabetes aged $\geq$40 years and high-dose statins for those with increased cardiovascular risk [e.g., LDL cholesterol $\geq$100 mg/dL (2.6 mmol/L)], high blood pressure, smoking, albuminuria, and family history of premature coronary artery disease) (5).

The typical pattern of dyslipidaemia seen in patients with T2DM is elevated TG and low HDL-C levels, although all lipoproteins have compositional abnormalities (4). Observational studies suggest that low HDL-C is one of the most important risk factor for CAD (6,7). It is well documented that raised LDL-C and TG are also associated with an increased risk of CAD (4,8). However, differences exist in the morbidity and mortality of diabetes patients between different ethnic groups. Compared to Caucasians, South Asians have a higher risk of developing CAD and other macro-vascular and micro-vascular complications related to diabetes (9). Change in the prevalence and pattern of dyslipidaemia could be a contributing factor for higher risk of CAD among South Asians.

The best time to look at the prevalence and pattern of diabetes dyslipidaemia is at the time of the diagnosis of diabetes as subsequent management with pharmacological agents or non-pharmacological measures can alter both pattern as well as the prevalence of dyslipidaemia. However, according to our knowledge, there were no previous studies on the prevalence and pattern of dyslipidaemia among Sri Lankans with newly diagnosed T2DM. Even for South East Asians, the pattern and the prevalence of dyslipidaemia among newly diagnosed patients with T2DM is not adequately investigated. The knowledge on the pattern and the prevalence of diabetic dyslipidaemia will be useful in the successful management of T2DM particularly in the local setting. Therefore, this study was designed to determine the prevalence and pattern of Dyslipidaemia among newly diagnosed patients with T2DM and evaluate the its associations with risk factors such as hypertension (HT), body mass index (BMI), waist circumference (WC), and fasting blood glucose (FBG).

Methods

This cross sectional study was conducted in newly diagnosed patients with T2DM presented to a Regional Diabetes Centre, Southern Province of Sri Lanka. This Regional Diabetes Centre attracts patients from whole Southern Province which has a total population of 2.5 million and account for 12% of Sri Lankan population. The study was carried out from January 2012 to July 2013. Subjects were recruited by convenient sampling method. Posters in public places and collaborations with general practitioners were used to recruit patients with new onset T2DM. Following patients were excluded from the study; patients currently on treatment (pharmacological or non-pharmacological) for dyslipidaemia, patients who have been treated for diabetes in past, those who were unwell due to hyperglycaemia or intercurrent illness, clinically apparent hypothyroidism, nephrotic syndrome and chronic kidney disease, those with extreme body habitus (BMI<18 or >40), and when type 1 diabetes or secondary causes for diabetes were more likely on clinical grounds than T2DM. A pretested interviewer-administered questionnaire was used to obtain demographic and medical information such as age, sex, ethnicity, tobacco smoking, and family history of dyslipidaemia, CAD, and metabolic syndrome. Weight, height, and WC were measured and BMI was calculated. All anthropometric measurements were performed by trained nurses adhering to the WHO guidelines, using calibrated equipment. Blood pressure was recorded using an electronic instrument (Omron Corporation, Tokyo, Japan), as the mean of two readings taken five minutes apart.

All chemical analyses were performed in the laboratory attached to the Regional Diabetic Center mentioned above and same method of biochemical analysis was used throughout the study period. Overnight fasting venous blood samples were collected to measure HDL-C and LDL-C, serum TG and glucose. Cholesterol esterase oxidase-peroxidase-amidopyrine method was used to assess serum cholesterol, and for measurement of serum TG glycerol phosphate oxidase-peroxidase-amidopyrine method was used. For HDL cholesterol, direct method poly-ethylene-glycol-pretreated enzymes were used. Approval of the Institutional Ethics Committee of the Faculty of Medicine, University of Ruhuna, was obtained prior to study commencement and written informed consent was obtained from all study subjects in the local language.

All the data were analysed using SPSS 17.0. Dyslipidaemia was diagnosed if any component of lipid profile exceeds recommended targets. Those with dyslipidaemia were further subdivided in to mixed dyslipidaemia (all three parameters outside the recommended ADA targets), combined dyslipidaemia (two parameter outside the

recommended target) or isolated dyslipidaemia (only one parameter outside the recommended target). Patients with combined dyslipidaemia were further classified in to different patterns of dyslipidaemia (high LDL and TG, high LDL and low HDL, high TG and low HDL). Significance of relationship between following factors with each lipid component level was calculated using Chi square test of independence. Age at presentation (<45 or ≥45 years), degree of hyperglycaemia at presentation (HbA_1C < 6.9% as lower degree of hyperglycaemia and HbA_1C value ≥7.9% as higher degree of hyperglycaemia), presence of global obesity defined as BMI more than 23kg/m^2, and presence of central obesity with WC exceeding 80cm in females and 90cm in males.

T-test and one way ANOVA were used to test significant as appropriate.

Results

Table 1 shows demographic characteristics of the 403 newly diagnosed patients with T2DM in the study. There were more male (71.7%) than female (28.3%), and nearly 60% of the male had younger onset of T2DM (<45 years). Females were significantly older and had lower level of HDL-C than males. Although there was a higher prevalence of central obesity in females (89%) compared with males (59%), the mean difference was not statistically significant.

Table 1: Baseline characteristics of the study sample according to gender

Variables		Male = 289		Female = 114		*p*
Number and percentages		n	%	n	%	
Age (years)	<45	168	58.1	42	36.8	-
	⩾45	121	41.8	72	63.1	-
BMI	<23	88	30.4	44	38.6	-
	⩾23	201	69.5	70	61.4	-
Waist Circumference (cm)*	Normal	120	41.2	13	11.4	-
	High	169	58.8	101	88.6	-
HbA_1C	⩽ 6.9%	77	26.6	34	29.8	-
	7-7.9%	132	45.6	52	45.6	-
	> 7.9%	80	27.6	28	24.5	-
		Mean	**SD**	**Mean**	**SD**	***p***
Age		43.3	10.6	47.2	10.8	0.001
BMI		24.5	4.9	25.0	4.8	0.36
Waist Circumference		90.3	11.1	91.4	10.4	0.34
HbA1c%		6.9	1.4	7.0	1.4	0.80

Mean levels of total cholesterol, HDL-C, LDL-C, and TG were 205.3± 41.8, 48.7±9.3, 130.6± 38.3, and 119.1± 54.8 respectively. Of note, the mean LDL-C of 130.6± 38.3 mg/dL was well above the LDL-C target of 100 mg/dL recommended by ADA.

Overall, the prevalence of Dyslipidaemia with at least one abnormal lipid parameter was seen in 89% of patients in the sample with higher prevalence observed in females (94%) than in males (87%). Raised LDL-C was the commonest abnormality affecting 84%; however, raised TG and low HDL-C were comparatively less common accounting for 19% and 18% respectively. Females had higher prevalence of unfavorable lipid abnormalities including raised LDL-C(91%) and low HDL-C(38%). However, raised TG was more prevalent in males than in females (**Figure 1**).

Table 2 presents the pattern of dyslipidaemia in newly diagnosed patients with T2DM according to their gender. Among males, isolated raised LDL-C was the commonest pattern seen around 60% and combined dyslipidaemia with raised LDL-C and TG was observedaround15%. Mixed dyslipidaemia with all three abnormal lipid parameters (TG, LDL-C and low HDL-C) was rare (1.4%) in males. In females too, isolated raised LDL-C was the most common pattern of dyslipidaemia (46.5%) followed by combined dyslipidaemia (32%) with raised LDL-C and low HDL-C. However, combination of raised LDL-C and TG was less common in females (7.9%) in compared to males (15.6%).

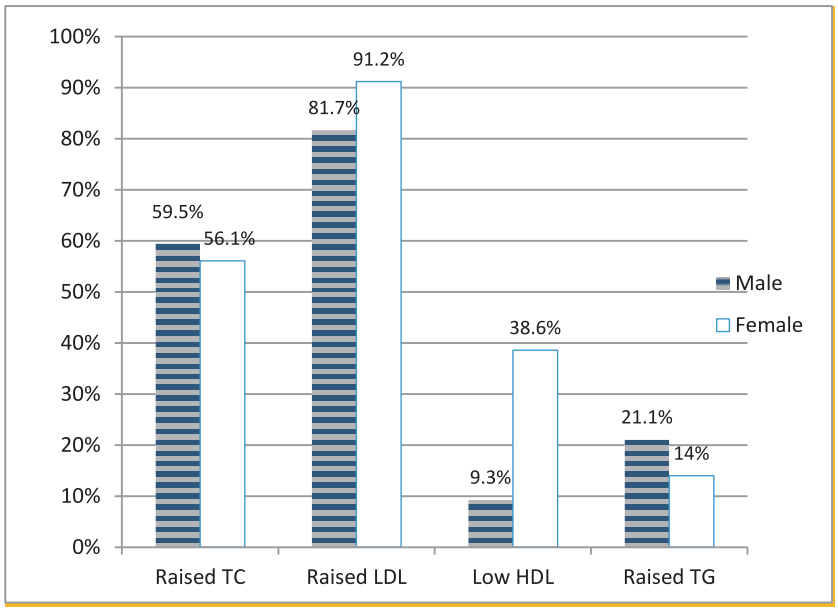

Figure 1: Lipid abnormalities according to gender

Table 2: Pattern of Dyslipidaemia according to gender

	Males(289)		Females(114)	
Pattern of dyslipidaemia	n	%	n	%
Isolated single parameter dyslipidaemia	184	63.7	57	50.1
Raised LDL-C	170	58.8	53	46.5
Raised TG-C	10	3.5	2	1.8
Low HDL-C	4	1.4	2	1.8
Combined dyslipidaemia	64	22.2	46	40.4
High TG and low HDL-C	2	0.7	0	0
HIGH TG and high LDL-C	45	15.6	9	7.9
High LDL and low HDL-C	17	5.9	37	32.5
Mixed dyslipidaemia (high TG, high LDL-C and low HDL-C)	4	1.4	5	4.4
Total	252	87.2	108	94.7

We analysed prevalence and pattern of dyslipidaemia according to degree of hyperglycemia at the time of diagnosis of T2DM. HbA_1C value less than or equal to 6.9% was considered as lower degree of hyperglycaemia whereas values 7.9% or more was considered as higher degree of hyperglycaemia. As shown in **Table 3** there was no significant effect of degree of hyperglycaemia on the pattern and the prevalence of dyslipidaemia. However, lower degree of hyperglycaemia was more commonly associated with isolated Dyslipidaemia even though it did not reach statistical significance.

We also evaluated whether the age at diagnosis of T2DM had any effect on the prevalence and pattern of dyslipidaemia. As shown in **Table 4,** raised TG was significantly different between groups with higher mean value observed in patients with younger (25-35 years) onset T2DM compared older onset. Even though not reaching significant level, other lipid parameters too (raised LDL, and low HDL) were higher in younger individuals.

Table 3: Lipid abnormalities according to degree of hyperglycaemia

Prevalence of dyslipidaemia	**Degree of hyperglycaemia**		
	$HbA_1C \leqslant 6.9\%$ (%)	$HbA_1C \geqslant 7.9\%$ (%)	*p*
Raised LDL	86.4	87.0	0.83
Raised TG	10.8	19.4	0.11
Low HDL	13.5	20.3	0.24
Total	88.2	90.7	0.48
Pattern of dyslipidaemia	%	%	*p*
Mixed dyslipidaemia	0	2.7	0.12
Combined dyslipidaemia	21.6	29.6	0.27
Isolated dyslipidaemia	67.5	59.2	0.09
No Dyslipidaemia	10.8	09	0.34

TC - total cholesterol, LDL - low density lipoprotein, HDL - low high density lipoprotein, TG -triglycerides

Table 4: Lipid abnormalities according to age at diagnosis

Age categories	**n**	**TC**			**LDL**			**TG**			**HDL**		
		Mean	**SD**	***p****	**mean**	**SD**	***p****	**mean**	**SD**	***p****	**mean**	**SD**	***p****
15 - 24	12	209.3	23.4	0.19	130.0	33.4	0.13	125.0	58.4	0.01	48.3	6.6	0.42
25 - 34	64	216.7	43.2		139.6	42.3		140.3	69.3		46.4	9.8	
35 - 44	140	207.4	47.5		131.4	42.9		124.4	63.8		47.7	9.2	
45 - 54	131	194.0	52.3		124.0	39.3		108.1	46.8		47.7	12.9	
55 - 64	60	198.5	44.1		125.4	41.0		105.1	30.4		50.1	10.0	

TC - total cholesterol, LDL - low density lipoprotein, HDL - low high density lipoprotein, TG - triglycerides.

*According one way ANOVA. ** Post Hoc test revealed that there was significant difference exist between age category of 25-34 with 45-54 ($p<0.01$) and with 55-64 ($p=0.01$).

We examined the prevalence of dyslipidaemia according to BMI and waist circumference. Raised LDL was the commonest abnormality in all BMI categories followed by raised TG. Overall BMI had no effect on the prevalence of dyslipidaemia. Central obesity measured according to waist circumference had no significant effect on the overall prevalence of dyslipidaemia.

Discussion

In the wake of rising incidence of diabetes and cardiovascular diseases in Sri Lanka, this study is a step towards evaluating the prevalence and the pattern of diabetic dyslipidaemia. Furthermore, this is the first paper on diabetes dyslipidaemia in Sri Lankans with newly diagnosed type 2 diabetes mellitus. This study revealed close to 90% patients had some form of dyslipidaemia at the time of diagnosis of T2DM. Transferred on to the total diabetes population in Sri Lanka, this figure may imply that approximately 1.8 million Sri Lankans with diabetes may be affected by dyslipidaemia.

The mean levels of total cholesterol and LDL-C found in our study were comparable to the mean total cholesterol levels and LDL-C reported in the United Kingdom Prospective Diabetes Study (UKPDS) (10,11). However, raised TG observed in our study (113mg/dL in males and 121mg/dL in females) was much lower than the mean TG levels of UKPDS (159mg/dL in both genders) (11). Mean HDL-C level of 51.5mg/dL in males and 48.6mg/dL in females found in our study were also different to the mean HDL-C levels of 39mg/dl in males and 43mg/dl in females reported in UKPDS study. The UKPDS study also reported higher prevalence of adverse Dyslipidaemia in females than in males (11). Such difference was not observed in our study; however there was a significantly lower HDL-C level observed in females in our study.

The most prevalent type of dyslipidaemia in this study was raised LDL followed by hyper-triglyceridemia. Prevalence of low HDL was comparatively low and seen in just 18% of the sample. These findings are different to diabetic dyslipidaemia described in Caucasians (4,11,13). However, some studies including one conducted in Sri Lanka also have reported higher LDL cholesterol level than TG in patients with T2DM (14). Raised LDL cholesterol with relatively lower TG was also reported among patients with diabetes in other developing countries such as Nigeria, and India (15,17). But, unlike in our study most of these studies showed higher prevalence of low HDL.

There could be many reasons for the different pattern of diabetic dyslipidaemia in the cohort of patients that we studied. Unlike some of the published studies on diabetic dyslipidaemia, we studied only the newly diagnosed patients with T2DM who were not on any treatment for dyslipidaemia. Therefore, the pattern of Dyslipidaemia observed in this study reflects the true picture of diabetes dyslipidaemia. Higher prevalence of TG with low LDL reported in previous studies could be an effect of statins as it lowers LDL more than TG. The typical changes of raised TG with low HDL-C seen in diabetic dyslipidaemia is thought to be due to insulin resistance together with dysfunction of the enzyme lipoprotein lipase (LPL). It was postulated that insulin resistance in adipocytes promote lipolysis, resulting in excessive free fatty acid (FFA) release into the blood and higher production of TG-rich very low-density lipoproteins (VLDL) by liver. Higher production of VLDL together with blunted LPL activity contributes raised TG levels (18). Therefore, one of the possibilities for comparatively lower levels of TG seen in our study is either lower degree of insulin resistance or higher LPL activity or both. Further studies are needed to evaluate insulin resistance among patients with raised LDL-C and raised TG to answer this question. Higher prevalence of raised LDL in this study may indicate higher prevalence of raised LDL in the general population. Even though the prevalence of lipid abnormalities in the general population of Sri Lanka is not well studied, studies conducted in urban India had shown higher prevalence of raised LDL in general population (19,20). One of the other possibilities is the rising incidence of obesity in the local population (21). As substantial proportion of subjects (60%) were obese in our study, it could contribute for raised LDL levels.

Gender differences in the pattern of altered plasma lipids observed in this study are similar to major epidemiological studies from Western populations. However, in contrast to females who were more

dyslipidemic with higher LDL and triglycerides in those studies, our study revealed higher proportions of males (21%) having raised triglycerides compared to females (14%). Our study also showed that diabetes occurring in young individuals (<45 years) had significantly higher prevalence of elevated triglycerides. Even though not reaching significant level, other lipid parameters too (raised LDL, and low HDL) were higher in younger individuals (<45 years). This may be significant in the light of the finding that new onset diabetes in the South Asians is occurring at a relatively younger age and they need to be treated accordingly with appropriate measures (22).

Other factors such as degree of hyperglycaemia at diagnosis, BMI, and WC showed no significant effect on prevalence and pattern of dyslipidaemia. Therefore, predicting underlying Dyslipidaemia based on BMI, and WC may not be appropriate.

Conclusions

The prevalence of dyslipidaemia is high among newly diagnosed patients with T2DM affecting over 90%. In both genders, the most common pattern of dyslipidaemia is isolated raised LDL cholesterol followed by combined dyslipidaemia with raised LDL and raised TG in males and combined dyslipidaemia with raised LDL and low HDL in females. Typical pattern of diabetic dyslipidaemia with raised TG and low HDL is not observed in the majority. Other associated and contributing factors of dyslipidaemia such as obesity, waist circumference, and degree of hyperglycaemia at diagnosis had no significant effect on the pattern and prevalence of dyslipidaemia. Based on the findings of our study, we recommend lipid profile to be carried out in all patients at the diagnosis of T2DM and decision to perform lipid profile should not be based on factors such as obesity and degree of hyperglycaemia.

Limitations

The main limitations of our study include its single center study design. Therefore, generalisation of our findings accurately to whole diabetes population of Sri Lanka may not be plausible. The other limitation is not performing lipoproteins and genetic studies for further characterization of dyslipidaemia.

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Neurotoxic effects of paraquat

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Paraquat (1, 1' - dimethyl - 4, 4' - dipyridyl) is a bipyridyl compound. It was first marketed in 1962 as a broad-spectrum, non-selective and contact herbicide after having been described first by Weidel and Rosso in 1882 (1).

Paraquat is highly corrosive. It is absorbed poorly after inhalation but is extremely toxic if ingested. After paraquat ingestion, oedema, burns or ulceration may be seen in the mucosa of the mouth, oesophagus, stomach and intestines. Death usually occurs within 48 hours of ingestion of 50 mg/kg. Self-ingestion of paraquat is a serious health problem in many developing countries as it is used for suicidal attempts. It was described that 15 ml of 20% paraquat or one mouthful is a lethal dose in adults (2). An antidote for paraquat has still not been found. The World Health Organization classifies paraquat as a Class 2 moderately toxic substance but 'Pesticide Action Network Asia & Pacific' believes it to be in Class 1 due to its acute toxicity, delayed effects, and lack of antidote. There is a lag time between exposure and development of symptoms, early exposure is most deleterious. Unborn foetus and children are at more risk (3). In 2010, the California Environmental Protection Agency showed if exposed to lower doses even, during critical periods of childhood brain development is adversely affected.

At lower doses death may be delayed for several weeks (1). Toxicity is due to the pulmonary accumulation of bipyridyl compound. Paraquat is transported actively into pulmonary cells resulting in pulmonary oedema or fibrosis. Centrizonal hepatic necrosis, proximal renal tubular damage, myocardial damage, and skeletal muscle damage with focal necrosis may also be seen after acute intoxication of paraquat (1).

The major cause of death in paraquat poisoning is respiratory failure due to an oxidative insult to the alveolar epithelium with subsequent obliterating fibrosis. Paraquat, once it accumulates in the lungs or renal cells, leads to redox cycling and generation of toxic reactive oxygen species. This can overwhelm cellular defense mechanisms and lead to lung damage and renal tubular necrosis.

Paraquat is neurotoxic *in vitro*, but the neurotoxic effect of paraquat in humans is not yet clear. It was shown that exposure of lab animals to paraquat causes reduction in neurotransmitters in brain (4). Stelmashook *et al* 2007 demonstrated that both mature and immature cerebellar granule neurons in rats are killed by paraquat (5). Kriscenski-Perry *et al* 2002 demonstrated that paraquat and thermal stress elicit synergistic effect in damaging spinal motor neurons in laboratory animals (6). *In vitro* studies by Niso-Santano M *et al*. (2006) showed low concentrations (25μM paraquat in to 5×10^4 cells/cm^2 rat brain neuroblast cells) of paraquat stimulate very early and rapid activation of intracellular signalling cascades leading to paraquat induced neural cell death (7).

Chen Q *et al.* 2010 showed that after treatment with paraquat which was given orally once daily for 28 consecutive days to mice, cells in the hippocampus were irregular, and cytoplasm was found to be condensed. Number of nissl bodies found there was reduced and apoptotic or necrotic neurons were observed. Increased response latency was also noted in animals given paraquat (8).

Peng J *et al*. (2008) demonstrated tyrosine hydroxylase (TH) positive neuronal cell death in primary mesencephalic neuron-glia in animals treated with 10 mg/kg paraquat twice per week for three weeks (9).

Animal studies by Fei Q *et al.* (2008), Kang M J *et al.* (2009) and Ren J *et al.* (2009) showed repeated doses of paraquat (10 mg/kg gavage daily for four months or 10 mg/kg intraperitoneal injection twice weekly for three consecutive weeks) induced damage to the cells in substantia nigra pars compacta (SN_{pc}) in mid brain sections from mice (10-12). Kang M J *et al.* (2009) used 10mg/kg paraquat by intraperitoneal injection twice weekly for three consecutive weeks and showed reduction of TH-positive neurons in SN_{pc} by 40% as compared to saline treated controls (11). They also demonstrated reduced levels of dopamine (DA) and homovanillic acid (metabolite of DA) in the SN_{pc} of paraquat treated mice. Apart from the neurotoxic effects of paraquat on SN_{pc} , Fei Q *et al.* demonstrated that paraquat induced neurotoxicity acts through a Bak-dependent mechanism as Bak deficient mice were resistant to paraquat induced neurotoxicity (10). Bak is constitutively present on the surface of mitochondria and trigger mitochondrial outer membrane permeabilization. Ultrastructural evidence shows astrocyte oedema, neuron apoptosis in rat brain visualized by electron microscopy (13,14).

Although paraquat elimination in laboratory animals and humans from blood and organs other than brain occurs in hours and days, Prasad K *et al*. (2007) showed that paraquat persists in the ventral mid brain of mice for a prolonged time with a half-life of approximately one month (9). This persistence may contribute to its prolonged adverse effects in the central nervous system.

To see the effect of paraquat in acute poisoning, Magnetic resonance imaging (MRI) has been performed on poisoned survived victims and two patients in acute post poisoning phase have showed abnormal signals in brain. Susceptibility weighted imaging (SWI) has elicited changes in the corrected phase values for the extrapyramidal ganglia of survivors and these values correlate with excessive ion deposition. Diffusion tensor imaging (DTI) has shown microstructural changes in the extrapyramidal ganglia and hippocampus after paraquat poisoning. Therefore neuroimaging has indirectly demonstrated that acute paraquat poisoning exerts sustained effect during acute and recovery stages of poisoning (15).

Two case reports of facial nerve palsy following subcutaneous (SC) injection of paraquat and ingestion of minute amount of paraquat were found in the literature (16,17). One case report was on a 30 year-old farmer who injected (SC) himself approximately one ml of 20% solution of Gramoxone (16). Two days after, he was admitted to hospital with right facial nerve palsy. His abdominal reflexes were reduced on the right side. Oppenheim's sign (dorsiflexion of the big toe on stroking downwards along the medial side of the tibia, seen in pyramidal tract disease) was present on the left side. On the seventh day of administration of poison the findings were no longer elicited. The patient died on the 18th day in severe respiratory distress. The second case report was on a 49 year-old male who had rolled a cigarette with unwashed spray nozzles contaminated with paraquat and four days later developed a right lower motor neuron facial nerve palsy (17). The subsequent cause of the disease was not described and this may be entirely coincidental.

Cerebral haemorrhage following acute ingestion of paraquat has been reported (18,19). Autopsy findings of a 44 year-old male who had ingested 2-3ml of 20% paraquat concentrated solution and died on the sixth day of ingestion showed oedematous brain with purpuric haemorrhage extensively involving the cerebrum, brain stem, cerebellum and spinal cord (18). The maximum diameter of hemorrhagic foci was 5mm and there were no lesions seen in major arteries, veins or sinuses of the brain. The purpuric haemorrhage almost distributed in the white matter of the brain. Nerve fibers around the lesion were distorted and disintegrated to various extents. Glial proliferation was sparse. Degenerative changes were observed in Purkinje cells and granular cells of the cerebellum. The cerebral haemorrhage may be due to direct toxic effects of paraquat or its metabolites and anoxic anoxemia. Saeed S A M *et al*. (2001) also reported an intracerebral bleeding following acute paraquat ingestion (19). The report was based on a 52 year-old male who had ingested about 160 ml of "Weed killer". During the acute illness he developed left hemiparesis and computed tomography (CT) confirmed an intracerebral haematoma in the region

of the right basal ganglia and external capsule. The patient recovered gradually including his neurological features.

Chronic exposure to paraquat is a potential etiological factor for the development of Parkinson's disease (20,21). The paraquat structure bears a close similarity to the Parkinsonian toxin, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) (20). It has been thought that paraquat gains access to dopaminergic neurons through dopamine transporter (22). Repeated doses of MPTP fed mice showed reduction of TH-positive neurons in substantia nigra similar to repeated dose of paraquat fed mice (12).

Peripheral burning sensation following acute paraquat ingestion reported by Gawarammana I.B. and Dawson A.H. may be due to involvement of sensory nerves (23).

In vitro and animal studies clearly show the neurotoxicity of paraquat. Deliberate ingestion of high doses of paraquat may cause neurotoxicity in humans; however detection would not be possible due to lack of survivors. Although it was suggested that chronic paraquat exposure is an etiology of sporadic Parkinson's disease, it is extremely difficult to correlate the two due to the difficulty in identifying the exposure state accurately and confirmation of damage is possible only at postmortem. The neurotoxic effects of acute paraquat exposure on humans have still not been clearly investigated.

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Dilemma of clinician; making clinical decisions sans supportive laboratory findings

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Introduction

Thyrotoxicosis is a prevalent condition with diverse clinical presentations. It is typically associated with low TSH and high free thyroxin levels. Making the diagnosis of thyrotoxicosis in the absence of typical TSH and thyroxin changes is a daunting task and demands very accurate interpretation of clinical information. Here we describe an atypical presentation of thyrotoxicosis where delayed diagnosis led to a potentially fatal outcome.

Case report

A 22 year-old mother of a child with a meningomyelocele, presented with fever, difficulty in breathing and productive cough of 4 days. She also complained of noticeable weight loss despite normal appetite over the preceding 5 years. Her bowel habits were normal and there was no indication of steatorrhoea during this illness. She did not complain of chronic cough or evening pyrexia and she denied experiencing tremors, palpitation or excessive sweating.

Initial examination showed an emaciated woman (BMI - 16.4kg/m^2) who was febrile, tachypnoeic with a respiratory rate of 32/min and pulse rate of 120/min. Her breath sounds were vesicular. Bilateral coarse crepitations were audible in middle and lower zones, bilaterally. Her neck muscles were weak and she had to support the chin to lift the head. Neurological examination revealed generalised muscle wasting, weakness with Grade 4 power and exaggerated tendon reflexes.

Her initial investigations revealed White cell count of 22.15x10^9/L (neutrophils - 85%), Hb - 10.7mg/dL, Platelet - 279x10^9/L, CRP - 48mg/dL, ESR - 12mm, Na^+ - 140mmol/L, K^+ - 3.9mmol/L. Liver function tests on admission revealed AST - 81U/L, ALT - 76U/L, Serum protein - 66g/L, Serum albumin - 41g/L, Total bilirubin - 6.1umol/L. Thyroid Function Tests (TFT) were normal in 3 occasions (done from two different labs) with a TSH - 1.75mIU/L (0.47 / 4.7), free T_4 - 14.9pmol/L (10-28.2). Her stool analysis revealed the presence of fat globules but her stool culture was normal.

While waiting for the lab results. Patient was thought to have community-acquired pneumonia and she was treated with oxygen inhalation, intravenous cefotaxime and clarithromycin. She, however, developed type II respiratory failure requiring intubation and ventilation. Although her chest infection resolved completely she could not be weaned off ventilator due to poor respiratory muscle effort. Investigations at this stage showed CPK level of 204U/L (24 - 195) and EMG was suggestive of myopathy. Her serum vitamin D3 was low 24.7nmol/L (75 - 150). She had a fasting blood sugar value of 68mg/dL with negative retro-viral antibodies.

Although thyrotoxicosis was the most plausible etiology of her clinical picture, repeatedly normal TSH and thyroxin levels prevented us treating her with antithyroid drugs which are known to have serious adverse effects. Gradual deterioration of her condition, however, forced us to accept our clinical instinct despite serious concerns among the other members of the multidisciplinary team about our clinical judgment. Accordingly, she was started on oral propylthiouracil 350mg/day, verapamil 40mg tid. She was treated with intravenous vitamin D 10000 IU single dose prior to antithyroid therapy

because of low Vitamin D level but did not lead to any clinical improvement. She gradually improved allowing us to extubate her and subsequently discharged on propylthiouracil, verapamil, 1α cholecalciferol and calcium lactate.

Discussion

Thyrotoxicosis is generally associated with elevated free T_4 / T_3 with low TSH levels. Our patient had normal TFT in three instances. Despite of repeatedly normal TFT, presence of symptoms and signs such as persistent tachycardia, weight loss, myopathy, exaggerated reflexes, fat globules in SFR, led to the provisional diagnosis of thyrotoxicosis.

Many case reports have been published revealing the presence of thyrotoxicosis with normal TFT (1,2). There have been cases with resistant thyrotoxicosis with normal TFT where careful clinical evaluation has led to the correct diagnosis and management of the patient. These patients have been monitored with clinical parameters (weight gain, pulse rate, improvement and resolution of other thyrotoxic symptoms). Drug doses have been adjusted according to the clinical rather than biochemical response and patients have completely recovered.

It has been shown that 46% of the patients with thyrotoxicosis have isolated fat globules in their faeces due to an unknown reason (3). Furthermore, thyrotoxic patients have low vitamin D level again due to unknown reasons (4) and calcium and vitamin D supplements have led to a better response to antithyroid drugs (5). Observational studies have shown that there is an increase incidence of meningomyelocoele among children born to thyrotoxic mothers. It has been found out that multiple genetic mutations are responsible for this association (6).

In addition to clinical parameters, patient had biochemical parameters supportive of thyrotoxicosis such as low vitamin D levels, fat globules in stool which are widely reported in the literature. She also had a child with a meningomyelocoele which is a well explained association.

Conclusions

It is possible for patients with clinically overt thyrotoxicosis to have normal TSH and thyroxin levels. In this situation, subtle clinical features can help clinical decision making and rescue the patient's life.

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A case of trigeminal neuralgia due to dolichoectasia of the vertebrobasilar arteries

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Introduction

Trigeminal Neuralgia (TN) is a debilitating pain syndrome usually caused by demyelination of trigeminal sensory fibres within the nerve root. In most cases, the trigeminal nerve root demyelination involves the proximal portion of the root, resulting from compression by an overlying artery or vein (1). Dolichoectasia is a very rare cause of compression of trigeminal roots leading to TN. Currently there is less than 10 reported cases of vertebrobasilar dolichoectasias complicated by trigeminal neuralgia reported in literature (2).

Dolichoectasia is a rare but recognized vascular anomaly usually occurring in the vertebrobasilar system of intracranial arteries (3). It is characterized by elongated and tortuous arterial vessels subsequently leading to thrombosis, micro-embolisation, and brainstem compression, with or without aneurysm formation. It has been observed to cause isolated or combined brainstem/cranial nerve syndromes, cervico-medullary junction compression, transient or permanent motor deficits, cerebellar dysfunction, central sleep apnoea and hydrocephalus. It has also given rise to ischaemic and hemorrhagic stroke and subarachnoid hemorrhage (4,5). Although, it is not commonly observed, it should be considered as a cause which could lead to significant neurological morbidity and mortality.

We report a patient with dolichoectasia of vertebra-basilar system presenting with debilitating TN, who subsequently improved with local anesthetic injections through radiographic guidance.

Case report

We present a 70 years-old male who presented with episodic left sided hemi-facial pains for the last two months. He is a patient with hypertension with a fairly good control. His episodes of pain started to occur once or twice a day initially. He described an excruciating electric shock like pain over the V1 and V2 areas of the trigeminal nerve dermatomes, which predominantly got precipitated by washing his face. Gradually, his pain worsened and frequency also increased to 10-20 episodes per day. During the exacerbations he took paracetamol, tramadol, carbamazepine and also oral morphine without much benefit. He was feeling depressed and anxious and avoided any activity which could precipitate another attack, including washing face and chewing food. He did not consent for very invasive surgical procedure.

We investigated him with non-contrast and contrast CT scan (**Figure 1**) and also with an angiogram of cerebral vessels (**Figure 2**). It showed a Vertebrobasilar dolichoectasia without any aneurysms or arterio-venous malformations. His basic blood investigations were all normal.

As the pain was resistant to maximum pain relief medication, including subcutaneous regular dose of Morphine, we arranged an injection of a local anesthetic agent (bupivacaine) combined with steroid through radiographic guidance, to the area around foramen ovale and repeated the injections weekly until maximum pain relief was achieved. With four weekly injections, the facial pains reduced significantly and we managed to maintain his pain relief with oral gabapentin and carbamazepine. Gradually, he could eat and wash his face and engage in usual activities of daily living. Within the last 2 years of clinic follow up, he required 2 - 3 injections in two episodes of exacerbations, but was otherwise uneventful.

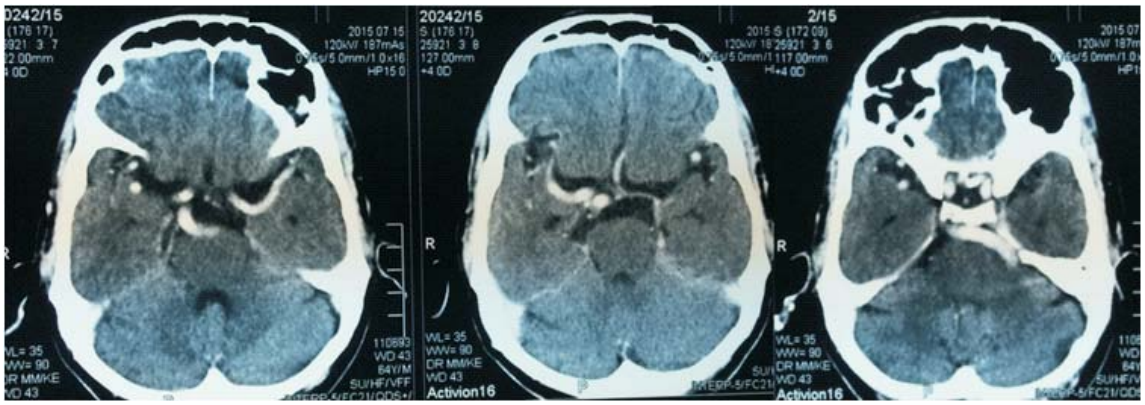

Figure 1: Contrast CT showing vertebrobasilar dolichoectasia

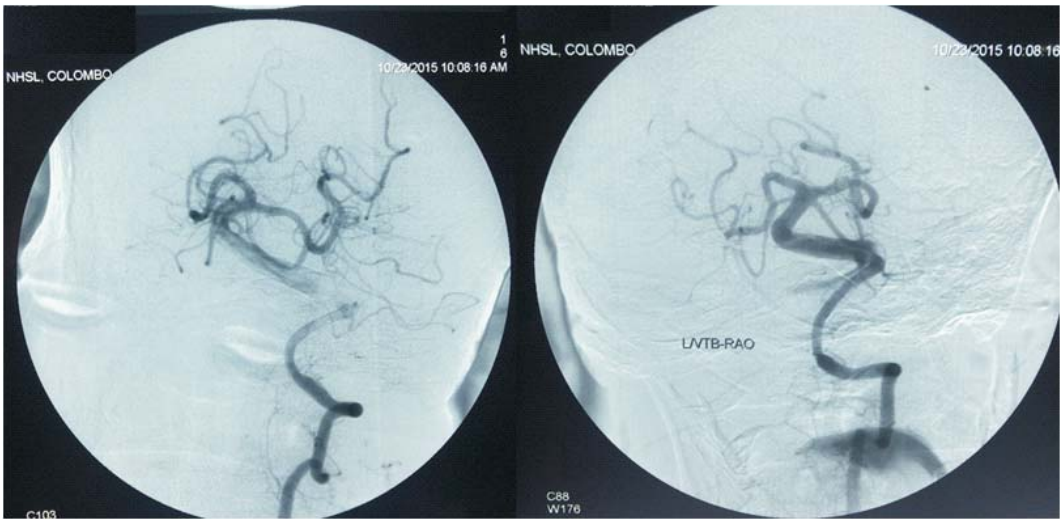

Figure 2: Angiography of cerebral vessels showing the elongated, tortuous arteries of circle of Willis. Vertebrobasilar dolichoectasia

Discussion

Dolichoectasia is a usually incidentally detected entity and is asymptomatic in majority. Vertebro-basilar dolichoectasia is an extremely rare entity with an expected incidence of 0.06 - 5.8%. The disorder is more common in males and is seen usually in 6^{th} - 7^{th} decade of life. The criteria for dolichoectasia include a diameter of more than 4.5 mm, basilar length >29.5 mm or intracranial vertebral artery length >23.5mm and deviation of the ectatic vessel of more than 1 cm beyond the shortest normal course (3).

Compressive etiology is the most common way leading to TN. So, microvascular decompression is considered the preferred treatment for medically resistant cases of TN and gamma knife therapy has emerged as a recommended alternative, particularly in elderly patients with comorbidities (8). However, over 30 years of follow up, the incidence of recurrence after microvascular surgery has been reported to range from 3 to 30% (9).

Our patient did not consent for surgery, so that we had to go ahead with an alternative mode of treatment. Therefore, local anesthetic injection combined with steroids was attempted as an option.

With this strategy, he showed a long lasting response and thereafter, he only necessitated few injections in the two exacerbations that he had over the next 2 years of follow up.

Conclusions

Dolichoectasia is a very rare but a noteworthy cause for Trigeminal Neuralgia (TN). It is important to be vigilant about the compressive causes which may lead to TN, especially when they are resistant to oral medication. When managing resistant cases, it would be beneficial to try less invasive methods such as, Trigeminal nerve blocks with local anesthetic and administering pain relief for neuropathic pain in patients who are not willing for invasive surgery.

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Where less is more; a case based discussion on the damage control resuscitation, a fundamental concept in the current management of major trauma

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Introduction

Systemic inflammatory response syndrome (SIRS) is a condition recognized recently. Inadequacies in resuscitation limited the survival of patient in the initial hours after major trauma until a relatively recent development changed the picture. Coagulopathy, acidosis and hypothermia (collectively called fatal triad) leading to SIRS followed by organ failure and even death is one of the most feared sequels of major trauma. Damage Control Resuscitation (DCR) was developed In order to prevent this 'dark' sequence by addressing its initiation during the immediate post-major trauma period. We discuss this novel and lifesaving concept using our experience in the successful management of a young man who sustained a major trauma.

Components of DCR are permissive hypotension until haemorrhage control, haemostatic resuscitation, limited use of crystalloids to avoid dilutional coagulopathy and damage control (Salvage) surgery to preserve physiology as well as to control haemorrhage.

DCR is the principle concept employed in the resuscitation of major trauma. This procedure saves lives increasingly and has gained acceptance globally. Our patient after suffering from a major trauma was successfully managed in a reasonably developed still less than ideal setting. Although perfection should be the aim, emergency health care systems in developing countries like Sri Lanka must embrace this concept and practice it as much as feasible for the benefit of many injured.

Case report

A 28 year-old three wheeler driver was admitted to Emergency Trauma Centre, Teaching Hospital, Karapitiya, Galle, about 30 minutes after his vehicle met with a head-on collision with a bus. Handle of the wheeler turned right angle during accident with its end creating an imprint on mid upper abdomen.

Initial inquiry did not reveal any airway or breathing problems but patient was in haemorrhagic shock with pulse rate of 125 beats per minute, blood pressure of 85/60mmHg and distended abdomen. Initial GCS was 14. His spine was immobilized although he did not have any evidence of spinal injury. He had no significant limb or other injuries except a few scattered abrasions.

Patient was managed at the resuscitation bay. Extended focused abdominal sonography (eFAST) revealed the presence of intraperitoneal free fluid. Patient was given1L of normal saline followed by one unit each of whole blood, fresh frozen plasma (FFP) and platelets. Systolic blood pressure was maintained around 100mmHg. He was taken to emergency theatre about 60 minutes after the injury for an exploratory laparotomy. Approximately 1.5L of intraperitoneal blood was removed. The patient had 5cm transverse laceration across stomach cutting across gastroepiploic vessels and lowers half of the body of pancreas sparing main pancreatic duct. He also had severe bruising of 3rd part of duodenum and mesentery of transverse colon. In addition large left sided retroperitoneal haematoma was found. Spleen was intact but the patient had 3cm through and through laceration involving left lobe of the liver. After initial packing, the gastric laceration was

repaired in two layers with 3/0 polygalactin. Pancreatic tear was over sawn with the same material. Gastroepiploic vessels and some minor bleeders were tied off. Exploration of haematoma around the 3rd part of the duodenum did not reveal any perforations. Left sided retroperitoneal haematoma was not explored as per trauma guidelines. Patient required 1 unit each of blood, FFP and platelets during the surgery and had 1L of Hartmann solution afterwards. Tranexamic acid was administered. Systolic blood pressure was kept between 100 and 110 during surgery and for 24 hours afterwards. Abdomen was closed with two drains- one each for lesser sac and pelvis.

Postoperatively patient was admitted to the intensive care unit where he stayed for seven days followed by another 12 days stay in high dependency unit. Patient was treated with nasogastric drainage and octreotide post operatively and serum amylase was repeatedly checked. He did not develop pancreatitis. Haemoglobin and other parameters did not drop after patient had one unit each of blood, FFP and Platelets on day two postoperative. Due to repaired large gastric laceration and concern about severely bruised duodenal wall succumbing to a delayed perforation, patient was maintained on parenteral feeding and nothing by mouth regime until 10th postoperative day. Gastrografin study via NG tube confirmed the patency of the duodenum after which fluid and solids were gently reintroduced. Pelvic drain was removed on the 5th postoperative day but drain in the lesser sac was removed only 13 days after oral feeding was established. CT - Intravenous urogram was performed on the 15th postoperative day due to initial suspicion of damage to the left kidney. It showed a non functioning necrotic fragmented left kidney indicating total avulsion at the time of injury. As his general condition improved steadily he was mobilized slowly and discharged home after a total of 28 days in the hospital.

Discussion

This young man presented in Class III haemorrhagic shock, intraperitoneal contamination and multiple intra abdominal organ injury posed a major challenge to clinicians. Permissive hypotension with limited crystalloids and early use of blood and blood components all warmed to body temperature as well as administration of tranexamic acid probably minimized the derangement of coagulation system and bleeding. The maintenance of relative hypotension during surgery and first 24 hours postoperatively too contributed to this favorable outcome. Other important management concepts employed include non-exploration of lateral retroperitoneal haematoma as well as a cautious approach to enteral feeding in the face of potential gastric anastomotic leak and the duodenal blowout. Octreotide and delayed feeding was also intended to minimize the risk of acute pancreatitis.

The concept of damage control in acute management of trauma originated from the realization that improper resuscitation along with prolonged and complex surgical procedures in a patient with major injuries worsens ones chances. It was found that such patients do better when initial surgery was confined to life saving temporalizing measures allowing physiology to stabilize the patient in an intensive care unit for 24-48 hours before definitive surgery. This earned the name Damage control surgery (DCS) or salvage surgery. Damage control, a naval term, is defined as “the capacity of a ship to absorb damage and maintain mission integrity” by permitting only minimal emergency repairs at middle of the sea enabling the ship to reach the harbor docks for definitive repairs (1).

Physiological insult by single overwhelming hit or two successive hits leads to the development of fatal triad which consists of Coagulopathy, Hypothermia and Acidosis. This in turn pushes the patient towards Systemic Inflammatory Response Syndrome (SIRS), multi-organ failure (MOF) and even Death. This dreaded path should be avoided in the management of trauma. The first hit corresponds to the magnitude of the initial injury while the second hit can be a massive blood transfusion, prolonged hypoxia, severe hypotension, lengthy surgery etc. Reversal of the effects of the first hit and prevention of a second hit are the conceptual background to DCR. Orderly rapid resuscitation guided by Advanced Trauma and Life support (ATLS) protocol plays a valuable role in this context.

It is said that medical science is the only field benefited from warfare. The concept of DCR which has emerged over the last 10 years is an offshoot of recent war experiences in middle east by armed forces of US and UK (2). This evolved naturally from the concept of DCS which has been in existence for

over the last 20 years. Now DCS is considered a component of DCR. DCR can be defined as a systematic approach to patients with exsanguinating trauma, incorporating several strategies to reduce morbidity and mortality. This objective is achieved via minimizing the occurrence of fatal triad of hypothermia, acidosis and coagulopathy.

Hypothermia has multi factorial origin in a trauma patient. It can be due to exposure to cold at scene, during transport or in the operating theatre. Administration of cold fluids and blood products as well as effects of drugs for sedation and anesthesia too contributes to this. Hypothermia increases bleeding by impeding platelet adhesion, dysregulation of coagulation factors and by interfering with fibrinolysis. Countermeasures include external rewarming such as use of blankets as well as internal rewarming strategies including warming of IV fluids.

Acidosis is again has multi factorial origin. Hypoxia, inadequate tissue perfusion, lactic acidosis as well as the use of excessive normal saline resuscitation with its supra physiological chloride levels all contribute. Acidosis decreases coagulation factor activity. Clinically the degree of base deficit and lactate level on admission tend to strongly correlate with worsened patient mortality. Correction of hypoxia and restoration of circulation are the best countermeasure against acidosis.

Coagulopathy in a trauma patient which is termed trauma induced coagulopathy (TIC) by Brohi *et al* (2003) is caused by multiple independent but interacting mechanisms(3). Acute Traumatic coagulopathy (ATC), the endogenous component of TIC is initiated within 4-5 minutes of injury and has an association with the magnitude of trauma and shock. This is characterized by isolated factor V inhibition, impaired platelet function, dysfibrinogenemia, hyperfibrinolysis and systemic anticoagulation (4,5). Exogenous causes of TIC include acidosis, hypothermia, and dilution by hypocoagulable fluid etc. INR of 1.3 and above is an indicator of coagulopathy (6). As coagulopathy appears to be the main obstacle of a patient trying to recover from the effects of major trauma, much research has been directed towards rapid diagnosis and early direct interventions.

Components of DCR are,

A) Permissive hypotension until haemorrhage control

B) Haemostatic resuscitation

C) Limited use of crystalloids and colloids to avoid dilutional coagulopathy.

D) Damage control (Salvage) surgery to preserve physiology and to control haemorrhage

(A) Permissive hypotension until haemorrhage control

Achieving normotension with aggressive fluid resuscitation can be harmful in trauma patients without haemorrhage control as it can increase haemorrhage via clot dislodgement and coagulopathy. Minimal normotension or permissive hypotension where systolic blood pressure is maintained around 90mmHg by controlled administration of fluid and blood components reduces bleeding and is preferred until haemorrhage is controlled. Head injury is a possible exception where systolic blood pressure around 100mmHg is accepted.

In our patient we maintained hypotension until about 24 hours after surgery giving opportunity for significant intraabdominal raw surfaces and retroperitoneal haematomas to stop oozing. In our opinion more studies are in order to search the value of permissive hypotension extending beyond surgery.

(B) Haemostatic resuscitation

Those who will require massive blood transfusion (>10 units within 24 hours) should be anticipated with the aid of scoring systems such as ABC (Assessment of blood consumption) and timely activation of Massive Blood transfusion Protocol (MTP) when signaled. Packed red cells, Fresh frozen plasma, platelets and calcium are main the components of MTP. Some of the adjuncts include Recombinant Factor VIIa, cryoprecipitate and tranesmic acid. Our patient probably had benefit of the latter which is proven to be useful by many studies (13). In ideal circumstances the use of type and quantity of blood and blood components during resuscitation, surgery and early postoperative period should be guided by use of thrombo-elastometry

providing objective timely information (12). In the absence of this facility, the use of packed red cells, fresh frozen plasma and platelets in ratio of 1:1:1 is shown by studies as the second best alternative (13). Our use of this protocol albeit using whole blood instead of packed cells did minimize the transfusion requirements and aided the survival of our patient. MTP is recognized to be economical on blood transfusion services. This was favored in our case as the patient who had lost 1.5 to 2L of blood (Class III shock) only required three units each of whole blood, FFP and platelets.

(C) Limited Use of crystalloids and colloids to avoid dilutional coagulopathy

Early activation of MTP avoids excess crystalloid administration (2). This minimizes several associated side effects, including reperfusion injury, increased leukocyte adhesion and inflammation, associated acidosis and resulting acute respiratory distress syndrome, systemic inflammatory response syndrome and multi-organ failure (8-10). Our patient had only 1L of normal saline and 1L of Hartmann solution during the first 24 hours of resuscitation. It also reduces the incidence of both visceral and abdominal wall edema allowing tension free abdominal wall closure i.e. reducing the incidence of abdominal compartmental syndrome.

(D) Damage control (Salvage) surgery to preserve physiology and control haemorrhage

Damage control surgery (DCS) aimed to do minimum, least time consuming maneuvers to buy time to restore physiology than the correction of disrupted anatomy. This has led to saving of many lives during the recent wars. Only 10 % of US soldiers wounded during 2003 - 2009 period died compared to 24% in the Vietnam War. However not all patients with trauma need damage control surgery as first surgery may accomplish goals in a short time. In our patient this was the case. Widely accepted damage control surgery trigger protocols include core temperature less than 35°C, pH less than 7.2, base deficit greater than 15 and significant coagulopathy (9-12). Some protocols have other conditions such as operating time exceeding 60 minutes.

Tools available for surgeons in DCS cover abdominal trauma, thoracic trauma, fractures, vascular injuries and scope is expanding. The range of maneuvers include packing of bleeding liver and pelvis, rapid stapling of segments of lacerated bowel to prevent contamination, pulmonary tractotomy to access depth and deal with bleeders, external fixation of fractures, use of temporary intravascular shunts, angioembolization and balloon catheters to occlude bleeding vessels.

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