SURGICAL OUTCOME OF INTRADURAL-EXTRA-MEDULLARYSPINAL TUMOUR: OUR EXPERIENCE IN DHAKA MEDICAL COLLEGE & HOSPITAL

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Abstract:

Introduction: *Surgical outcome of spinal tumours varies depending on a number of factors such as: site of tumour compression within the spinal canal, the histological characteristics of tumours, the neurological progression and initial response to corticosteroid therapy, patient's age, comorbidity, tumour extension, involvement of neighbor structures and organs etc.*

Materials & Methods: *The 46 patients with intradural extramedullary (IDEM) spinal tumour underwent surgery by our team in 7 years (2010-2017) were reviewed retrospectively.*

Discussion: *Analysis of the surgical outcome of our spinal tumour patients was done on different variables like age, sex, presenting symptoms, neuro imaging, comorbidities etc. The aim of surgery was decompression of the spinal cord and total removal of the tumour.*

Conclusion: *The aim of this study is to analyze the data to make conclusion for more effective strategy as per site, size, type, resectibility and histological variety to establish an effective treatment protocol and prevention of per-operative and post-operative complications. Intradural extramedullary tumor can be radically resected with no mortality and minimal peri-operative morbidity*

Key Words: *Spinal tumours, spinal cord compression,surgical outcome, intradural extramedullary, IDEM.*

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Introduction:

Surgical outcome of spinal tumours varies depending on a number of factors such as: site of tumour compression within the spinal canal, the histological characteristics of tumours, the neurological progression and initial response to corticosteroid therapy, patient's age, co morbidity, tumour extension, involvement of neighbor structures and organs etc. Treatment of spine and spinal cord tumors is complex and a multidisciplinary approach is required[1]. Treatment options are surgery, radiation therapy and chemotherapy[2].This study was conducted to analyze factors with impact on the functional outcome in a series of 46 surgically treated patients with spinal tumours and to pointout the characteristics of the different histologicalentities.

The signs and symptoms of intradural extramedullary tumors are not specific to tumors and are similar to those caused by any spinal disorder that produces symptoms of spinal cord or nerve root compression. Because of the slow growth of these tumors, symptoms may be subtle and progress slowly over time before diagnosis[3]. The benign nature of ordinary spinal schwannomas is well documented[4-7]. Total surgical removal can usually be achieved

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and short-term outcome is favorable in those who are not too severely crippled before operation[5,7].

Intradural-extramedullary (ID-EM) tumors are the most commonly observed intradural spinal tumors, comprising over 60% of tumors found within the spinal canal [8]. While consisting of a heterogeneous group of pathological entities, the vast majority of these lesions are one of three types: meningiomas, schwannomas or neurofibromas [9].

Fortunately, the more common tumors are typically benign and thus, surgical excision represents the possibility of a curative result[10]. Surgical outcomes have generally been quite positive, with multiple studies quoting gross total resection rates approaching 100% with minimal morbidity and mortality regardless of histologic subtype [11,12].

Materials & Methods:

The 46 patients with intrdural extramedullary spinal tumours underwent surgery by our team in 7 years (2010-2017) were reviewed retrospectively.

Characteristics of patients:

Variable	Number (%)
Age	
<20	4 (8.69%)
21-40	10 (21.74%)
41-60	26 (56.52%)
61-80	6 (13.04%)
Sex	
Male	22 (47.83%%)
Female	24 (52.17%)
Presenting Symptom	
Back Pain	46 (100%)
Radicular Pain	35 (76.09%)
Motor deficit	40 (86.96%)
Sensory deficit	40 (86.96%)
Autonomic disturbance	25 (54.35%)
Neuro-imaging	
Plain X-ray	46 (100%)
CT scan	4 (8.69%)
MRI	46 (100%)
Co-morbidity	
Hypertension	20 (43.48%)
Diabetes	9 (19.57%)
COPD	2 (4.35%)

The aim of surgery was total removal of the tumor andspinal with minimal neurological deficit and nerve root preservation.. Most of the cases were done by laminectomy or laminoplasty under microscope.

Results:

Many factors have influenced the outcome of surgical treatment. The most important are the histological characteristics of tumor, spinal segment affected and the degree of decompression.

Trait	Number (%)
Spinal level	
Cervicomedulary Junction	3 (6.52%)
Cervical	10 (21.74%)
Cervico-dorsal junction	3 (6.52%)
Dorsal spine	27 (58.7%)
Conus level	3 (6.52%)
Nature	
Meningioma	17 (36.96%)
Schwannoma	20 (43.48%)
Neurofibroma	8 (17.39%)
Myxopapillary Ependymoma	1 (2.17%)

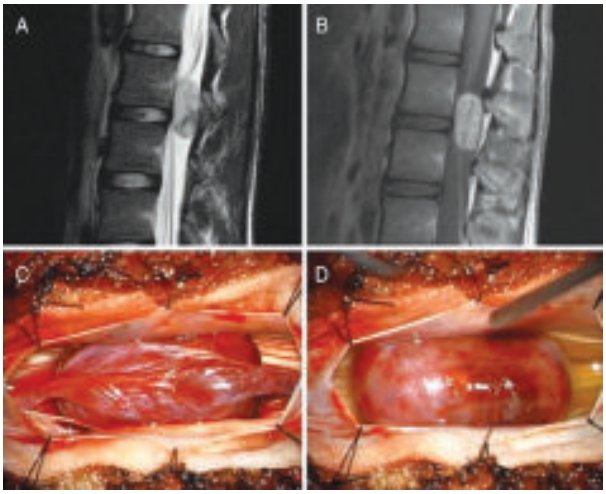

Fig.-1: *Intrdural Extramedullary (IDEM) Spinal Tumor*

Satisfactory postoperative outcome corresponds with the level of resection (e.g. total removal of meningiomas or neurofibromas leads to full recovery).

Extent of tumor resection:

Trait	Number (%)
Gross total	36 (78.26%)
Near total	8 (17.39%)
Subtotal	2 (4.35%)

Patient onset of improvement:

Trait	Number (%)
Immediate improvement	16 (34.78 %)
Improvement at discharge (7 days)	19 (41.30%)
Improvement at first month follow-up	7 (15.22%)
No improvement	3 (6.52%)
Deterioration	1 (2.17%)

The most frequent difficulties encountered duringsurgery were the per operative bleeding,anesthetic hazardin previously pulmonary compromised patient,difficulties when undergoing spinal instrumentation dueto tumor infiltration etc.

Postoperative complications include:

Complication	Number (%)
CSF leakage	1 (2.17%)
Wound infection	2 (4.35%)
Pseudo-meningocele	1 (2.17%)

Discussion:

The optimal surgical approach provides maximal exposure with the least manipulation of the neural elements. For most intradural extramedullary tumors, resection can be accomplished with a dorsal midline approach. As a general rule, lesions dorsal to the spinal cord can be reached easily using a dorsal midline approach, whereas lesions ventral and lateral to the spinal cord may require more lateral dissection to provide the best trajectory to the tumor[13].

In our study, the most of the patients were female 24 (52.17%) and belong to the age group of 41-60 years (47.67%).Similar scenario regarding age and sex was reported in Islam MR et al [2].

The respondents of our study presented with variable types of symptoms, among which pain contributes as 100%, motor deficit in 40 cases (86.96%) and sensory deficit in 40 cases (86.96%). . In our study 27 cases were at dorsal spine involvement which was highest in location (58.7%). Regarding nature of tumor the most frequent cases were Schwannoma 20 (43.48%) followed by meningioma 17 (36.96%), neurofibroma 8 (17.39%) and myxopappilary ependymoma 1 (2.17%)

The extent of tumor resection and decompression correlates directly with a good outcome. The extent of tumor excision was found to positively correlate with postoperative improvement. In our study 36 cases (78.26%) were underwent operation with gross total removal of tumor, 8 cases (17.39%) were underwent operation with near-total removal of tumor and 2 cases (4.35%) were underwent operation with sub-total resection of tumor.

In our study 19 patients (41.30%) were discharged at 7th post-operative day with significant improvement. In 16 patients (34.78 %) of our study, immediate post-operative improvement were observed. There was improvement in 7 cases (15.22%) at first month after post-operative, there was no improvement in 3 cases (6.52%) deterioration in 1 cases (2.17%).

Postoperative complications vary 10-52%[14-29]. In our study there were different type of post-operative complication like CSF leakage in 1 case (2.17%), wound infection in 2 cases (4.35%), pseudo-meningocele in 1case (2.17%).

Conclusion:

To bring good surgical outcome, to reduce postoperative mortality and peri-operative morbidity in case of intradural extra-medullaryspinal tumors, each neurosurgeon has to perform meticulous anatomical dissection mandatorily.

Besides this, thorough perioperative planning, meticulous microsurgical techniques and early mobilization & rehabilitation are essential for good clinical outcomes[30].

References:

1. T. Avramov, G. Kyuchukov, I. Kiryakov, N. Obreshkov, D. Handjiev, R. Nedelko Clinic of Neurosurgery and Neurology, St. Anna Hospital, Varna Department of Neurosurgery, Eye diseases and ENT, Medical University "Prof. P. Stoyanov", Varna, Bulgaria: Results of Spinal Tumors Surgery: Journal of IMAB - Annual Proceeding (Scientific Papers) 2009, book 1.
2. Islam MR, Siddique MSA, Ahmed M, Khan AS, Afreen S, Das S , Sarker AC:Spinal Tumor Surgery 6 Month Follow up in 34 Cases: Bang. J Neurosurgery 2014; 3(2): 46-50.
3. Cavalcanti DD, Martirosyan NL, Verma K, et al. Surgical management and outcome of schwannomas in the craniocervical region. J Neurosurg. 2011;114:1257-1267.
4. Hori T, Takakura K, Sano K: Spinal neurinomas—clinical analysis of 45 surgical cases. Neurol Med Chir 24:471–477, 1984
5. Iraci G, Peserico L, Salar G: Intraspinal neurinomas and meningiomas.A clinical survey of 172 cases. Int Surg 56:289–303,1971
6. Levy WJ, Latchaw J, Hahn JF, et al: Spinal neurofibromas: a report of 66 cases and a comparison with meningiomas. Neurosurgery 18:331–334, 1986.
7. Salah S, Horcajada J, Perneczky A: Spinal neurinomas. A comprehensive clinical and statistical study on 47 cases. Neurochirurgia 18:77–84, 1975.
8. Matti T. Seppälä, M.D., Matti J. J. Haltia, M.D., Risto J. Sankila, M.D., Juha E. Jääskeläinen, M.D., and Olli Heiskanen, M.D. Long-term outcome after removal of spinal schwannoma: a clinicopathological study of 187 cases.J Neurosurg 83:621–626, 1995.
9. Klekamp J, Samii M. Surgery of Spinal Tumors. Berlin: Springer, 2007.
10. Aghayev K, Vrionis F, Chamberlain MC. Adult intradural primary spinal cord tumors. J Natl Compr Canc Netw. 9: 434–447, 2011.
11. Albanese V, Platania N. Spinal intradural extramedullary tumors.Personal experience. J Neurosurg Sci. 46: 18-24, 2002.
12. Riad H, Knafo S, Segnarbieux F, Lonjon N. Spinal meningiomas:surgical outcome and literature review. Neurochirurgie. 59: 30-34,2013.
13. Gezen F, Kahraman S, Canakci Z, et al. Review of 36 cases of spinal cord meningioma. Spine (Phila Pa 1976). 200;25:727-731.
14. CahillDW, Kumar R: Palliative subtotal vertebrectomy with anterior and posterior reconstruction via a single posterior approach.J Neurosurg 1999, 90: 42-47.
15. Cooper P, Errico T, Martin R et al: A systematic approach to spinal reconstruction after anterior decompression for neoplastic disease of the thoracic and lumbar spine.Neurosurgery 1993, 32: 18(Medline)
16. Gilbert RW, Kim JH, Posner JB: Epidural spinal cord compression from metastatic tumor : diagnosis and treatment. Ann Neurol 1978, 3: 40-51 (Medline)
17. Han IH, Kuh SU, Chin DK, Jin BH, Cho YE: Surgical treatment of primary spinal tumors in the medullaris. J Kor Neurosurg Ass, 2008, 44(2): 72-77
18. Hufana V, Tan JSH, Tan KK: Microsurgical treatment for spinal tumors. Surg Med J, 2005, 46(2):74-77
19. Klekamp J, Samii H: Surgical results for spinal metastases.
20. Acta Neurochir (Wien) 1998, 140: 957967(Medline)
21. Klimo P Jr, Kestle JR, Schmidt MH: Treatment of metastatic spinal epidural disease: a review of the literature.Neurosurg Focus, 2003, 15(5): 1-9
22. Maranzano E, Latini P: Effectiveness of radiation therapywithout surgery in metastatic spinal cord compression:final results from a prospective trial.Int J Radiat Oncol BiolPhys 1995, 32: 959-967(Medline)
23. McCormick PC, Stein BM: Spinalcord tumors in adults.In Youmans JR ,ed Neurological Surgery. Philadelphia. WB Saunders, 1998, 3102-3122
24. Schwartz TH, McCormick PC : Intramedullary spinal cordtumors.Special issue. J Neurooncol 2000, 47: 187-317
25. Schwartz TH, McCormick PC : Intramedullary ependymomas: Clinical presentation, surgical treatment, strategies and prognosis. J Neurooncol 2000, 47:211218
26. Sciubba DM, Petteys RJ, GarcesAmbrossi GL, Noggle JC, McGirt MJ et al: Diagnosis and management of sacral tumors. J Neurosurg: Spine ,2009, 10(3) : 244-256
27. Solero CL, Formari M, Giombini S, Lasio G, Oliveri G, Cimino C et al: Spinal meningeomas: review of 174 operated cases.Neurosurgery 1989, 25: 153-160
28. Sundaresan N, Digiacinto GV, Hughes JE et al: Treatment of neoplastic spinal cord compression: results of prospective study. Neurosurgery 1991, 29: 645-650
29. Sundaresan N, Steinberger AA, Moore F et al : Indications and results of combined anterior-posterior approaches for spine tumor surgery.J Neurosurg 1996, 85:438-446.
30. Kenan Arnautovic, Aska Arnautovic: Extramedullary Intradural Spinal Tumors: A Review Of Modern Diagnostic And Treatment Options and A Report of z Series, Bosnian Journal of Basic Medical Sciences 2009; 9 (supplement 1): S40-S45.

SERUM LIPID STATUS IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME

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Summary:

Objective: *The aim of this study was to evaluate the serum lipid status in patients with PCOS and to compare the lipid status between PCOS patients and woman without PCOS.*

Methods: *This cross sectional analytical study was carried out in 50 women diagnosed as polycystic ovary syndrome on the basis of Rotterdam Criteria (group I) and 50 women of reproductive age group without polycystic ovary syndrome (group II) attending the outpatient department of Obstetrics and Gynaecology of Dhaka Medical College Hospital, Dhaka during the period of July 2013 to June 2015.*

Results: *The mean total cholesterol, triglycerides and LDL were significantly ($p<0.005$) higher in group I but mean HDL cholesterol was not significantly ($p>0.05$) associated with PCOS. Patients with raised total cholesterol : HDL ratio having the risk of developing dyslipidemia estimated to be 11.16 (95% CI = 3.9-33.1) times higher in PCOS patients than that in the group II. In multivariate logistic regression analysis of lipid profile, only raised LDL-C (>130 mg/dl) was found to be significantly associated with PCOS ($p<0.05$).*

Conclusion: *High LDL level was more associated with PCOS followed by TC, TG and TC:HDL ratio. This study demonstrated a higher level of dyslipidemia specially in PCOS with higher BMI.*

Key words: *Polycystic Ovary Syndrome, Dyslipidemia.*

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Introduction:

Polycystic ovary syndrome (PCOS) is the most prevalent female endocrinopathy and the largest single cause of anovulatory infertility[1]. Its association with menstrual disturbance and altered hormonal parameters leads many affected women of reproductive age to attend a gynaecology, endocrinology or infertility clinic. The incidence of polycystic ovary syndrome (PCOS) is 5-10% in women of reproductive age[1]. Insulin resistance is a key pathophysiology of PCOS and dyslipidemia in women with PCOS may therefore be consistent with that found in the insulin resistant state: de-creased levels of high density lipoprotein-cholesterol (HDL-C) and apolipoprotein (Apo) A-I and increased levels of triglycer-ides (TG), ApoB and very low-density lipoprotein[2,3,4]. There may be a disturbance of adrenocortical function in the prepubertal and postpubertal phase of life initially, followed by a shift to the ovarian dominance, which is associated with a non-cyclical pattern of ovarian function[5]. The end result would be the increased androgen production in the ovary and the increased peripheral production of oestrogen[5].

Women with polycystic ovary syndrome appear to be at increased cardiovascular risk due, in part, to dyslipidemia characterized by increased plasma triglyceride and reduced high density lipoprotein (HDL) cholesterol levels.

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A recent study of premenopausal women showed that those with the polycystic ovary syndrome had a higher prevalence of coronary artery calcification as detected by electron-beam computed tomography[7]. A predisposition to macrovascular disease and thrombosis in women with the polycystic ovary syndrome has also been described[8, 9].

Both insulin resistance and hyperandrogenemia contribute to this atherogenic lipid profile. Testosterone decreases lipoprotein lipase activity in abdominal fat cells and insulin resistance impairs the ability of insulin to exert its antilipolytic effects[10, 11, and 12]. Insulin resistance leads to increased catecholamine induced lipolysis in adipocytes resulting in increased free fatty acids in circulation. This results in increased VLDL production by the liver resulting in hypertriglyceridemia[13]. Efforts should be directed toward reducing obesity in PCOS to improve the metabolic disturbance in addition to ameliorating the presenting symptoms[13].

Materials and Method:

This cross sectional analytical study was carried out in the Obstetrics and Gynaecology department of Dhaka Medical College, Dhaka, during July 2013 to June 2015 with an aim to evaluate the lipid status in patients with PCOS and to compare the lipid status between PCOS patients and women without PCOS.

According to the Rotterdam criteria (ASRM/ ESHRE, 2003), patients with following characteristics were included in the study as PCOS patients.

1. Oligomenorrhoea (Menstrual cycle interval more than 35 days but less than 6 months).
2. Elevated LH level and LH/FSH ratio e" 2 with one or some of the following features:

- Characteristic enlargement of ovaries by USG.
- Hirsutism
- Obesity
- Infertility
- Stria

In this study, dyslipidemia were considered if Total cholesterol (TC)/HDL ratio is>4.5.

A total of 50 women diagnosed as polycystic ovary syndrome on the basis of Rotterdam criteria considered as group I and 50 women of reproductive age group without polycystic ovary syndrome considered as group II attending the out patient department were enrolled in this study.

Patients with adrenal or ovarian androgen producing tumours, hypothyroidism, overt diabetes, cardiovascular disease, Cushing's syndrome, familial hypercholesterolemia or hypertriglyceridemia, hyperprolectinaemia, postmenopausal women, pregnant and lactating women, those on lipid lowering drug, androgen containing drug, oral contraceptives, cortisone, synthetic progestogen or danazol were excluded from the study.

Data were collected using a structured questionnaire containing all the variables of interest, by interview and laboratory investigations. Statistical analyses were carried out by using the Statistical Package for Social Version (SPSS) version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). A descriptive analysis was performed for all data. The mean values were calculated for continuous variables. The quantitative and qualitative observations were indicated by frequencies, percentages with 95% CI. Chi square test and odds ratio with 95% CI were used to analyze the categorical variables shown with cross tabulation and unpaired t-test was used to analyze the continuous variable expressed as mean (±SD). Multiple logistic regression analysis was done for prediction of dyslipidaemia in PCOS. A P-value was considered to be statistically non significant if >0.05 and statistically significant if d" 0.05.

Ethical consideration:

Prior permission was taken from Ethical Review Committee (ERC), Dhaka Medical College (DMCH) Hospital, Dhaka to undertake this study. Keeping compliance with Helsinki Declaration for Medical Research Involving Human Subjects 1964, all the study subjects were informed verbally about the study design, the purpose of the study and potential benefits for the community. PCOS patients and women

without PCOS who gave informed consent to participate in the study were included as study sample.

Results:

Majority 19 (38.0%) patients belonged to age 26-30 years in group I and 18(36.0%) in group II. Mean age was found 27.98±4.5 years in group I and 26.92±4.8 years in group II. Mean age difference was not statistically significant (p>0.05) between two groups. Almost three-fourth (74.0%) patients belonged to BMI e"25.0 kg/m^2 in group I and 38(76.0%) patients belonged to BMI 18.5-24.9 kg/m^2 in group II (table 1). Mean BMI was found 28.0±3.7 kg/m^2 in group I and 24.4±2.8 kg/m^2 in group II. Mean BMI was statistically significant (p<0.05) between two groups. Mean total cholesterol was found 217.7±21.8 mg/dl in group I and 180.5±17.7 mg/dl in group II. Mean triglycerides were found 193.4±25.6 mg/dl in group I and 140.5±12.8 mg/dl in group II. Mean LDL-cholesterol was found 171.0±21.0 mg/dl in group I and 117.6±28.4 mg/dl in group II which were statistically significant (p-value, 0.001) but mean HDL-cholesterol was not statistically significant (p>0.05) between two groups. (Table 2)

The risk of developing dyslipidemia with raised total cholesterol, triglyceride, LDL and total cholesterol / HDL ratio was estimated to be 47.25(95% CI = 12.69-100.0), 23.92(95% CI = 7.58-79.70), 82.25(95% CI = 18.02-100.0) and 11.16(95% CI = 3.90-33.10) times higher in PCOS patients than that in the group II. More than two-third (68.0%) of the patients had raised total cholesterol: HDL ratio in group I and 8(16.0%) in group II. (Table 3) In multivariable logistic regression analysis of lipid profile, only raised LDL-C (>130mg/dl) was found to be statistically significant (p < 0.05). Other lipid profiles were not significantly associated with PCOS. (Table 4)

Table 1

Distribution of the study patients by BMI (n=100)

BMI (kg/m^2)	Group I (n=50)		Group II (n=50)		OR	95% CI	P
	n	%	n	%		(lower-upper)	value
≥25.0 (over weight &obese)	37	74.0	12	24.0	9.01	3.34-24.96	[a]0.001[s]
18.5-24.9 (normal)	13	26.0	38	76.0			
Mean±SD	28.0	±3.7	24.4	±2.8			[b]0.001[s]
Range (min-max)	20.3	-34.7	20.3	-32.1			

s= significant, OR= odds ratio, [a]P value reached from chi square test
[b]P value reached from unpaired t-test

Table-II

Distribution of the lipid profile of study patients (n=100)

Lipid profile	Group I(n=50)		Group II(n=50)		P value
	Mean	±SD	Mean	±SD	
Total cholesterol (mg/dl)	217.7	±21.8	180.5	±17.7	0.001[s]
Range (min-max)	160	-260.0	130	-210.0	
Triglycerides (mg/dl)	193.4	±25.6	140.5	±12.8	0.001[s]
Range (min-max)	126.0	-218.0	120.0	-176.0	
HDL-cholesterol (mg/dl)	46.84	±4.0	47.35	±6.4	0.633[ns]
Range (min-max)	38.0	-56.0	32.0	-60.0	
LDL-cholesterol (mg/dl)	171.0	±21.0	117.6	±28.4	0.001[s]
Range (min-max)	124.0	-202.0	68.0	-178.0	

s=significant; ns=not significant P value reached from unpaired t-test

Table-III

Risk of developing dyslipidemia in subjects with PCOS (n=100)

Lipid profile	Group I(n=50)		Group II(n=50)		OR	95% CI (lower-upper)	P value
	n	%	n	%			
Total cholesterol (mg/dl)							
>200	42	84.0	5	10.0	47.25	12.69-100.0	0.001[s]
≤200 (normal)	8	16.0	45	90.0			
Triglycerides (mg/dl)							
>150	42	84.0	9	18.0	23.92	7.58-79.70	0.001[s]
≤150 (normal)	8	16.0	41	82.0			
HDL-cholesterol (mg/dl)							
<40	1	2.0	5	10.0	0.18	0.01-1.73	0.092[ns]
≥40 (normal)	49	98.0	45	90.0			
LDL-cholesterol (mg/dl)							
>130	47	94.0	8	16.0	82.25	18.02-100.0	0.001[s]
≤130 (normal)	3	6.0	42	84.0			
Total cholesterol: HDL ratio							
>4.5 (dyslipidemic)	34	68.0	8	16.0	11.16	3.90-33.10	0.001[s]
≤4.5 (normal)	16	32.0	42	84.0			

s=significant; ns=not significant, P value reached from chi square test

Table-IV

Multivariable logistic regression analysis of Lipid Profile (n=100)

	B	S.E	P value	OR	95% CI for OR	
					Lower	Upper
LDL-cholesterol (>130 mg/dl)	3.268	0.865	0.001[s]	26.3	4.8	143.1
Triglycerides (>150 mg/dl)	-2.848	2.127	0.181[ns]	0.1	0.0	3.7
Total cholesterol (>200 mg/dl)	2.728	1.508	0.070[ns]	15.3	0.8	293.8
HDL-cholesterol (<40 mg/dl)	-2.517	1.468	0.086[ns]	0.1	0.0	1.4
Total cholesterol/HDL ratio (>4.5 mg/dl)	1.026	2.019	0.611[ns]	2.8	0.1	145.8

s=significant; ns= not significant

Discussion:

Insulin resistance is a key pathophysiology of PCOS and dyslipidemia in women with PCOS may therefore be consistent with that found in the insulin resistant state: decreased levels of high-density lipoprotein-cholesterol (HDL-C) and apolipoprotein (Apo) A-I, and increased levels of triglycerides (TG), ApoB and very low-density lipoprotein (VLDL) [4,14].

Three-fourth (74.0%) patients belonged to BMI ≥25.0 kg/m^2 in group I and 38(76.0%) patients belonged to BMI 18.5-24.9 kg/m^2 in group II. Mean BMI was found 28.0±3.7 kg/m^2 in group I and 24.4±2.8 kg/m^2 in group II. Mean BMI was statistically significant (p<0.05) between two groups. Overweight or obese had 9.01 times increased risk to develop PCOS with 95% CI 3.34-24.96% in this study. Similarly, in another study the mean BMI was 26.76 ±6.08 kg/m^2 in PCOS group and 24.73±5.66 kg/m^2 in control group[15]. The difference was statistically significant (p<0.05) between two groups. On the other hand, Manjunatha et al. (2014), Fulghesu and Magnini (2012) and Iuhas et al. (2012) observed statistically significant difference between two groups regarding the mean BMI[16, 17, 18].

Rotterdam guidelines suggested evaluation for the metabolic syndrome and indirectly indicated

the need to measure only HDL-C and triglycerides with relatively little attention to other lipid parameters. However, during past decade, a large number of studies found an increase of LDL-C levels in women with PCOS[28, 19]. Therefore, recently both the American College of Obstetricians and Gynecologists (ACOG) (ACOG practice bulletin 2009) and the Androgen Excess and PCOS Society (Wild et al. 2010) guidelines have recommended that women with PCOS should have a complete fasting lipid and lipoprotein evaluation as part of their cardiovascular risk assessment[20,21].

In this study, mean total cholesterol was 217.7±21.8 mg/dl varied from 160 – 260 mg/dl in group I and 180.5±17.7 mg/dl varied from 130 – 210 mg/dl in group II. The mean total cholesterol was significantly (p value-0.001) higher in group I. Similarly, Manjunatha et al. (2014) showed mean serum total Cholesterol 202.16 ±16.12 mg/dl in study group and 170.8±9.87 mg/dl in control group.

Mean triglycerides was 193.4±25.6 mg/dl varied from 126 – 218 mg/dl in group I and 140.5±12.8 mg/dl varied from 120 – 176 mg/dl in group II which was significantly (p-value 0.001) higher in group I. Manjunatha et al. (2014) found that the mean serum triglycerides was 120.13±12.88 mg/dl and 98.3±18.19 mg/dl in study group and control group respectively[16]. The difference was statistically significant ($p<0.05$) between two groups, which is consistent with the current study.

Mean LDL-cholesterol was 171.0±21.0 mg/dl varied from 124 – 202 mg/dl in group I and 117.6±28.4 mg/dl varied from 68 – 178 mg/dl in group II which was significantly (p-value 0.001) higher in group I.

In this present study, it was observed that the mean HDL-cholesterol was not significantly ($p>0.05$) associated with PCOS. Manjunatha et al. (2014) found that the mean HDL-Cs were 39.16±6.01 mg/dl and 55.45±4.11 mg/dl in study group and control group respectively[16]. The difference was statistically significant ($p<0.05$) between two groups which is comparable with the current study.

Al-Hakeim et al. (2009) mentioned that there is a significant increase ($p<0.05$) in total cholesterol, TG and LDL-C in PCOS patients as compared with control group while HDL-C and serum calcium is decreased significantly in patients group in comparing with control group[22]. Similar observations were also reported by Wild et al. (2010), Moran et al. (2010); Manjunatha et al. (2014)[10, 23,16].

However, some other studies showed different profiles. Bickerton et al. (2005) found that there were no significant differences in lipid or lipoprotein concentrations between the women with PCOS group and controls[24]. Yilmaz et al. (2005) found no difference in serum TC, LDL-C, TG, levels between PCOS and control groups, whereas HDL-C was lower[25]. Vrbikova et al. (2003) showed serum TC and TG did not differ significantly between PCOS and healthy women groups while HDL-C was lower and LDL-C was higher in PCOS than in controls[26].

In this study, the frequency of raised total cholesterol, raised triglycerides and raised LDL were higher in group I compared to group II. More than eighty percent (84.0%) of the patients had raised total cholesterol and raised triglyceride. The risk of developing dyslipidemia was higher in PCOS patients than that in group-II.

Wild et al. (2011) showed triglyceride levels were 26 mg/dl (95% confidence interval [CI] 17–35) higher and HDL-cholesterol concentrations were 6 mg/dl (95% CI 4–9) lower in women with PCOS[27]. Iuhas et al. (2012) reported that both total cholesterol and LDL-cholesterol were positively associated only with the presence of PCOS ($p<0.05$ for total cholesterol, $p<0.05$ for LDL-cholesterol)[18]. No association was observed between HDL-cholesterol levels and the presence of PCOS.

Conclusions:

This study was undertaken to evaluate the lipid status in patients with polycystic ovary syndrome. Most of the patients were in 3rd decade. High LDL level was more associated with PCOS followed by TC, TG and TC:HDL ratio. This study demonstrated a higher level of dyslipidemia specially in PCOS with higher BMI.

References:

1. Saghafi-Asl M, Pirouzpanah S, Ebrahimi-Mameghani M, Asghari-Jafarabadi M, Aliashrafi S, Sadein B 2013, Lipid profile in relation to anthropometric indices and insulin resistance in overweight women with polycystic ovary syndrome. Health Promot Perspect. 2013;3:206-216.
2. Sniderman AD, Scantlebury T, Cianflone K, Hypertriglyc-eridemic hyperapob: the unappreciated atherogenic dys-lipoproteinemia in type 2 diabetes mellitus, Ann Intern Med 2001;135:447-459.
3. Barter PJ, Brewer HB Jr, Chapman MJ, Hennekens CH, Rader DJ, Tall AR, Cholesteryl ester transfer protein: a novel target for raising HDL and inhibiting atherosclero-sis, Arterioscler Thromb Vasc Biol 2003;23:160-167.
4. Brunzell JD, Ayyobi AF, Dyslipidemia in the metabolic syndrome and type 2 diabetes mellitus, Am J Med 2003;115(8A):24S-28S.
5. Polycystic Ovary Syndrome. In: Malhotra N, Kumar P, Malhotra J, Bora NM, Mittal P, ed. Jeffcoate's Principles of Gynaecology. 8th ed. New Delhi: Jaypee Brothers Medical Publishers Pvt. Ltd; 2014:360-368.
6. Mahnaz L, Valizadeh N, Heshmat R, et al. Evaluation of dyslipidemia in polycystic ovary syndrome. Journal of Diabetes and Metabolic Disorders 2004;4:102.
7. Christian RC, Dumesic DA, Behrenbeck T, Oberg AL, Sheedy PF, Fitzpatrick LA. Prevalence and Predictors of Coronary Artery Calcification in Women with Polycystic Ovary Syndrome, J Clin Endocrinol Metab 2003;88(6):2562-2568.
8. Yildiz BO, Haznedaroglu IC, Kirazli S, Bayraktar M, Global fibrinolytic capacity is decreased in polycystic ovary syndrome, suggesting a prothrombotic state, J Clin Endocrinol Metab 2002;87:3871-3875.
9. Orio F Jr., Palomba S, Spinelli L, Cascella T, Tauchmanova L, Zullo F et al. The Cardiovascular Risk of Young Women with Polycystic Ovary Syndrome: An Observational, Analytical, Prospective Case-Control Study, J Clin Endocrinol Metab 2004;89(8):3696–3701.
10. Wild S, Pierpoint T, Jacobs H, McKeigue P. Long-term consequences of polycystic ovary syndrome: results of a 31 year follow up study, Hum Fertil (Camb) 2000;3:101-105.
11. Talbott EO, Zborowskii JV, Boudraux MY. Do women with polycystic ovary syndrome have an increased risk of cardiovascular disease? Review of the evidence Minerva Ginecol 2004;56:27-39.
12. Legro RS. Polycystic ovary syndrome and cardiovascular disease: a premature association, Endocr Rev 2003;24:302-312.
13. Asmathulla S, Rupa Vani K, Kripa S, Rajarajeswari R. Insulin resistance and its relation to inflammatory status and serum lipids among young women with PCOS, Int J Reprod Contracept Obstet Gynecol 2013;2(3):325-329.
14. Taskinen M. LDL-cholesterol, HDL-cholesterol or tri-glycerides: which is the culprit? Diabetes Res Clin Pract 2003;61(Suppl. 1) S19-26.
15. Sarapatkova H, Sarapatka J, Frysak Z. The importance of lipid spectrum changes in women with polycystic ovary syndrome (PCOS). Bratisl Lek Listy 2014;115(9)569-572.
16. Manjunatha S, Bennal AS, Hiremath S, Veena HC. 2014, Effect of PCOS on Lipid Profile. Sch J App Med Sci 2014;2(3D):1153-1155.
17. Fulghesu A, Magnini R. 'Obesity Related Lipid Profile and Altered Insulin Incretion in Adolescent with Policystic Ovary Syndrome, Dyslipidemia', From Prevention to Treatment. Prof Roya Kelishadi 2012;2:978-983.
18. Iuhas CI, Costin N, Mihu D. 2012, Lipid Parameters in Patients with Polycystic Ovary Syndrome, Appl Med Inform 2012;31(4):27-32.
19. Roa Barrios M, Arata-Bellabarba G, Valeri L, Velazquez- Maldonado E. Relationship between the triglyceride/high-density lipoprotein-cholesterol ratio, insulin resistance index and cardiometabolic risk factors in women with polycystic ovary syndrome, Endocrinol Nutr 2009;56:59–65.
20. ACOG practice bulletin no. 108: polycystic ovary syndrome, Obstet Gynecol 2009;114:936–9.
21. Wild R, Carmina E, Diamanti-Kandarakis E, et al. Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: a position statement by the Androgen Excess & Polycystic Ovary Syndrome (AE-PCOS) Society. J Clin Endocrinol Metab 2010;95:2038–2049.
22. Al-Hakeim HK, Shaba'a SM, Kadhem MA. Is lipid profile in women with polycystic ovary syndrome related to calcium or magnesium in serum? J Kerbala University 2009;7(2):150-157.
23. Moran LJ, Misso ML, Wild RA, Norman RJ. Impaired glucose tolerance, type 2 diabetes and metabolic syndrome in polycystic ovary syndrome: a systematic review and meta-analysis, Hum Reprod Update 2010;6:347-363.
24. Bickerton AS, Clark N, Meeking D, et al. Cardiovascular risk in women with polycystic ovarian syndrome (PCOS), J Clin Pathol 2005;58(2):151-154.
25. Yilmaz M, Biri A, Bukan N, et al. Levels of lipoprotein and homocysteine in non-obese and obese patients with polycystic ovary syndrome, Gynecol Endocrinol 2005;20(5):258-263.
26. Vrbikova J, Cifkova R, Jirkovska A, et al. 2003, Cardiovascular risk factors in young Czech females with polycystic ovary syndrome, Hum Reprod 2003;18(5):980-984.
27. Wild RA, Rizzo M, Clifton S, Carmina E. 2011, Lipid levels in polycystic ovary syndrome: systematic review and meta-analysis, Fertil Steril 2011;95:1073-1079.
28. Legro RS, Kunselman AR, Dunaif A. Prevalence and pre-dictors of dyslipidemia in women with polycystic ovary syndrome, Am J Med 2001;111:607-613.

CASE REPORTS

LACTOBACILLUS SPECIES AS A CAUSE OF URINARY TRACT INFECTION

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Abstract

Lactobacillus *is a genus of Gram-positive, facultative anaerobic or microaerophilic, rod-shaped, non-spore-forming bacteria.[1] In human, they constitute a significant component of microbial flora at a number of body sites, such as the digestive system, urinary system, and genital system.* Lactobacillus *species are normally a major part of the vaginal microbial flora.[2,3,4] As a normal bacterial flora of the vagina the organisms are typically considered contaminants when cultured from urine specimens of female patients. Here we describe the case of a female patient with chronic pyuria and urinary tract symptoms in which* Lactobacillus spp. *was determined to be the causative microorganism. After proper treatment the patient gets well soon.*

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Case Report

A seventy years old lady admitted to Asgar Ali Hospital with incontinence of urine, recurrent peripheral vertigo and recurrent UTI. She had history of subtotal thyroidectomy , osteoporosis of knee joint and unable to talk and walk and several other co-morbidities including diabetes mellitus, hypertension , dementia and hyperlipidimea. Data was collected from HMIS Internet support of our hospital, the patient took an executive visit for her UTI in January 8th 2017, her urine revealed the evidence of UTI and culture yielded the growth of *Esch.coli* >10^5CFU/ml which was not an ESBL, and was sensitive to other drugs. In 18th of the same month the patient came to OPD, that time she complained lower abdominal pain and incontinence and treated with Meropenem. Her urine examination was done on 25th January 2017, and urine still revealed 40-50 pus cells/ HPF. In 22nd February, patient again came to OPD with same complains. Her urine had 8-10 pus cells and culture yielded *Klebsiella pneumoniae* 105 CFU/ml and which was a CRE, she treated with nitrofurantoin. She visited again to OPD in March 2017, Ecsh.coli and Enterobacter spp were isolated from her urine in that occasion, both having 104 CFU/ ml, Enterobacter spp. was ESBL positive. After that she visited to OPD for 2 occasions in month May and 10th November with same complains and same number of pus cells but culture yielded no growth and her symptoms such as nocturia, increase frequency and dysurea did not resolved. In November 19th of 2017 she came to emergency, was not vitally stable then immediately transferred to ICU. Before starting of antibiotics urine was sent for RME, Gram stain and culture and sensitivity. After sending the sample, injection ceftriaxone was started. Her urine showed plenty of pus cells and Gram stain revealed plenty of large Gram positive bacilli both in centrifuge and uncentrifuge urine. Due to confusion regarding organism, after removal of the catheter, re-catheterization had been done, and sample was collected from new catheter after proper irrigation with normal saline and maintaining of strict aseptic precausion. Urine examination such as RME, Gram stain and culture were repeated. Same findings were observed.

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Urine was inoculated in blood, Mc Conkey's and chocolate agar media .After 48 hours of incubation with 5% CO2, pure faint alpha hemolytic colonies appear on blood and chocolate agar media and colony count was 10^5 CFU/ml there was no mixed growth and no growth on Mc Conkey's agar media. Gram stain was done from the colonies, Gram positive large bacilli appeared which was catalase negative , oxidase negative. On the basis of these characteristics together and very characteristics Gram stain morphology, the organisms was presumptively identified as a *Lactobacillus* species, which was sensitive to penicillin, amplicillin, ceftriazone, clindamycin, linezolid, rifampicin and gentamycin, and resistant to tetracycline, cefixime, meropenem, cotrimoxazole, nitrofurantoin, vancomycin , ciprofloxacin and levofloxacin. Lactobacilli spp. are phenoltypically resistant to vancomycin. Patient was treated with injectable ceftriaxone followed by oral Cefixime. On 25/11/17 urine RME, Gram stain and culture were done, revealed 5-6/ pus cells in per HPF and urine Gram stain and culture did not show any evidence of organisms.

Discussion

Urinary tract infections caused by *Lactobacillus* spp. are exceedingly uncommon. Our review of the literature revealed previously published case report of a 66-year-old diabetic male who developed acute renal failure and sepsis in a setting of ureteral obstruction. The patient's urine and blood yielded pure cultures of *Lactobacillus gasseri*, and following treatment with amoxicillin, the patient recovered fully[5]. Another report showed An 85 years old female with recurrent urinary tract infections, lastly lactobacilli was isolated from her urine which was also identified by bacterial 16S rRNA gene sequencing. Analysis of the isolate's 16S rRNA gene sequence revealed it to be *Lactobacillus debrueckii*.[6] Lactobacilli are rod-shaped bacteria that are part of the intestinal and vaginal normal flora, and are usually considered beneficial because they produce vitamin K, the enzyme lactase that helps to digest dairy products, and anti-microbial substances, such as acidolin and acidolphillin, which prevent the growth and colonization of harmful bacteria. However, in rare cases, lactobacilli can cause serious infections of the bloodstream, urinary tract and internal organs, especially in immunocompromised individuals. Lactobacilli are generally considered to be of low virulence, rarely causing infection in humans. Blood stream infection has been described primarily in immunocompromised patients following dental manipulations, oral trauma, or endoscopic procedures and as a result of both gastrointestinal tract fistulas and gynecologic neoplasms[7,8]. Subsequent development of endocarditis has been observed in bacteremic patients with preexisting valvular defects (8). Lactobacilli have also been shown to cause neonatal meningitis after vertical transmission of organisms from mother to infant during birth[7,8].

Antibiotics are the mainstay of treatment for lactobacillus infections. Penicillin is the common antibiotic used and can be administered orally or intravenously, depending on the condition of the patient. According to John Hopkins Point of Care Information Technology Center, the typical duration of penicillin treatment is about six weeks for infections of the bloodstream and heart[9]. Penicillin and its derivative ampicillin can also be used to treat lactobacilli infections of stomach. It is also important to note that almost all the strains of lactobacilli are resistant to vancomycin, so it is not recommended to treat lactobacilli infections[9].

For patients with penicillin allergies, gentamicin is the alternate choice, and can be administered intravenously to patients with blood and heart infections. The John Hopkins Point of Care Information Technology Center also prescribes oral clindamycin to treat gum and teeth infections caused by lactobacilli species[9].

Conclusion

In conclusion, we report a case of a patient with recurrent urinary tract infections in which *Lactobacillius spp.* was determined to be the etiologic agent. *Lactobacillus* spp. should not be regarded as simply a contaminant but as an unlikely, yet significant, cause of urinary tract inflammation and symptoms.

References

1. Makarova, K.; Slesarev, A.; Wolf, Y.; Sorokin, A.; Mirkin, B.; Koonin, E.; Pavlov, A.; Pavlova, N.; et al. (October 2006). "Comparative genomics of the lactic acid bacteria". Proc Natl Acad Sci U S A. 103 (42): 15611–6. doi:10.1073/pnas.0607117103. PMC 1622870/ . PMID 17030793.
2. Petrova, Mariya I.; Lievens, Elke; Malik, Shweta; Imholz, Nicole; Lebeer, Sarah (2015). "Lactobacillus species as biomarkers and agents that can promote various aspects of vaginal health". Frontiers in Physiology. 6. doi:10.3389/fphys.2015.00081. ISSN 1664-042X.
3. Ma, Bing; Forney, Larry J.; Ravel, Jacques (20 September 2012). "Vaginal Microbiome: Rethinking Health and Disease". Annual Review of Microbiology. 66 (1): 371–389. doi:10.1146/annurev-micro-092611-150157. ISSN 0066-4227. PMC 3780402/ . PMID 22746335.
4. Fettweis, JM; Brooks, JP; Serrano, MG; Sheth, NU; Girerd, PH; Edwards, DJ; Strauss, JF; Jefferson, KK; Buck, GA (2014). "Differences in vaginal microbiome in African American women versus women of European ancestry". Microbiology. 160 (Pt 10): 2272–82. doi:10.1099/mic.0.081034-0. PMC 4178329/ . PMID 25073854.
5. Dickgiesser, U., N. Weiss, and D. Fritsche. 1984. Lactobacillus gasseri as the cause of septic urinary infection. Infection 1214-16. [PubMed]
6. Benjamin W. Darbo; Brian K.Petreije; Gray V. Doern. "Lactobacillus delbrueckii as the Cause of Urinary Tract Infection". J.Clin Microbiology.2009 Jan; 47(1):275-277.
7. Cannon, J. P., T. A. Lee, J. T. Bolanos, and L. H. Danziger. 2005. Pathogenic relevance of Lactobacillus: a retrospective review of over 200 cases. Eur. J. Clin. Microbiol. Infect. Dis. 24:31-40.CrossRefMedlineGoogle Scholar
8. Winn, W., Jr., S. Allen, W. Janda, E. Koneman, G. Procop, P. Schreckenberger, and G. Woods. 2006. Koneman's color atlas and textbook of diagnostic microbiology, 6th edition. Lippincott Williams & Wilkins, Baltimore, MD.
9. https://www.livestrong.com › Diseases and ConditionsWhat Are the Treatments for a Lactobacillus Infection? by SHAMALA PULUGURTHA Last Updated: Aug 14, 2017

POLYCYTHAEMIA RUBRA VERA WITH INCISIONAL HERNIA SURGERY-A VERY RARE CASE REPORT

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Abstract:

Polycythaemia rubra vera is a chronic myeloproliferative disorder that is characterized by excessive red cell production and unlike other forms of polycythaemia, it can cause both bleeding and thrombosis in the same patient. Only few cases have been reported in the literature where polycythaemia rubra vera with surgery was performed successfully .The ideal peri-operative management is currently unknown. Here we present a case of 50 yrs old lady with polycythaemia rubra vera underwent open mesh repair for incisional hernia. After operation, the patient developed hemorrhagic complications needing resuscitation with blood and plasma expander. The patient was managed efficiently. Considering its very rarity, we are reporting the case.

Key words: *Polycythaemia vera (PV).*

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Introduction:

Polycythemia vera (PV) is presented by both spontaneous thrombosis and hemorrhage[1]. In general, the thrombotic tendency has been more discussed and relatively little emphasis has been placed on the hemorrhagic aspect. Burris and Arrowsmith have recently published their experience with surgery on 68 patients with PV[2]. This is the only report in the recent surgical literature which has discussed this problem. They observed the thrombotic tendency to be the most common postoperative complications and did not find any instance of hemorrhagic events. The purpose of this paper is to present a case of PV in which the postoperative course was complicated by hemorrhage and to suggest a more comprehensive preoperative evaluation and optimization which would help to prevent both hemorrhagic and thrombotic complications.

Primary polycythemia (polycythemia vera) is considered as a hematopoeitic stem cell disorder giving rise to proliferation of a clone of hematopoietic precursors leading to an excess production of erythrocytes with thrombocytosis and leucocytosis in some patients. Though the incidence of complications that are associated with polycythemia vera (PV) is found low, the risk of perioperative morbidity and mortality is found to be substantial if complications occur. Attention has always been on other hematological disorders, especially anemia inspite of lack of serious complications associated with anemia in perioperative period. Shift of attention towards less frequently encountered bleeding disorders such as PV should draw attention of not only the anesthesiologist but also the physicians and surgeons directly concerned with the patient. Normal stem cells are found in the bone marrow of patients with PV besides abnormal clonal

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stem cells which interfere with or suppress normal stem cell growth and maturation. The origin of the stem cell transformation remains unknown. Several studies suggest that a mutation on the Janus kinase-2 gene (*JAK2*) is the most likely candidate gene involved in PV pathogenesis, as *JAK2* is directly involved in the intracellular signaling following exposure to cytokines to which PV progenitor cells display hypersensitivity[3].

Polycythemia can be divided in two groups: PV (PV primary or true) and non vera types. PV is considered as a disorder of the blood-producing cells of bone marrow which results in overproduction of red blood cells. In polycythemia vera, the extra mass of red blood cells increases the volume of blood and makes it more viscous, as a result it flows less easily through small blood vessels. The cause is unknown. Non Vera types are further sub-divied into secondary and relative polycythemia Secondary are usually caused by oxygen deprivation, as seen in living at high altitudes, smoking, chronic pulmonary disease and cyanotic heart disease. Relative polycythemia occurs mainly as a result of dehydration that is caused by the use of diuretics, or, drinking too little fluids or sweating a lot. All the non vera types have underlying causes and are not true PV[3]. Though the incidence of PV is not constant worldwide, approximately 1.9 in 100,000 (person each year) are diagnosed each year. It can occur in all age groups though incidence goes up with age[3] .

Case report :

A 50 yrs old lady coming from Norshingdi admitted into BSMMU on 12 July 2016 for open mesh repair. She has been also suffering from PV for last 1 yr and was on medical therapy and regular phlebotomy. Her past history included hypertension and carrier of hepatitis-C virus for last 2 yrs without any hepatic complications. She had a history of open total abdominal hysterectomy 2 yrs ago without any significant events. She had no history of smoking, COPD, heart disease. She is a housewife. Her weight is 50 kg and height is 162 cm.

On examination, She was of average body built, having plethoric face and conjuctival injection. She had an overall dusky cyanotic complexion. Her pulse was 60/min and BP -120/80 mmHg. Splenomegaly was found 3 cm from left costal margin along its long axis. A slightly tender spherical swelling present in right iliac fossa at the right end of previous pfannestial incision scar which was reducible and gap about 3x4 cm .Pre-operative investigation findings are listed in Table I.

Table-I

Preoperative investigation profile

Lab variable	Value	Normal range
Hb	17.2 gm/dl	11-15 gm/dl
WBC	$13x10^9$/l	$4-11x10^9$/l
Platelet count	$350x10^9$/l	$150-450x10^9$/l
ESR	34 mm in 1st hour	Up to 20 mm in 1st hour
Hct	79%	35-45%
PT	14 sec	12-14 sec
INR	1.1	0.8-1.2
APTT	32 sec	32-35 sec
Bleeding time	03 min	2-7 min
Cloting time	83 u/l	5-11 min
Albumin	39 gm/l	30-35 gm/dl
Alkaline phosphatase	05 min	15-65 u/l
SGPT	23 u/l	30-60 u/l
SGOT	30u/l	30-60 u/l
HBsAg	Negative	
AntiHcv	Positive	
PCR for HCV RNA	Undetectable	
S.Creatinine	0.76 mg/dl	0.6-1.2 mg/dl
RBS	5.5 mmol/l	
USG of W/A	Splenomegaly	
JAK-2	Positive	

After proper pre-operative optimization, she underwent open prolene mesh repair by on-lay position technique. Considerable attention was paid to meticulous technique and haemostsis. There was no preoperative adverse events.

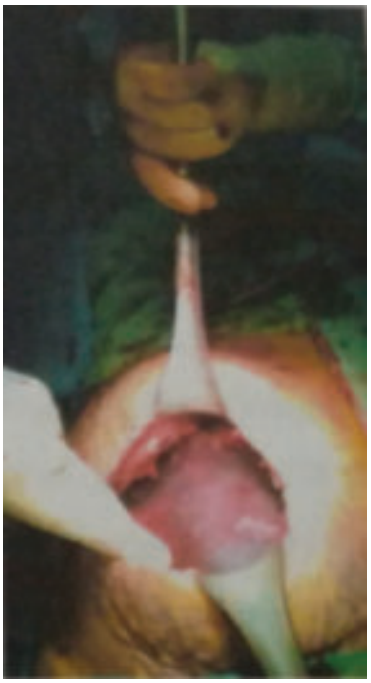

Fig.-1: *During hernia surgery*

Immediate recovery room, patient's vital sign was within normal limit but drain tube collection was 100ml (2 hours after operation) which was fresh blood and about 1400 ml blood drained on "0" POD (postoperative day).We consult with hematologist .Two unit fresh blood transfused and blood sent for coagulation profile. Laboratory exam revealed coagulation profile including bleeding time, clotting time, prothombin time, APTT, FDP, D-dimer, plasma fibrinogen and von Willebrand factor were normal but it was noted that clot did not retract and easily dispersed.

On 1st and 2nd POD, fresh blood was seen through drain tube that measured about 1200 ml and 800ml respectively. On 4th POD, drain tube collection was nil but haematoma formed beneath subcutaneous layer. On 7th POD, she was taken to operation theatre and clot was evacuated under general anaesthesia. On careful inspection, no bleeding point could be found. After 2nd time exploration, patient was stable, minor sero-sanguinous fluid drained through drain tube but uneventful recovery.

Discussion

There are several identified causes of morbidity and mortality associated with PV. Thrombosis is seen in 15-60% of patients, depending on control of the disease. It is the principal reason of death in 10-40% of patients. Venous thromboses have caused pulmonary emboli, renal failure from renal vein or renal artery thrombosis, intestinal ischemia resulting from mesenteric vascular thromboses, or peripheral arterial emboli. Hemorrhagic complications occur in 15-35% of patients and result in death in 6-30% of these patients. Peptic ulcer disease is found in association to PV at a 3- to 5-fold higher rate in compared to the general population. This has been due to increased histamine serum levels. Myelofibrosis and pancytopenia may occur in 3-10% of patients, usually in late stage of disease, which can be considered as the spent phase of PV. In these cases, bleeding and infectious complications may become the most serious health threats, and red cell transfusion may be required to maintain adequate red blood cell counts and to improve fatigue and other anemia-related symptoms. Acute leukemia or a myelodysplastic syndrome develops in 1.5% of patients who are treated with phlebotomy alone. The risk of transformation rises up to 13.5% in 5 years with treatment using chlorambucil and up to 10.2% within 6-10 years in patients treated with P-32 (radioactive Phosphorus- 32). At 15 years, transformation risk for Hydroxyurea (HU) is 5.9%, which, although not statistically significant, is worrisome [3.]

Diagnostic criteria by polycythaemia vera study group are as follows - **Category A** (total red blood cell mass – in males, more than or equal to 36 mL/kg and in females, greater than or equal to 32 mL/kg, arterial blood oxygen saturation greater or equal to 92% and splenomegaly) and **Category B** (thrombocytosis with platelet count greater than 400,000/iL, leukocytosis with a white blood cell count greater than 12,000/iL, increased leukocyte alkaline phosphatase (ALP) greater than 100 U/L, serum vitamin B-12 concentration more than 900 pg/mL or binding capacity more than 2200 pg/mL). The diagnosis is established with A1 plus A2 plus A3 or A1 plus A2 plus any 2 criteria from category-B. With the establishment of polymerase chain reaction (PCR)-based methods for detecting the *JAK2* V617F mutation, this

may become the first molecular diagnostic marker for PV[3].

Venesection of 300–500 mL is performed weekly or twice weekly to achieve a haematocrit of less than 0.45, and thereafter every 3–6 months to maintain the haematocrit at this level. Iron deficiency may occur and requires cautious treatment. Low-dose aspirin (100 mg/day) reduces thrombotic complications. Cytoreductive therapy should be considered when venesection is poorly tolerated. There is symptomatic or progressive splenomegaly, thrombocytosis or the presence of symptoms that may indicate disease progression (e.g. night sweats; weight loss)[4,5].

It is preferred to maintain blood results at reference range levels by regular evaluation and treatment. Fasting for prolonged time without adequate replacement should be avoided as this can lead to dangerously high hematocrit levels in patients already predisposed to hypercoagulability. Fasting, even for not more than 4-6 hrs should always be accompanied by adequate pre operative hydration. During operation the patients' baseline hypercoagulability rises by a hundred fold. Aggressive hydration should be continued throughout the surgery and adequate urine output must be ensured. Emergent surgery may require intraoperative phlebotomies. This must be done with extreme caution taking care to replace lost volume and avoiding vasoconstriction from volume depletion that can risk multiorgan ischemia or intraoperative thrombus formation[6,7,8,9].

Monitoring using central venous line is advised in all patients to monitor not only fluid status but also for the provision of a large gauge central venous line for rapid infusion rates that may be required in such patients[10,11]. Monitoring the vitals and clinical evaluation of patient for the possibility of stroke or hemorrhage should continue from the intraoperative through the postoperative period[7,12,13].

All patients with PV who present for surgery, either elective or emergency, are advised to be admitted to the intensive care unit in the immediate post operative period for minimum forty eight hours with strict vitals observation and concurrent clinical and laboratory evaluation[14,15]. Early ambulation and aggressive use of analgesics preferably opioids is recommended to prevent stasis of blood flow and discourage formation of deep venous thrombosis to which these patients are at increased risk. Compression stockings to avoid clot formation and use of peripheral local anesthetic blocks to relieve postoperative pain and thus allow early ambulation should be undertaken in these patients[3,16].

Conclusion

Patient's diagnosed with PV are at increased risk of perioperative thrombosis and hemorrhage. Follow-up in the post-operative period may be complicated by pulmonary or cerebral thrombosis or embolisms or hemorrhage. It might be concluded that PV is a risk factor for haemorrhagic events that requires meticulous attention to perioperative assessment of patient blood profile and subsequently tailored treatment strategies in order to avoid substantial morbidity and mortality.

Reference(s)

1. Passamonti F, Malabarba L, Orlandi E, et al.(2003). Polycythemia vera in young patients: a study on the long-term risk of thrombosis, myelofibrosis and leukemia. Haematologica 88 (1): 13–8.
2. Berlin NI (1975). Diagnosis and classification of polycythemia. Semin Hematol 12: 339.
3. Khan FA, Khan RA, Iqbal M, Hussain S. Polycythemia vera: Essential management protocols. Anaesth Pain & Intensive Care 2012;16(1):91-9
4. Ruggeri M, Rodeghiero F, Tosetto A. Post surgery outcomes in patients with polycythemia vera and essential thrombocythemia: a retrospective survey. Blood 2008 Jan 15;111(2):666-71.
5. Weinfeld A, Swolin B, Westin J. Acute leukaemia after hydroxyurea therapy in polycythaemia vera and allied disorders: prospective study of efficacy and leukaemogenicity with therapeutic implications. *Eur J Haematol* 1994;52(3):134-9.
6. Fruchtman SM, Pettit RM, Gilbert HS, et al, and the Anagrelide Study Group. Anagrelide: analysis of long-term safety and leukemogenic potential in myeloproliferative diseases (MPDs) [abstract]. *Blood* 2002;100:70a.
7. Fruchtman SM, Petitt RM, Gilbert HS, Fiddler G, Lyne A, and the Anagrelide Study Group Leukemia

Research. Anagrelide: analysis of long-term efficacy, safety and leukemogenic potential in myeloproliferative disorders. *Leuk Res.* 2005;29(5): 481-91.

8. Landolfi R, Marchioli R, Kutti J, et al. Efficacy and safety of low-dose aspirin in polycythemia vera. *N Engl J Med.* 2004;350(2):114-24.
9. Squizzato A, Romualdi E, Middeldorp S. Antiplatelet drugs for polycythaemia vera and essential thrombocythaemia. Cochrane database sys rev. 2008 Apr 16;(2):CD006503.
10. Dan K, Yamada T, Kimura Y Clinical features of polycythemia vera and essential thrombocythemia in Japan: retrospective analysis of a nationwide survey by the Japanese Elderly Leukemia and Lymphoma Study Group. Int J Heamatol 2006;83(5):443-9.
11. Fruchtman SM, Mack K, Kaplan ME, et al. From efficacy to safety: a Polycythemia Vera Study Group report on hydroxyurea in patients with polycythemia vera. *Semin Hematol* 1997;34(1):17-23.
12. Berk PD, Goldberg JD, Donovan PB, et al. Therapeutic recommendations in polycythemia vera based on Polycythemia Vera Study Group protocols. *Semin Hematol* 1986;23(2):132-43.
13. Landolfi R, Cipriani MC, Novarese L. Thrombosis and bleeding in polycythemia vera and essential thrombocythemia: pathogenetic mechanisms and prevention. Best pract clin res heamatol. 2006; 19(3):617-33.
14. Elliott MA, Pardanani A, Lasho TL. Thrombosis in myelofibrosis: prior thrombosis is the only predictive factor and most venous events are provoked. Heamatologica 2010;95(10):1788-91.
15. De Stefano V, Za T, Rossi E. Recurrent thrombosis in patients with polycythemia vera and essential thrombocythemia: incidence, risk factors, and effect of treatments. Heamatologica 2008;93(3):372-80.
16. Beer PA, Erber WN, Campbell PJ. How I treat essential thrombocythemia. Blood 2011;117(5):1472-82.