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MGM Institute of Health Sciences (Deemed University u/s 3 of UGC Act 1956) is committed to promote excellence in medical education and research finding better, safer and affordable ways of diagnosing, treating and preventing diseases. With this view in mind, the university has launched a quarterly peer-reviewed scientific journal "MGM Journal of Medical Sciences" in 2014. It publishes original research papers, review articles, interesting case reports, pictorial reviews, letters to editor, book reviews and notices of important professional meetings and conferences. All submitted articles are scrutinized by peer-reviewers and the editorial team, before being published. From time to time, this journal may bring out special issues focusing on specific themes. A section may also be devoted exclusively to young researchers and students to stimulate their innovative and creative ideas.

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From the Editor's Desk

It is being increasingly recognized that active student engagement in teaching-learning processes in higher educational institutions is of paramount importance to achieve excellence in desired outcomes. This is particularly relevant to medical education. In spite of stringent rules, regulations, policies and curricula prescribed by regulatory bodies and councils for imparting medical education and training in medical schools, we find that desired outcomes in respect of knowledge and clinical skills acquired by medical graduates are still not up to the mark. There are significant gaps. Our medical schools may be staffed with best of faculties, state-of-art equipments, good hospitals and top class infrastructure, what they lack is active and optimum student engagement in all academic and other activities of the institution. Students are the most important stake-holders of medical schools. They should have representation in all policy making academic committees of the institution. They should participate in designing curricula. Their feedback will help in improving teaching methodologies and in assessment procedures. They should be engaged in research activities under guidance of and in collaboration with their teachers. They should be encouraged and supported to participate in local, regional, national and international medical conferences and meetings. They should be made to participate in delivery of healthcare to communities. Their representatives must be allowed to sit in the governing bodies of the institutions. Their opinions should be given due weightage in framing new policies and rules. Their feedback about teaching faculty must be given due consideration in granting promotion to the faculty.

In one of the articles published in this issue of MGMJMS, engagement of medical students with curriculum has been discussed comprehensively by two reputed authorities in medical education namely: John Dent and Catherine Kennedy from Association for Medical Education in Europe (AMEE). I am sure our esteemed readers, who are keen to see improvement in the quality of medical education in our country, will benefit from this article. In addition, as usual, this issue contains a mix of interesting papers from various disciplines of medical sciences. We gratefully acknowledge the cooperation of all the contributors who have been submitting papers for MGMJMS. Our sole criteria for publication are quality and factual data.

Shibban K Kaul MS MCh FIACS
Editor-in-Chief
MGM Journal of Medical Sciences
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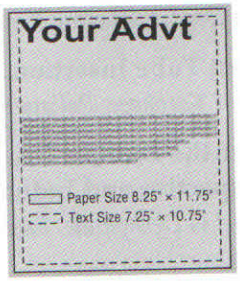

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ORIGINAL ARTICLE

Adenocarcinoma with Unknown Primary: Diagnostic Implications using Immunohistochemistry

[1]Nidhi Anand, [2]Saumya Shukla, [3]Anshima Singh, [4]Nuzhat Husain

ABSTRACT

Carcinoma of unknown primary site (CUP) is a heterogeneous group of cancers defined by the presence of metastatic disease with no identifiable primary tumor at presentation. We undertook this study to assess the utility of immunohistochemistry (IHC) for the determination of primary tumor site in adenocarcinomas. This retrospective study included 51 cases with a morphological diagnosis of metastatic adenocarcinoma with unknown primary. Basic IHC panel that included cytokeratin 7 (CK-7), cytokeratin 20 (CK-20), pan-cytokeratin (pan-CK), thyroid transcription factor-1 (TTF-1), and caudal type homebox 2 (CDX-2) was used. Additional extended panel with specific IHC markers was used in cases where the primary could not be determined using the basic panel. The male-to-female ratio was 1.4:1 with mean age of 50 years. The most common metastatic site was lymph node followed by liver. A conclusive diagnosis using IHC was achieved in 30 cases (58.82%). Specific diagnosis could be made in 8 cases (16%) using basic IHC panel.

Extended panel yielded specific diagnosis in additional 22 cases (43.13%). Primary site could not be determined using even both the panels in 21 cases (41.18%). The panels for identification of the primary need to be flexible depending on the site of metastasis, age/sex of the patient, and detailed history, which may determine sensitivity and specificity of primary detection.

Keywords: Adenocarcinoma, Immunohistochemistry, Neoplasms, Unknown primary.

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INTRODUCTION

Carcinomas of unknown primary sites are defined as a heterogeneous group with metastatic disease for which the site of origin cannot be identified at the time of diagnosis despite careful clinical examination and laboratory test.[1] The CUPs account for approximately 3% of all malignant neoplasms while adenocarcinoma accounts for about 50% of all CUPs. In this era of personalized medicine with targeted therapy being available, it is essential for a pathologist to identify the organ of origin, as it has a significant impact on overall survival.[1,2]

The role of a pathologist in identifying the organ of origin in cases of CUPs is expanding. Recent advances in IHC and the development of numerous organ-specific IHC antibodies have been of great help in this regard.[2,3] Current study was undertaken with the objective to identify the primary tumor site in cases of CUPs with adenocarcinoma phenotype.

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MATERIALS AND METHODS

This was a retrospective tertiary care center, hospital-based study that included 51 cases diagnosed as metastatic adenocarcinoma in which the primary site of tumor was unknown. Testing with A panel of IHC markers was performed that was categorized into two groups: (1) basic IHC panel and (2) extended IHC panel (Table 1).

Immunohistochemistry testing was done by the standard protocol. The tissue section on coated slides was fixed overnight at 60°C in a dry oven, deparaffinized in xylene and rehydrated through graded ethanol series. Sections were blocked with 3% hydrogen peroxide in methanol for 30 minutes to quench any endogenous peroxidase activity, if present, and were then processed for antigen retrieval in Pascal (DAKO Cytomation, California) by placing in sodium citrate buffer (pH-6.0). Sections were incubated for an hour with primary antibodies, followed by treatment with polymer-based secondary antibody kit (Dakopatts, Envision kit, Denmark). Bound antibody was visualized using diaminobenzidine, according to the manufacturer's instructions. Sections were counterstained with hematoxylin and mounted. Positive and negative controls were run with all batches by including and omitting primary antibodies respectively.

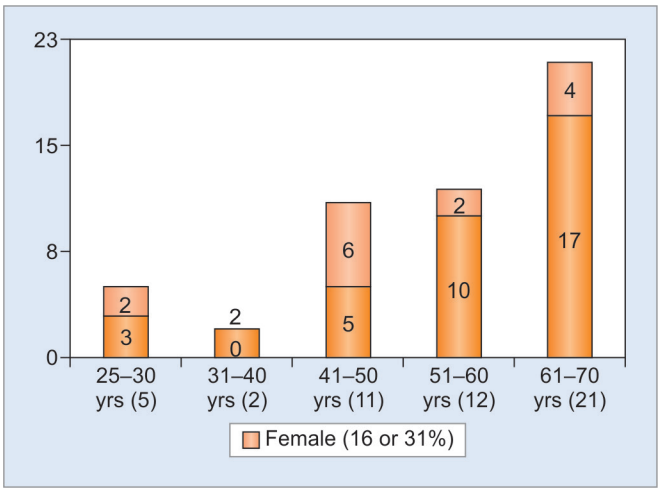
The IHC results were interpreted under light microscopy. The results were analyzed in terms of the utility of the basic panel and the extended IHC panel for the identification of primary site in cases of CUPs with adenocarcinoma phenotype.

RESULTS

This retrospective tertiary care center, hospital-based study included 51 cases of metastatic adenocarcinoma in

Table 1: List of IHC antibodies used for identification of primary tumor site

Name	*Clone*	*Supplier*	*Dilution*
Basic IHC panel			
Pan-CK	AE1/AE3	Dako	Ready to use
CK-7	OV-TL 12/30	Dako	Ready to use
CK-20	Ks20.8	Dako	Ready to use
TTF-1	8G7G3/1	Dako	Ready to use
CDX-2	DAK-CDX2	Dako	Ready to use
Extended IHC panel			
Thyroglobulin	DAK-Tg6	Dako	1:100
WT-1	6F-H2	Dako	Ready to use
Vimentin	V9	Dako	Ready to use
Synaptophysin	DAK-SYNAP	Dako	Ready to use
Epithelial membrane antigen (EMA)	E29	Dako	Ready to use
ER	EP1	Ventana Medical Systems	Ready to use
PSA	Anti-PSA	Dako	Ready to use
CK-5/6	D5/16 B4	Dako	Ready to use
Placental alkaline phosphatase (PIAP)	8A9	Dako	Ready to use
Carcinoembryonic antigen (CEA)	II-7	Dako	Ready to use
CD-34	QBEnd10	Dako	Ready to use
Hepatocellular carcinoma antigen (HCC-Ag)	OCH1E5	Dako	Ready to use
p-63	4A4	Biogenix	Ready to use
S-100	Anti-S-100	Dako	Ready to use
CD-10	56C6	Dako	Ready to use
Glial fibrillary acidic protein (GFAP)	Anti-GFAP	Dako	Ready to use
GCDFP	Anti-GCDFP	Dako	Ready to use
Leukocyte common antigen (LCA)	2B11 + PD7/26	Dako	Ready to use



Graph 1: The age and gender distribution

which the primary site of tumor was unknown. The male-to-female ratio was 1.4:1. The mean age of the patients in the study was 50 years (Graph 1).

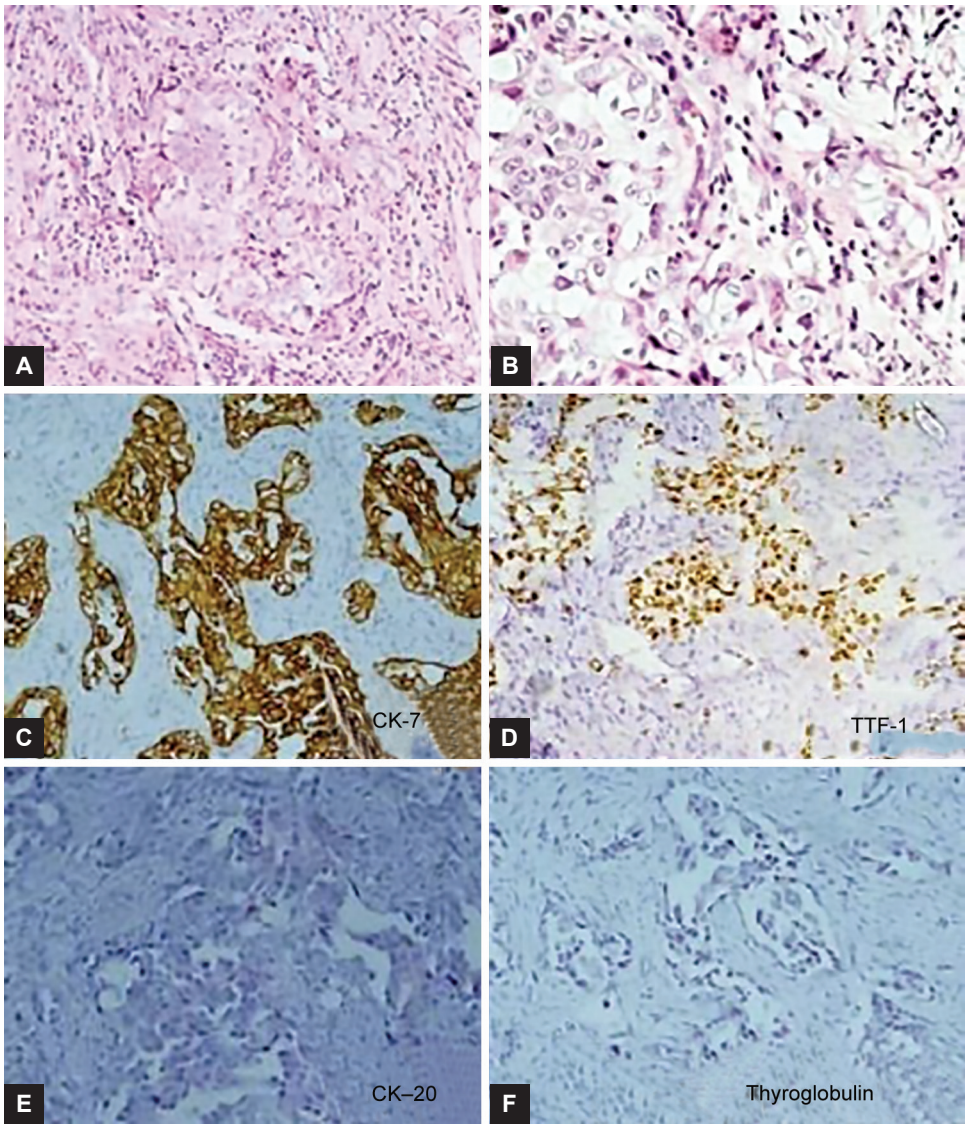
The most common metastatic site was lymph node followed by liver. A conclusive diagnosis using IHC was achieved in 30 cases (58.82%). The most common primary site was lung in 46.67% (n = 14), followed by the gastrointestinal tract (GIT) in 23.33% (n =7), thyroid in 10% (n = 3), breast in 6.67% (n = 2), ovary (n = 2) in 6.67%, prostate (n = 1) in 3.33%, and kidney (n = 1) in 3.33% (Figs 1 to 3).

The basic IHC panel constituted of CK-7, CK-20, TTF-1, CDX-2, and pan-CK. Specific diagnosis using this basic panel could be made in 8 cases (15.68%). Primary site could be identified with the extended panel in an additional 22 cases (43.13%). Primary site could not be determined using even both the panels in 21 cases (41.18%).

DISCUSSION

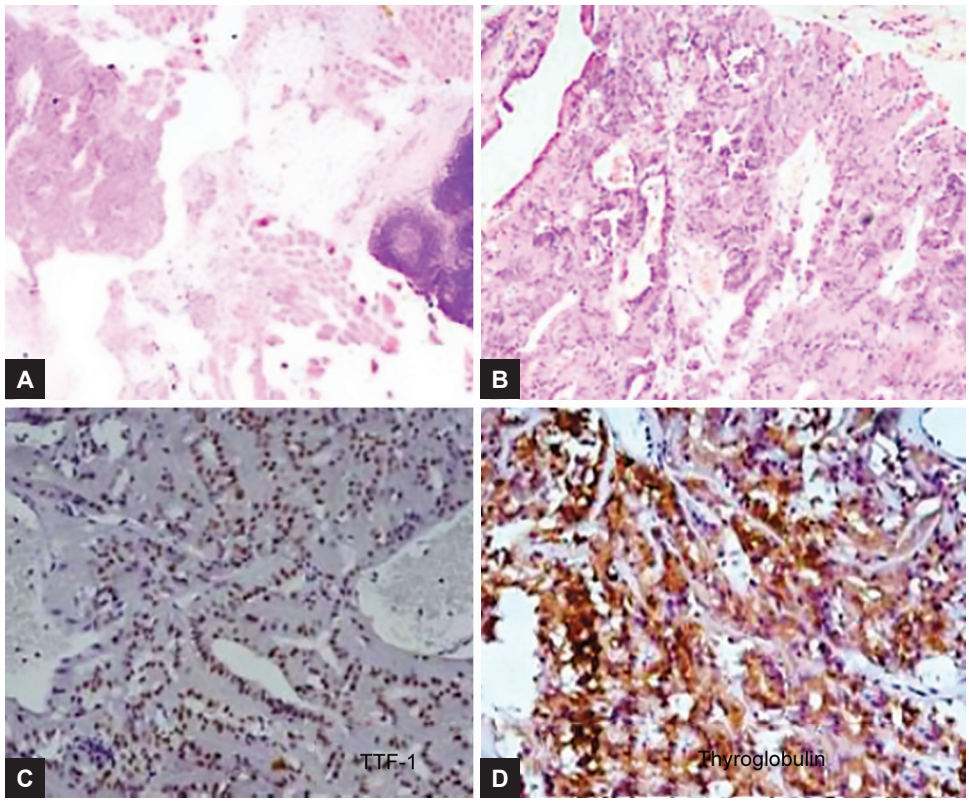
In this study, the utility of IHC panel in the diagnosis of primary tumor site in metastatic adenocarcinoma has been evaluated and validated. Through recent advancements in IHC, additional organ-specific antibodies have become available including estrogen receptors (ER), mammaglobin, gross cystic disease fluid protein-15 (GCDFP-15), CDX-2, TTF-1, Wilms' tumor susceptibility gene 1 (WT-1), paired box gene 8, prostate-specific antigen (PSA), and uroplakin with conventional antibodies including CK-7 and CK-20. Use of these biomarkers has the potential to identify the primary tumor site with greater sensitivity and specificity.[1,2] Improving treatment of CUPs requires identification of the primary tumor site using molecular markers and application of primary tumor site-specific treatment.[4]

In this study, two panels for IHC were designed and staining was performed in a sequential pattern. The basic panel was done initially to narrow down the

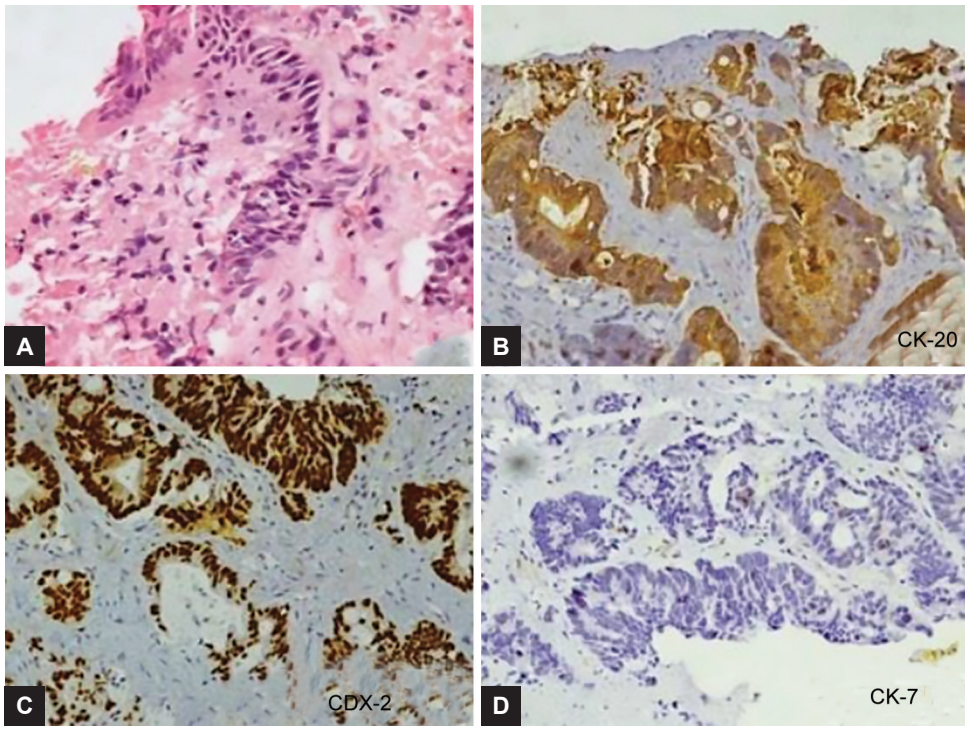


Figs 1A to F: (A and B) Cervical lymph node biopsy with tumor cells arranged in nests and acini (hematoxylin and eosin, A = ×100, B = ×200) with positivity for CK-7 (C) and TTF-1 (D) and negative staining for CK-20 (E) and thyroglobulin (F) indicative of primary in the lung (CK-7 = 3,3′-Diaminobenzidine (DAB) ×100, TTF-1 = DAB ×100, CK-20 = DAB ×100, thyroglobulin = DAB × 100)

probability of the primary site by using CK-7 and CK-20. The common CK-7-positive tumors are lung, thyroid, breast, ovary, upper GIT, and pancreaticobiliary tract, while CK-20 expression is commonly present in lower GIT along with urothelium, though it can be identified heterogeneously in other sites also. The primary site could be determined in 15.68% of cases using the basic panel. In the remaining cases, an extended panel was performed that included more organ-specific antibodies. An accurate diagnosis suggestive of the primary site could be achieved in additional 43.13% of cases using the extended panel. The overall diagnostic efficacy of IHC in the diagnosis of primary tumor sites in cases of CUPs with adenocarcinoma phenotype was 58.82% in the present study. In the study conducted by Hashimoto et al, the diagnostic efficacy was 81.7%.[1,5,6] The use of sequential IHC is important, as it aids in saving both time and resources. Utilization of an extensive panel of IHC in the beginning may lead to wastage of resources and may also cause exhaustion of the tissue biopsy. It is essential to treat all biopsies as precious samples, as molecular diagnosis is essential for the use of targeted therapy.[7] The College of American Pathologists recommends testing for actionable targets in multiple cancers like lung, colon, breast, stomach, and thyroid. Hence, it is essential to perform a robust panel of IHC for the detection of primary site in cases of CUPs but in a sequential pattern. Identifying patients with prognostically favorable disease is important in cases of CUPs, as they may get substantial benefit from directed treatment and achieve prolonged survival.[8,9] Panels for identification of the primary need to be flexible depending on the site of metastasis, age/gender of the patient, and detailed history which may improve sensitivity and specificity of primary detection.[10]



Figs 2A to D: (A and B) Cervical lymph node with nodal and extranodal deposits of tumor cells with papillary architecture (hematoxylin and eosin, A = ×50, B = ×100). (C and D) TTF-1 and thyroglobulin positivity is indicative of a primary in the thyroid (TTF-1 = 3,3′-Diaminobenzidine (DAB) × 100, thyroglobulin = DAB × 100)



Figs 3A to D: Biopsy from the lumbar spine with nests and clusters of neoplastic cells with positive staining for CK-20 and CDX-2 and negative staining for CK-2 (A = hematoxylin and eosin ×100, CK-20 = DAB × 100, CDX-2 = DAB × 100, CK-7 = 3,3′-Diaminobenzidine (DAB) × 100)

CONCLUSION

Immunohistochemistry can be of great help in making correct diagnosis of the primary tumor site in patients presenting with metastatic adenocarcinoma with unknown primary. To save time and resources, it is essential that sequential testing be done with basic and extended panel of IHC antibodies. Current advances in targeted therapy that has improved patient survival demand that we identify the primary site in these patients because this therapy in primary tumor is site-specific. In our study, conclusive diagnosis could be obtained in 58.82% of cases of adenocarcinoma with unknown primary by using IHC out of a total of 51 patents.

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ORIGINAL ARTICLE

Satisfaction with Life among Dialyzed Patients: A Cantril Ladder Survey

[1]Leszek Sulkowski, [2]Maciej Matyja, [3]Jerzy A Walocha, [4]Artur Pasternak

ABSTRACT

Introduction: End-stage renal disease (ESRD) patients consider hemodialysis (HD) to be an invasive and time-consuming procedure. The total success of HD depends not only on the medical parameters, but also on the patients' satisfaction with life (SwL). The purpose of this study was to evaluate ESRD patients' self-reported SwL and compare it with patient-related and dialysis-related factors.

Materials and methods: Fifty-nine patients [average age = 63.3 (standard deviation, SD = 12.3), 19 women (32.2%)] were evaluated in the survey. Both the present and expected 5-year SwL scores were evaluated according to the Cantril ladder (CL).

Findings: The relations between the present and expected 5-year CL-SwL scores and gender, education, fulfillment of medical recommendations, months on dialysis, type of vascular access, urea reduction ratio (URR), and ultrafiltration (UF) were excluded. The results indicated highly positive relationships between high expected 5-year CL-SwL scores and being in a relationship, having a kidney graft performed in the past, and willingness to have a kidney graft performed in the future. The group of ESRD patients who were not in a relationship, did not undergo kidney grafts in the past, did not want to undergo a kidney graft in the future, and the eldest patients expected their SwL in 5 years to be significantly lower.

Practical implications: Cantril ladder is a useful tool for SwL measurements among ESRD patients. The ESRD patients who expected their SwL in 5 years to be significantly lower (who were not in a relationship, did not undergo a kidney graft, did not desire a kidney graft, and the eldest patients) must be provided with psychological support.

Originality: This article fills the gap in the ESRD patients' quality of life assessment. The self-reported present SwL was evaluated along with expected 5-year SwL.

Keywords: Cantril ladder, End-stage renal disease, Hemodialysis, Quality of life, Satisfaction with life, Vascular access.

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Conflict of interest: None

INTRODUCTION

During the past decades, both the prevalence and the costs of ESRD have increased.[1] The number and age group of patients who undergo HD have been increasing.[2,3] Hemodialysis prolongs lives[4] and improves the health of ESRD patients.[2] But it also may lead to emotional disturbances and changes in social life and roles. Hemodialysis may cause social isolation, decreases in both physical and mental health,[2] fatigue, depression,[5] and cognitive impairment.[6,7] The ESRD patients on chronic HD are less active than healthy controls.[2] Even the early stages of ESRD reduce the quality of life due to rather obvious risk factors of ESRD patients (i.e., senility, unemployment, and lower socioeconomic status).[8,9] Additionally, multiple comorbidities, such as diabetes, hypertension,[6] anemia,[7,10] cerebrovascular diseases, hyperparathyroidism, and depression,[7] have been detected among ESRD individuals. Patients consider HD to be an invasive and time-consuming procedure.[6] Patients are exposed to large osmotic, fluid, and uremic toxin fluctuations.[6] Consequently, all of the above-mentioned factors lead to poorer quality of life compared not only with the general population but also with patients with other chronic diseases.[8,11] Aside from effective HD, a high SwL is an important factor of general satisfaction with renal replacement treatment.[11,12] Therefore, the total success of HD depends not only on the medical parameters of the dialysis but also on the patients' frame of mind, satisfaction with treatment, and their overall health. Improving patients' SwL and well-being leads to improving the overall effect of HD.[2] For this reason, the subjective measures of SwL have received increasing attention.[13]

The purpose of this study was to provide information about ESRD patients' self-reported SwL scores and compare the results with the patient-related and dialysis-related factors. A better understanding of these relationships might lead to improvements of the SwL scores of ESRD patients[14] and the overall effects of HD.

MATERIALS AND METHODS

Data were collected in a single, outpatient, hospital-based HD center. A total of 135 patients, 18 years or older, were hemodialyzed at the time of data collection in May 2016. Each patient was asked to participate in a survey and received a questionnaire that included a survey, demographic and clinical questions and a CL measure. The entire questionnaire required approximately 30 minutes.

Following HD, many patients felt tired and in need of rest or sleep. These could have been caused by kidney failure itself or the HD treatment. The recovery time after HD increased with the durations of both ESRD and HD.[12] The cognitive functions of the ESRD patients reached higher levels approximately 24 hours after HD.[7] Accounting for the information mentioned earlier, the patients were asked to complete the questionnaires one day after HD when the ESRD patients' cognitive functions were potentially the best.

Of the 135 patients who received the questionnaires, 59 patients (43.7%) expressed their desire to participate and were evaluated in the survey (Table 1). The study was performed on a group of 19 women (32.2%) and 40 men (67.8%) who ranged in age from 28 to 84 with an average age of 63.3 (SD = 12.3). The patients answered questions regarding their demographic details (age, gender, and marital status), medical history (months on dialysis, vascular access, kidney graft, and fulfillment of medical recommendations). The presented data were compared with clinical information evaluating the quality of HD treatment including the dialyzer clearance of urea/dialysis time (Kt/V), URR, UF, and duration of a single HD (Table 1).

The SwL was evaluated by the CL, which is a subjective, nondisease-specific, self-reported measure.[13,15] The

Table 1: Demographic, clinical, and dialysis-related factors affecting the CL ratings of SwL

			CL score					
			Present			*Expected in 5 years*		
		Participants		*Sample mean vs population mean t-test*	*Sample mean vs sample mean t-test*		*Sample mean vs population mean t-test*	*Sample mean vs sample mean t-test*
	n (%)	*M [range] (SD)*	*Mean (SD)*	*p-value*	*p-value*	*Mean (SD)*	*p-value*	*p-value*
	59 (100)		6.1 (2.1)			4.8 (2.7)		
Gender and age (years)	59	63.3 y [28–84 y] (12.3)	6.1			4.8		
Male	40 (67.8)	63.5 y [28–84 y] (12.7)	6.1 (2.1)	NS		4.6 (2.7)	NS	
Female	19 (32.2)	63.1 y [37–80 y] (11.4)	6.2 (2.0)	NS	N/S (*vs* male)	5.0 (2.6)	NS	N/S (*vs* male)
<50	8 (13.6)	39.8 y (7.5)	6.0 (2.0)	NS		5.0 (3.0)	NS	
50–60	13 (22.0)	57.6 y (2.0)	6.7 (1.6)	NS		5.8 (2.5)	NS	
61–70	23 (39.0)	65.2 y (2.6)	6.7 (1.7)	NS		5.4 (2.1)	NS	
71–80	12 (20.3)	76.7 y (2.3)	5.0 (2.1)	NS		2.7 (2.3)	<0.01	
>80	3 (5.1)	83.0 (1.4)	4.3 (2.9)	NS		2.3 (1.2)	NS	
Marital status	58		6.1			4.6		
Unmarried	6 (10.3)		5.1 (1.7)	NS		4.8 (2.7)	NS	
Married	40 (69.0)		6.5 (1.7)	<0.02		5.2 (2.5)	<0.02	
Widow/widower	8 (13.8)		5.5 (2.7)	NS		3.5 (2.9)	NS	
Single	4 (6.9)		4.8 (2.9)	NS		2.0 (1.0)	<0.02	
Married/in a relationship	40 (69.0)		6.5 (1.7)	<0.02	<0.01 (*vs* not in a relationship)	5.2 (2.5)	<0.02	<0.03 (*vs* not in a relationship)
Not in a relationship	18 (31.0)		5.2 (1.7)	<0.02		3.6 (2.5)	NS	
Education	58		6.1			4.7		
Elementary school	12 (20.7)		5.1 (2.2)	NS		3.9 (2.7)	NS	
Middle school	19 (32.8)		6.5 (2.0)	NS		5.0 (2.5)	NS	
High school	16 (27.6)		6.1 (1.8)	NS		4.8 (2.7)	NS	
University	11 (19.0)		6.6 (1.8)	NS		4.9 (2.5)	NS	
Months on dialysis	55	48.9 [1–317] (64.3)	6.2			4.8		
<12	16 (29.1)	8.1 (3.8)	6.1 (1.7)	NS		4.2 (1.9)	NS	
13–60	27 (49.1)	32.4 (15.2)	6.1 (2.4)	NS		4.7 (2.9)	NS	
>61	12 (21.8)	140.6 (84.7)	6.8 (1.6)	NS		5.7 (2.8)	NS	
<24	28 (50.9)	12.6 (6.5)	6.3 (2.1)	NS		5.0 (2.3)	NS	

(Cont'd…)

(Cont'd…)

			CL score					
			Present			Expected in 5 years		
		Participants		Sample mean vs population mean t-test	Sample mean vs sample mean t-test		Sample mean vs population mean t-test	Sample mean vs sample mean t-test
	n (%)	M [range] (SD)	Mean (SD)	p-value	p-value	Mean (SD)	p-value	p-value
25–47	9 (16.4)	35.4 (4.8)	4.9 (2.5)	NS		3.3 (2.9)	NS	
>48	18 (32.7)	112.4 (79.9)	6.7 (1.8)	NS		5.2 (2.8)	NS	
Dialysis duration (hours)	58		6.2 (2.1)			4.7 (2.7)		
<4	14 (24.1)		6.0 (2.7)	NS		3.9 (2.5)	NS	
4	35 (60.4)		5.9 (1.8)	NS		4.7 (2.7)	NS	
>4	9 (15.5)		7.7 (1.0)	<0.01		5.9 (2.5)	NS	
Vascular access	57							
AVF	53 (93.0)		6.2 (2.1)	NS		4.8 (2.7)	NS	
Wrist	26 (49.1)		6.0 (1.9)	NS		4.4 (2.3)	NS	
Forearm	14 (26.4)		6.7 (2.5)	NS		4.9 (3.0)	NS	
Elbow	11 (20.7)		6.0 (1.8)	NS		5.0 (2.9)	NS	
Arm	2 (3.8)		4.5 (1.5)	NS		4.5 (3.5)	NS	
Not tunneled catheter	2 (3.5)		4.0 (0)	NS	N/S (*vs* AVF)	2.5 (0.5)	NS	N/S (*vs* AVF)
Tunneled catheter	2 (3.5)		8 (0)	NS	N/S (*vs* AVF)	5.5 (1.5)	NS	N/S (*vs* AVF)
Kidney graft in the past	59		6.1			4.8		
Yes	5 (8.5)		7.0 (1.8)	NS	N/S (*vs* "no")	7.6 (2.4)	NS	<0.02 (*vs* "no")
No	54 (91.5)		6.1 (2.1)	NS		4.5 (2.5)	<0.01	
Willingness to kidney graft	56		6.1			4.8		
Yes	32 (57.1)		6.5 (1.8)	NS	N/S (*vs* no)	5.4 (2.7)	NS	<0.04 (*vs* no)
No	24 (42.9)		5.6 (2.2)	NS		3.4 (2.0)	<0.01	
Fulfillment of medical recommendations	55		6.3				4.9	
Yes	39 (70.9)		6.3 (2.2)	NS		5.2 (2.7)	NS	N/S (*vs* no)
No	16 (29.1)		6.3 (1.7)	NS		4.2 (2.5)	NS	
Partly	7 (13.5)		6.7 (1.7)	NS		4.1 (2.5)	NS	
Irregularly	10 (19.2)		6.1 (1.8)	NS		5.1 (2.9)	NS	
Regularly	35 (67.3)		6.2 (2.2)	NS		4.7 (2.6)	NS	
Kt/V	57	1.31 [0.82–1.89] (0.34)	6.2			4.7		
<1	6 (10.5)	0.88 (0.11)	5.5 (1.9)	NS		3.3 (1.9)	NS	
1–1.5	40 (70.2)	1.23 (0.13)	6.2 (2.1)	NS		4.6 (2.7)	NS	
>1.5	11 (19.3)	1.78 (0.42)	6.6 (2.0)	NS		6.2 (2.4)	<0.05	
<1.2	22 (38.6)	1.04 (0.12)	6.2 (2.1)	NS		4.5 (2.5)	NS	
1.2–1.3	13 (22.8)	1.26 (0.03)	6.2 (2.0)	NS		5.0 (2.8)	NS	
>1.3	22 (19.3)	1.52 (0.17)	6.1 (2.1)	NS		4.8 (2.8)	NS	
URR	58	0.66 [0.42–0.90] (0.07)	6.2			4.7		
<0.6	15 (25.9)	0.56 (0.04)	6.2 (2.2)	NS		4.4 (2.4)	NS	
0.6–0.7	28 (48.3)	0.66 (0.02)	6.1 (2.0)	NS		4.6 (2.6)	NS	
0.7–0.8	13 (22.4)	0.73 (0.03)	6.1 (2.2)	NS		5.3 (2.9)	NS	
>0.8	2 (3.4)	0.85 (0.05)	7.0 (1.0)	NS		4.5 (2.5)	NS	
UF (mL)	58	2,298 [300–4,200] (910)	6.1			4.8		
<1,000	8 (13.8)	650 (206)	5.5 (1.9)	NS		4.0 (2.4)	NS	
1,000–2,000	12 (20.7)	1,675 (200)	6.3 (2.4)	NS		4.8 (2.8)	NS	
2,000–3,000	25 (43.1)	2,532 (260)	6.2 (2.2)	NS		4.6 (2.6)	NS	
>3,000	13 (22.4)	3,438 (253)	6.5 (1.6)	NS		5.2 (2.7)	NS	

N/S: Not significant

CL was chosen because it is fast and easy to explain to the patients. During the survey, the patients received two pictures of the ladder. The hypothetical rungs of the ladders were numbered from 0 to 10. The patients were informed that the top of the ladder represented the best possible SwL, and the bottom rung represented the worst possible SwL. Higher scores indicated higher SwL. On the first ladder, the patients were asked to indicate how they felt and to express their personal stance at that particular moment. On the second ladder, they were asked to indicate their expected stance in 5 years.[15]

Statistical Analysis

Demographic information was analyzed using the frequencies and average calculations. The SD were computed for continuous variables. The variables were compared with Student's t-tests. Both the sample means *vs* the population means and the sample means *vs* the sample means of two independent groups were compared with t-tests. A p-value less than 0.05 was considered to be statistically significant.

FINDINGS

Of the 135 patients who received HD thrice a week in a single outpatient center in May 2016, 59 patients returned the questionnaires and were further evaluated. Among the study participants, there were 40 males (67.8%) and 19 females (32.2%) who ranged in age from 28 to 84 (average age, 63.3 years and SD = 12.3; Table 1).

The factors that may have affected the SwL as assessed by the CL (CL-SwL) and the CL-SwL expected in 5 years were analyzed. The following factors were considered: gender, age (10-year categories), marital status, education, months on dialysis, duration of a single HD, vascular access, kidney graft in the past, graft willingness in the future, fulfillment of medical recommendations, and dialysis adequacy (i.e., Kt/V, URR and UF; Table 1); t-tests were used to describe differences in the CL-SwL scores.

Initially, the influence of each factor on both the present and expected 5-year CL-SwL scores was evaluated. There were no statistically significant relationships in either the present or expected 5-year CL-SwL scores and the factors of gender, education, months on dialysis, type of vascular access [arteriovenous fistula (AVF), not tunneled catheter, or tunneled catheter], fulfillment of medical recommendations, URR, or UF (Table 1).

A group of ESRD patients (71–80 years) rated their SwL expected in 5 years as significantly lower ($p < 0.01$). For the other age groups, there were no significant differences. Despite the low rating of the SwL expected in 5 years in the oldest group (>80 years), the group size was too small (three patients) to prove a significant difference.

The strong relationship between marital status and both present and expected 5-year CL-SwLs has been demonstrated (Table 1). The married group rated both their SwL at present ($p < 0.02$) and expected in 5 years ($p < 0.02$) significantly higher than the groups of single, unmarried, and widows/widowers in one group. The differences between in a relationship and not in a relationship were even more significant ($p < 0.01$ for present CL-SwL and $p < 0.03$ for the expected 5-year CL-SwL).

The patients whose dialysis took over 4 hours rated their present SwL higher ($p < 0.01$) than others, while there were no differences in the CL-SwL expected in 5 years (Table 1). Former kidney grafts did not significantly affect the present CL-SwL score. However, the patients who had undergone a kidney graft in the past expected their SwL to be significantly higher in 5 years ($p < 0.02$). Similarly, the willingness to undergo a kidney graft did not change the present CL-SwL, but the individuals who did not desire a kidney graft rated their expected in 5 years CL-SwL as significantly lower ($p < 0.01$ *vs* total population, $p = 0.035$ *vs* yes to kidney graft; Table 1).

A Kt/V over 1.5 was associated with a significantly higher expected 5-year CL-SwL ($p < 0.05$), while there was no significant relation between Kt/V and the present CL-SwL (Table 1).

DISCUSSION

The ESRD is an important cause of morbidity and mortality,[10] and it is associated with an increased risk of cognitive impairment.[6] One-third of ESRD patients who are dialyzed thrice a week exhibit moderate-to-severe cognitive impairment. This occurs despite the meeting of HD quality standards.[16]

Hemodialysis is an example of a passive treatment. The patients have to come to the HD center for several hours thrice a week. Patients are connected to blood purification systems by medical staff and have to meet other dialyzed patients. Between the HD sessions, the patients are expected to adhere to a restricted diet and to take medications.[17]

The SwL scores of ESRD patients were evaluated with a CL survey. Despite its simplicity, the CL survey is the most important one. The CL survey is easy to understand, fast to perform, and easy to repeat. We accounted for the self-reported CL-SwL scores rated by the patients. Next, we compared the SwL ratings with the demographic factors and clinical parameters (Table 1).

Dialysis adequacy was assessed according to Kt/V.[18] Additionally, the URR and UF were evaluated. A Kt/V over 1.5 was associated with significantly higher CL-SwL scores expected in 5 years ($p < 0.05$), while there was no significant relation between Kt/V and the present CL-SwL (Table 1). We did not find significant relations between

the present or expected 5-year CL-SwL scores and URR or UF (Table 1).

According to the patients, the vascular access method influences their lifestyles. The hospitalization of ESRD patients contributes to complications of vascular access in 15 to 20% cases.[4] Arteriovenous fistulas, compared with arteriovenous grafts and central venous catheters, are associated with better clinical outcomes and lower costs.[4] The ESRD, HD, and vascular access have major influences on the quality of life.[12] However, we excluded the relations between the present and expected 5-year CL-SwL scores with the type of vascular access (Table 1). This means that the type of vascular access affects the costs but not the self-reported CL-SwL scores.

Additionally, we did not find significant relationship between present or expected 5-year CL-SwL scores and gender, education, months on dialysis, or fulfillment of medical recommendations (Table 1). These factors were not associated with SwL.

Both an age of 61 to 70 years and dialysis lasting over 4 hours were associated with significantly higher present CL-SwL ($p < 0.05$ and $p < 0.01$ respectively), while undergoing a kidney graft in the past and the willingness to undergo a kidney graft in the future were associated with significantly higher expected 5-year CL-SwL ($p < 0.02$ and $p < 0.04$ respectively). Being in a relationship was associated with both significantly higher present and expected 5-year CL-SwL scores ($p < 0.02$ and $p < 0.02$ respectively; Table 1).

An age of 71 to 80 years old, the absence of a kidney graft in the past and the unwillingness to have a kidney graft done in the future were associated with significantly lower ($p < 0.01$, $p < 0.01$, and $p < 0.01$ respectively) expected 5-year CL-SwL scores, while not being in a relationship was associated with significantly lower present and expected 5-year CL-SwL scores ($p < 0.01$ and $p < 0.03$ respectively; Table 1).

CONCLUSION

- CL is a useful tool for SwL measurement. It is a single, meaningful, self-reported method that is fast and easy to perform with ESRD patients.
- The relationship between present and expected 5-year CL-SwL scores and patient- related factors, such as gender, education, fulfillment of medical recommendations, and dialysis-related parameters including months on dialysis, type of vascular access, URR, and UF were excluded.
- The results indicated a highly positive relationship between high expected 5-year CL-SwL and the following factors: being in a relationship, having a kidney graft performed in the past and willingness to have a kidney graft done in the future.
- Despite the relations to dialysis parameters, the group of ESRD patient who were not in a relationship, those who did not undergo kidney grafts in the past, those who did not desire a kidney graft in the future, and the eldest patients expected their SwL in 5 years to be significantly lower. Psychological support should be offered to these ESRD patients first.

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ORIGINAL ARTICLE

Fine Needle Aspiration Cytology of Follicular-patterned Thyroid Lesions

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ABSTRACT

Introduction: Fine needle aspiration cytology (FNAC) plays a vital role in diagnosing thyroid lesions. However, follicular-patterned lesions need to be evaluated meticulously due to markedly overlapping cytomorphological features.

Aim: To study the role of FNAC in follicular-patterned lesions of thyroid.

Materials and methods: A retrospective and prospective study of 50 cases in which thyroid FNAC showed follicular-patterned lesions along with histopathological correlation wherever available was done over a period of 3 years (January 2013–December 2015).

Results: Out of 50 cases of follicular-patterned lesions, 44 cases were reported as adenomatous goiter (AG), 3 cases each of follicular neoplasm (FN), and follicular variant of papillary thyroid carcinoma (FVPTC) on FNAC. Out of total 24 cases available for histopathological correlation, 5 cases (20.83%) showed discordance and the possible causes for the discordance were analyzed. The diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value were 83.3, 42.9, 100, 100, and 81.0% respectively.

Conclusion: Diagnosing follicular-patterned lesions on FNAC is challenging and will remain a "gray zone" for all cytopathologists. Scrupulous and thorough examination of all cytological smears should be done for predominant follicular pattern along with cytomorphological and background details to differentiate follicular-patterned thyroid lesions in order to minimize false-negative diagnosis on FNAC.

Keywords: Fine-needle aspiration cytology, Follicular-patterned lesions, Thyroid.

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INTRODUCTION

Thyroid nodular lesions are common clinical problems and need to be evaluated meticulously. Fine needle aspiration cytology of thyroid gland is primarily a "screening test" but is also helpful in diagnosing many thyroid lesions. Follicular-patterned lesions of thyroid fall in the "gray zone" of cytopathology. The differential diagnosis of the follicular-patterned lesions of thyroid comprises of AG/hyperplastic nodule, FN, and FVPTC.[1,2] Various cell patterns are seen on aspirates of thyroid follicular cells by FNAC. These include follicular pattern, which consist of normofollicular/macrofollicular and microfollicular pattern, papillary, syncytial, cystic, and dispersed pattern.[3]

Follicular-patterned lesions are the major cause of false-positive and false-negative results at FNACs. This is because of overlapping cytologic features found in follicular-patterned lesions. This present study was conducted to discuss the cytomorphological features of various follicular lesions and to find out the diagnostic pitfalls while reporting and decreasing the false-negative rates and increasing the sensitivity of FNAC in diagnosing follicular-patterned thyroid lesions.

In this study, the cytological diagnosis was given by observing the predominant follicular cell pattern, cellular details, and the background elements.

MATERIALS AND METHODS

A retrospective and prospective study of 50 cases of FNAC of follicular-patterned thyroid lesions was conducted over a period of 3 years (January 2013–December 2015). Institutional ethical committee approval was obtained prior to the commencement of the study. All the FNA smears of each case were studied thoroughly by correlating with age, sex, clinical details, and cytomorphological features and a definite cytological diagnosis was offered. The inclusion criteria of the present study were patients above the age of 15 years and cytological smears showing predominant follicular pattern on thyroid FNAC. Exclusion criteria were (a) patients less than 15 years and (b) inadequate smears.

The cytological diagnosis was correlated with histopathological diagnosis of those cases whose surgical specimens were received at our laboratory. The aims and objectives were to study the role of FNAC in the diagnosis of follicular-patterned thyroid lesions, to study cytomorphological features of various follicular-patterned lesions of thyroid, and to recognize diagnostic difficulties

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Table 1: Incidence of follicular-patterned thyroid lesions

Type of lesions	*No. of cases*	*Percentage*
AG	44	88
FN	3	6
FVPTC	3	6
Total	50	100

Table 2: Distribution of AG cases according to cytomorphological features

Cytological features	*Parameters*	*No. of cases*	*Percentage*
Cellularity	High	25	56.82
	Moderate	19	43.18
Predominant pattern	Macrofollicular	20	45.45
	Microfollicular	24	54.55
Colloid	Scanty	17	38.64
	Moderate	17	38.64
	Abundant	10	22.72
Macrophages	Present	15	34.10
	Absent	29	65.90
Hurthle cells	Present	16	36.36
	Absent	28	63.64

Table 3: Cytological–histological corelation

Cytological diagnosis	*No. of cases*	*Histopathological diagnosis*	
		Concordance	*Discordance*
AG	21	17	4
FN	1	0	1
FVPTC	2	2	0
Total	24	19	5

Table 4: Cytomorphological features of FN on FNAC

Cellularity	*Pattern*			*Colloid*	*Hurthle cells*	*Nuclear features*
	Macrofollicular	*Microfollicular*	*Other*			
H	0	3	SS (1)	+	–	Nuclear overlapping and crowding
H	0	3	SS (1)	–	–	Nuclear overlapping and crowding
H	1	3	SS (1)	–	–	Nuclear overlapping and crowding

(–): Absent; (+): Scanty; (++): Moderate; (+++): Abundant; 0: Absent; 1: Occasional; 2: Frequent; 3: Predominant; SS: Singly scattered; H: High; M: Moderate

Table 5: Cytomorphological features of FVTPC on FNAC

Cellularity	*Pattern*			*Colloid*	*Hurthle cells*	*Nuclear features*
	Macrofollicular	*Microfollicular*	*Other*			
M	0	3	SYN (1) SS (1)	–	–	Anisonucleosis, round, increased N:C ratio, intranuclear cytoplasmic inclusions, nuclear grooves, powdery chromatin, prominent nucleoli
H	0	3	–	–	–	Nucleomegaly, increased N:C ratio, intranuclear cytoplasmic inclusions, nuclear grooves, powdery chromatin, prominent nucleoli
H	1	3	SYN (1)	–	–	Round, increased N:C ratio, intranuclear cytoplasmic inclusions, nuclear grooves, powdery chromatin, prominent nucleoli

(–): Absent; (+): Scanty; (++): Moderate; (+++): Abundant; 0: Absent; 1: Occasional; 2: Frequent; 3: Predominant; SS: Singly scattered; SYN: Syncytial; H: High; M: Moderate

and pitfalls related to FNAC diagnosis. The results were analyzed using Microsoft Excel.

OBSERVATION AND RESULTS

Results are summarized in Tables 1 to 5 and three representative smears are shown in Figures 1 to 3.

There were a total of 24 cases where cytohistological correlation was available. Of these 21 cases had AG, 2 FVPTC, and 1 FN. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 42.9, 100, 100, 81 and 83.3% respectively.

DISCUSSION

A palpable thyroid nodule whether benign or malignant has always been a matter of concern and requires

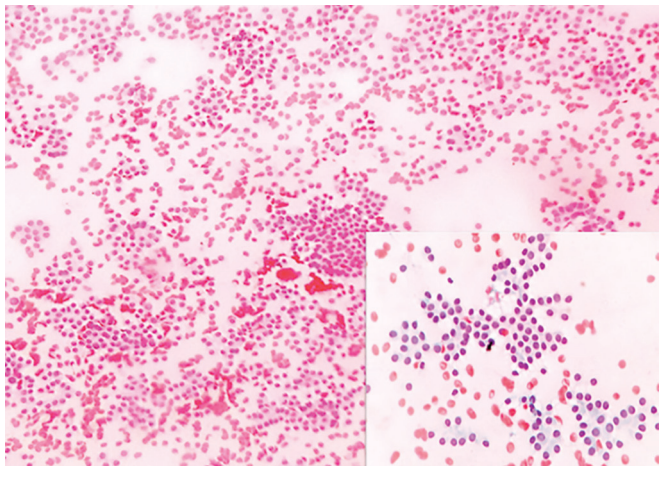

Fig. 1: Adenomatous goiter showing high cellularity. Inset showing macrofollicular and microfollicular pattern on a background of thin colloid. Papanicolaou stain, ×10

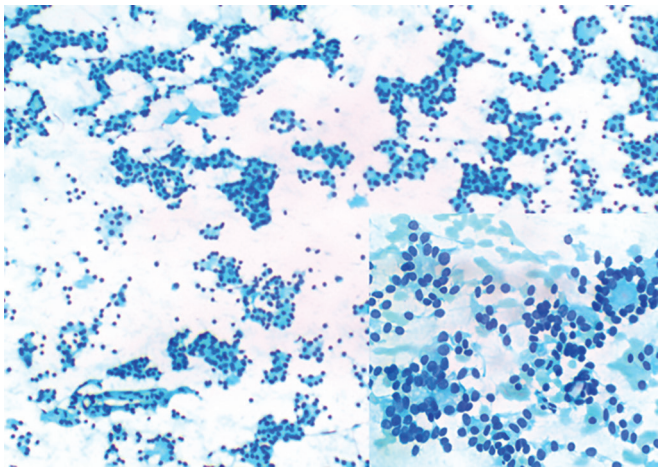

Fig. 2: Follicular neoplasm with high cellularity and cells arranged in predominantly microfollicular pattern, Papanicolaou (PAP) stain, ×10. Inset showing cellular overcrowding and overlapping, PAP stain, ×40

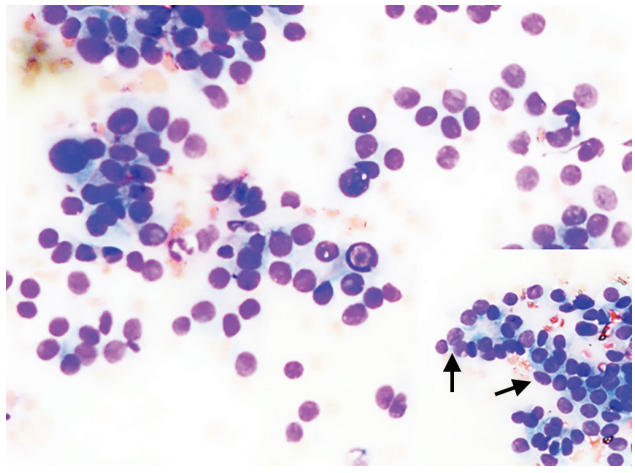

Fig. 3: Follicular variant of papillary thyroid carcinoma showing classical intranuclear cytoplasmic inclusions, ×40. Inset: Nuclear grooves (arrows), ×40. May–Grünwald Giemsa stain

thorough evaluation and management. Fine needle aspiration cytology being a simple, outpatient diagnostic procedure helps in providing a definitive diagnosis in all thyroid lesions so that further management can be appropriately carried out. On cytology, a thyroid lesion is designated as follicular when growth pattern of the lesion is either follicle forming or follicular patterning. The follicles are classified further based on their size as microfollicles or macrofollicles.[4]

This retrospective and prospective study was carried out over a period of 3 years (January 2013–December 2015). Out of a total of 348 cases of thyroid FNACs, 50 showed follicular-patterned thyroid lesions which included AG, FN (follicular adenoma and follicular carcinoma), and FVPTC.[1,2,5]

The incidence of follicular-patterned thyroid lesions was 14.36%, falling within the reported incidence of 5 to 29%.[6] Among the follicular-patterned thyroid lesions, the incidence of AG was 88% followed by FN (6%) and FVPTC (6%) (Table 1).

In this study, the patients ranged in age from 15 to 62 years with a mean age of 37.18 years. The commonest age group was 31 to 40 years (21 cases, 42%) followed by 21 to 30 years (10 cases, 20%), 41 to 50 years (8 cases, 16%), 51 to 60 years (5 cases, 10%), 11 to 20 years (4 cases, 8%), and 61 to 70 years (2 cases, 4%). Out of these 50 cases, 46 (92%) were females and 4 (8%) males, with male to female ratio of 1:11.5 showing female preponderance. The study conducted by Deveci et al[7] showed patients ranging in age from 16 to 87 years with an average age of 52 years and female preponderance where 372 cases were females and 87 were males. The study conducted by Mateša et al[8] also showed female preponderance with a male to female ratio of 1:4.8.

Out of these 50 cases, histopathological correlation was available in 24 (48%) cases. On histopathological examination, concordance was seen in 19 cases and discordance in 5 cases. Out of five discordant cases, three cases diagnosed as AG on FNAC were reported as follicular adenoma, one case diagnosed as AG on FNAC was FVPTC, and one case diagnosed as FN was FVPTC on histopathology.

Adenomatous Goiter

Adenomatous goiter in our study comprised the largest population of cases of follicular-patterned lesions with an incidence of 88% (44 cases) on FNAC, while other authors showed an incidence of 40 and 58.9%.[1,5] Of these, 41 patients were females and 3 males. Majority belonged to the age group of 31 to 40 years (18 cases, 36%) followed by 41 to 50 years (8 cases, 16%), 21 to 30 years (7 cases, 14%), 51 to 60 years (5 cases, 10%), 11 to 20 years (4 cases, 8%), and 61 to 70 years (2 cases, 4%).

Cytological smears of the 44 cases of AG in the present study showed 25 cases (56.82%) with high cellularity and 19 cases (43.18%) had moderate cellularity. About 24 cases (54.55%) showed predominantly microfollicular pattern and 20 (45.45%) macrofollicular pattern (Fig. 1); 17 cases (38.64%) showed moderate amount of colloid, 17 (38.64%) showed scanty colloid, and 10 (22.72%) abundant colloid. Macrophages, including cyst macrophages and hemosiderin-laden macrophages, were seen in 15 cases (34.10%) and were absent in 29 (65.90%) cases. Hurthle cells were present in 16 cases (36.36%) and were not seen in 28 cases (63.64%) (Table 2).

Among the 25 cases of AG with high cellularity, background and accompanying components, such as abundant colloid, cystic changes, stromal fragments, and follicular cells in honeycomb arrangement were observed. These were labeled as benign lesions.

Histopathological reports were available for 24 patients out of the total 50. Of these 24 cases, 17 were consistent

with AG and 4 showed discordance. Of the four discordant cases, three were diagnosed as FA and one as FVPTC (Table 3). Greaves et al[2] also observed similar discordance wherein three out of five lesions were diagnosed as AG on FNAC but turned out to be FA by histology. Guhamallick et al[9] observed similar discordance. Discordance in our cases might have occurred due to aspiration from colloid-rich macrofollicular areas of the neoplasm. This may be resolved by giving multiple passes through various sites of the lesion under ultrasound guidance.

Follicular Neoplasm

Incidence of FN was 6% (3 cases) of the total 50 cases of follicular-patterned lesions. Out of these, two cases (4%) were in the age group of 31 to 40 years and one case (2%) was in the age group of 21 to 30 years. Shobha et al,[1] in their study of 30 cases of follicular-patterned lesions, encountered 17 cases (56.66%) of FN. Of the three cases of FN, two were females and one was male.

All three cases of FN showed high cellularity, predominant microfollicular and dispersed pattern, nuclear overlapping, and crowding with no colloid (Fig. 2). However, one case showed macrofollicular pattern and scant colloid (Table 4). All these were diagnosed as FN on FNAC. Out of these three cases, histopathology was available only in one case and was diagnosed as FVPTC on histopathology. In Bommanahalli et al[10] study, out of the 12 cases of cytologically diagnosed FNs, three cases were confirmed to be as FVPTC on histopathology. This could be avoided by repeat aspirations from different parts of thyroid nodule.[9]

Follicular Variant of Papillary Thyroid Carcinoma

The incidence of FVPTC was 6% (3 cases) out of total 50 cases of follicular-patterned lesions. The studies done by other authors showed a higher incidence of FVPTC among the follicular-patterned lesions of thyroid. Shobha et al[1] found only one case of FVPTC out of 30 cases accounting to 3.34% of all the follicular-patterned lesions. In our study, all the three cases of FVPTC were females, two in the age group of 21 to 30 years and one in the age group of 31 to 40 years with a mean age of 29 years.

Smear examination of FVPTC cases in this study showed moderate to high cellularity with predominantly follicular pattern, characteristic nuclear features of PTC, and absence of colloid (Table 5). These findings correspond to published literature, in which cytological examination in FVPTC is characterized by hypercellularity with a prominent microfollicular pattern with a few syncytial follicular cells, but no obvious papillae and typical nuclear features in a proportion of cells, viz., pale powdery chromatin, intranuclear inclusions, nuclear grooves, and chewing gum colloid.[11,12]

Out of three cases of FVPTC, histopathology was available in two cases with 100% concordance. We gave a definitive diagnosis of FVPTC on FNAC based on moderate to high cellularity, typical nuclear features of papillary carcinoma with a predominant follicular pattern, and syncytial and dispersed pattern in one (Fig. 3). Third case of FVPTC which was wrongly diagnosed as AG on FNAC, discordance was due to absence of classic nuclear features of PTC, probably due to geographical miss on FNAC. Geographical miss can be resolved by performing ultrasound-guided aspiration. Wu et al[13] reported that the cytological diagnosis of FVPTC could be difficult because of the paucity of nuclear changes of PTC which can be mistaken as hyperplastic nodule. Baloch and Livolsi[4] diagnosed such lesions as suggestive of PTC and recommended intraoperative frozen sections or touch preparations for definitive diagnosis. Similar admixture of patterns was observed by Manimaran et al[14] in their study of 22 cases of FVPTC.

In this study, all the cases showed nuclear grooves and inclusions, nucleomegaly, powdery chromatin, and prominent nucleoli. Similar observations were made by Manimaran et al[14] and Aron et al.[15] Hurthle cells and psammoma bodies were not seen in any of our cases. Manimaran et al[14] reported similar results.

The sensitivity of a particular test is the statistical index of the diagnostic efficacy of the particular test. In the context of FNAC, it implies that if FNAC is positive, it definitely means the presence of disease, but if it is negative, it does not rule out the disease. In the present study, the sensitivity and specificity were 42.9 and 100% respectively. The study done by Shobha et al[1] showed a higher sensitivity of 70.6% and a specificity of 100%. Sharma[16] showed a sensitivity and specificity of 63.6 and 82.4% respectively. Overall diagnostic accuracy on FNAC for follicular-patterned lesions was 83.3%, whereas other authors showed a diagnostic accuracy of 80, 77, and 79%.[1,5,16] The positive and negative predictive values in our study were 100 and 81% respectively, whereas Sharma[16] showed a value of 43.75 and 91.3% respectively.

CONCLUSION

Fine needle aspiration cytology is a simple and inexpensive method of diagnosing non-neoplastic and neoplastic lesions of thyroid gland. The FNAC has low sensitivity for differentiating follicular adenoma from follicular carcinoma and hence, histopathological examination remains the gold standard for differentiating these two lesions. Due to overlapping cytomorphological features of benign and malignant follicular-patterned lesions, one should carefully look for nuclear features specific for

papillary thyroid carcinoma. Diagnosing follicular-patterned lesions on FNAC is challenging and will remain a "gray zone" for all cytopathologists. To decrease the rate of false-negative cases, FNAs should be performed under ultrasound guidance from different parts of the lesion. Scrupulous and thorough examination of all cytological smears should be done for predominant follicular pattern along with cytomorphological and background details to differentiate follicular-patterned thyroid lesions in order to minimize false-negative diagnosis on FNAC.

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ORIGINAL ARTICLE

Indian Teaching Hospitals and Quality Health Care from Global Perspective: A Reality Check in Maharashtra, India

[1]Archana Mishra, [2]Prakash P Doke

ABSTRACT

Teaching hospitals are the apex body of Indian hospital system and are expected to lead from the front in offering quality health care services in a safe environment by qualified and skilled staff. In this study, we conducted a reality check on some teaching hospitals in Maharashtra to assess gaps between declared policies and actual results achieved. We studied three parameters, i.e., human resource management (HRM), quality and safety, and communication and patient relations through three indicators, viz., policies, practices, and services from the Joint Commission International Accreditation (JCIA) standards in concurrence with National Accreditation Board for Hospitals (NABH). A total of 11 teaching hospitals were selected randomly across Maharashtra. The requisite data for the study were collected through personal interview from medical superintendents, employees, and patients. The responses were coded as: 10 (full compliance), 5 (partial compliance), and 0 (no compliance) as per NABH evaluation criteria.

The study shows that while teaching hospitals are maintaining most of the policies, they are poor in translating the standards into practices and services. Teaching hospitals need to lay greater emphasis on continuous training and development of their employees that should be focused on improving quality of patient care as per global standards as far as possible.

Keywords: Globalization, Health care, Quality, Standards, Teaching hospitals.

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INTRODUCTION

With changing global economic scenario, Indian patients too expect and deserve health care of global standards. This calls for greater integration, transparency, and accountability in health care entities.[1,2] Teaching hospitals have to play a pivotal role in the national health care system of the country by bringing improvements in the quality of medical education and research.[1,3]

In India, there are 63,985 seats for Bachelor of Medicine and Bachelor of Science (MBBS) courses in 460 medical colleges across the country.[4] Each medical college has an integrated teaching hospital. These hospitals are pillars to the health care system in India.[5] Studies show that teaching hospitals are overburdened as referral centers.[6] Moreover, they lack adequate resources in terms of equipment and skilled manpower[7,8] due to financial constraints.[9] These hospitals also need to use their resources strategically to meet the needs of health care delivery system.[10-12]

The Medical Council of India (MCI) has given guidelines about infrastructural norms in terms of space, manpower, equipments, and other facilities. Corporate hospitals in India are continuously improving their patient care services by improving efficiency and reducing procedural errors.[13,14]

In this study, we tried to conduct reality check in some selected teaching hospitals between policies as per global standards and their actual performance.

MATERIALS AND METHODS

The study population was teaching hospitals in Maharashtra. The respondents during the survey were 11 medical superintendents, 30 employees (doctors, nurses, and others) and 30 patients from each teaching hospital.

Three parameters, HRM, quality/safety, and communication system, were measured, based on standards (chosen from JCIA and NABH)[15,16] and indicators (policies, practices, and services). These standards [HRM (16), quality (28), and communication (23)] and indicators were optimized during the pilot study (Table 1).[7] There were three questionnaires to assess the status of teaching hospitals.

- Questionnaire A: Medical Superintendent,
- Questionnaire B: Employees (doctors, nurses, and others), and
- Questionnaire C: Patients.

The schema of the study is shown in Flow Chart 1.

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Table 1: Selected parameters and standards from JCIA and NABH

Indicators	*Code*	
Standards of HRM		
Policy (Questionnaire: A)	HRM1	Recruitment and selection policies (need assessment, advertising, interview, selection, and induction)
	HRM 2	Policies for defining/documenting job description for all employees
	HRM 3	Policies for maintaining personnel file for all employee
	HRM 4	Policies for handling grievances of employees
	HRM 5	Policies defined/documented for employees' education/training
	HRM 6	Performance appraisal/career development policies for employees
Practices (Questionnaire: B)	HRM 7	Existing recruitment and selection procedures as per defined policies
	HRM 8	Employees' knowledge/awareness about job description
	HRM 9	New employees' induction/orientation program
	HRM 10	Clarity of mission/goal of the hospital among employees
	HRM 11	Awareness among employees about Standard Operating Procedures of the department
	HRM 12	Employees' awareness and participation in performance appraisal/career development program
	HRM 13	Employees' involvement in organization through suggestions/complaints
Services (Questionnaire: C)	HRM 14	Assessment of competency of doctors through patients' feedback
	HRM 15	Assessment of competency of nurses through patients' feedback
	HRM 16	Assessment of competency of other staff through patients' feedback
Standards of quality/safety		
Policy (Questionnaire: A)	Qua 1	Defined quality assurance and continuous monitoring policies
	Qua 2	Defined managerial policies for continual improvement
	Qua 3	Policies for communicating to staff and patient for safety norms
	Qua 4	Defined and documented preventive and breakdown maintenance
	Qua 5	Defined and documented hospital infection control policies
	Qua 6	Defined and documented biomedical waste management
Practices (Questionnaire: B)	Qua 7	Awareness in employees for quality assurance plan in hospital
	Qua 8	Awareness in employees for risk management initiatives in hospital
	Qua 9	Education activities for staff and patient for safety
	Qua 10	List of personnel responsible for quality program
	Qua 11	Awareness among employees for cleaning and sterilization
	Qua 12	Preventive and breakdown maintenance procedures
	Qua 13	Awareness among employees for hospital infection control
	Qua 14	Awareness among employees for biomedical waste management
	Qua 15	Maintaining dignity and privacy of patients in the hospital
	Qua 16	Awareness among employees for informed consent
	Qua 17	Awareness for risks/benefits of informed consent
Services (Questionnaire: C)	Qua 18	Emergency and patient information support system for patients
	Qua 19	Effective front office facilities
	Qua 20	Importance of cleanliness and better ambiance in the hospital
	Qua 21	Effective diagnosis facilities
	Qua 22	Effective treatment facilities
	Qua 23	Effective food and beverages facilities
	Qua 24	Effective security and parking facilities
	Qua 25	Effective waste management and sterilization services
	Qua 26	Hospital is safe from fire, security threats, etc.
	Qua 27	Staff washes hands, wear gloves, mask, and gowns for the procedures
	Qua 28	Employees guide for necessary precautions for infection safety to the patients
Standards of communication (information to patients)		
Policy (Questionnaire: A)	Com 1	Defined policies for patient and family's rights during the care plan
	Com 2	Defined policies for patient/family involvement in decision making
	Com 3	Defined policies for grievances redressal of patients
	Com 4	Defined policies for patient's follow-up and feedback
	Com 5	Defined policies for confidentiality/security of information.
	Com 6	Defined policies for communication of financial implications

(Cont'd…)

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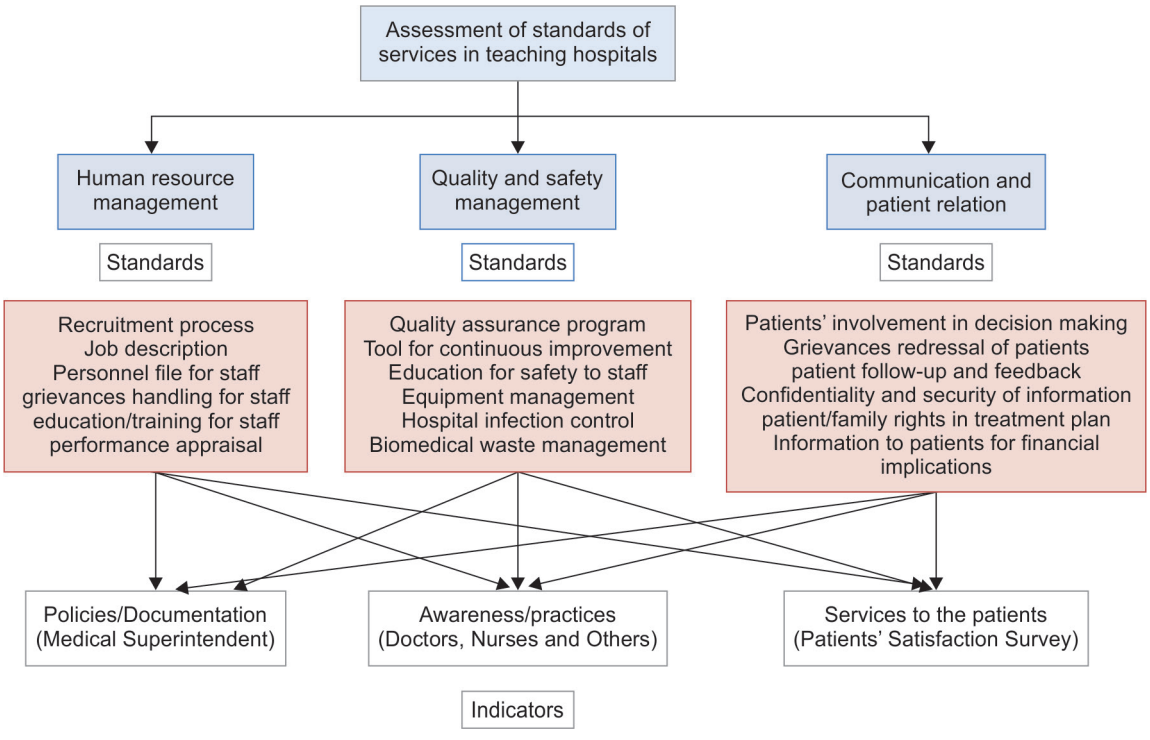
Indicators	*Code*	
Practices (Questionnaire: B)	Com 7	Practices of patient's follow-up and feedback
	Com 8	Maintaining confidentiality and security of information
	Com 9	Access to information from the medical records
	Com 10	Practices for communication of financial implications
Services (Questionnaire: C)	Com 11	Information for treatment and involved in decision-making
	Com 12	Hospital pay attention to privacy/confidentiality
	Com 13	Proper attention for complaints/feedbacks
	Com 14	Inform for course of treatment/follow-up
	Com 15	Informed about financial expenses for treatment plan
	Com 16	Cost-effective services
	Com 17	Visit again/recommend to others
	Com 18	Doctor informed you for treatment and procedures
	Com 19	Nurses informed you for treatment and procedures
	Com 20	Other staff informed you about the procedures
	Com 21	Doctors are courteous and genuine
	Com 22	Nurses are courteous and genuine
	Com 23	Other employees are courteous and genuine

Flow Chart 1: Schema of the study



Data Analysis and Interpretation

Data were quantified as per JCIA scoring criteria as shown in Table 2.

Evaluation of Feedbacks

All three questionnaires (A, B, and C) were evaluated together statistically, considering 10 as an ideal score. The operational definition of gap was adopted from JCIA as follows:

- One or more standards were scored less than 5.

Table 2: Scoring criteria for the responses of the policies, practices, and services in teaching hospitals

Evaluation criteria	*Answered*	*If the response were/ compliance*	*Score*
Fully met	Promptly yes	"Always/mostly"/90%	10
Partially met	Partly/hesitantly yes	"Usually/sometimes"/ 50–89%	5
Not met	No/not answered	"Rarely/never"/less than 49%	0
Not available	Do not know/ missing data	Do not know/missing data	0

Table 3: Human resource management score (policies, practices, and services) for teaching hospitals in Maharashtra from 2010 to 2013

Indicator	*H1*	*H2*	*H3*	*H4*	*H5*	*H6*	*H7*	*H8*	*H9*	*H10*	*H11*	*Average*
Policies	5.83	5.83	5.83	5.83	5.83	5.83	6.67	7.50	6.67	5.83	7.50	6.29 ± 1.96
Practices	4.05	3.57	3.57	3.55	3.76	3.71	4.19	4.10	4.26	4.05	4.40	3.93 ± 2.1
Services	3.94	2.33	3.83	4.44	3.56	3.00	4.44	2.44	3.50	3.61	6.11	3.75 ± 0.76
Mean score for policies, practices, and standards with standard deviation												4.65 ± 1.42
Mean	4.61	3.91	4.41	4.61	4.38	4.18	5.10	4.68	4.81	4.50	6.01	4.65 ± 0.55

Table 4: Quality score (policies, practices, and services) for teaching hospitals in Maharashtra from 2010 to 2013

Indicator	*H1*	*H2*	*H3*	*H4*	*H5*	*H6*	*H7*	*H8*	*H9*	*H10*	*H11*	*Mean*
Policy	4.17	3.33	4.17	3.33	4.17	3.33	6.67	6.67	6.67	5.00	7.50	5.00 ± 1.58
Practices	4.73	4.15	4.24	4.21	4.24	4.11	4.47	4.95	4.45	4.56	5.00	4.47 ± 0.32
Services	1.76	0.74	1.11	1.05	1.24	1.09	1.76	1.02	1.62	1.79	2.76	1.45 ± 0.56
Mean scores for standards (with standard deviation)												3.64 ± 1.85
Mean	3.55	2.74	3.17	2.86	3.22	2.84	4.30	4.21	4.25	3.78	5.09	3.64 ± 0.76

Table 5: Communication (policies, practices, and services) for teaching hospitals in Maharashtra from 2010 to 2013

Indicator	*H1*	*H2*	*H3*	*H4*	*H5*	*H6*	*H7*	*H8*	*H9*	*H10*	*H11*	*Mean*
Policy	3.33	0.83	0.83	0.83	0.83	0.83	5.00	5.00	5.00	5.00	5.00	2.95 ± 2.09
Practice	3.83	3.83	3.83	3.92	4.04	3.83	5.42	5.17	5.17	5.58	6.08	4.61 ± 0.87
Service	2.99	1.90	2.58	2.81	2.69	2.32	3.37	2.08	3.35	3.56	4.86	2.95 ± 0.83
Mean score for indicators (with standard deviation)												3.51 ± 1.56
Mean	3.38	2.19	2.41	2.52	2.52	2.33	4.60	4.08	4.50	4.72	5.31	3.51 ± 1.16

- Aggregate score of one or more parameters of the study was less than 8.

Limitations of the Statistical Analysis

The data were categorized into three codes: 0, 5, and 10; so, statistical test does not register significant gap in many cases.

RESULTS AND DATA ANALYSIS

Human Resources Management

Table 3 shows the indicators and hospitals (H1, H2, …, H11). The mean scores of HRM for the policies, practices, and services are shown in the last column and mean scores for each hospital are in the last row in Table 3. The statistical test ($F_{(2, 30)} = 39.90$, $p < 0.001$) confirmed that the policy/documentation standards were rated significantly different from knowledge/awareness/practices and services of HRM.

Quality/Safety

Table 4 shows the indicators and hospitals (H1, H2, …, H11). The mean scores of quality/safety for the policies, practices, and services are shown in the last column and the mean scores for each hospital are in the last row in Table 4. The statistical tests were also conducted to ascertain the gaps among the employees based on their profile, which shows that there was a significant difference between nurses and other staff ($t_{(20)} = 2.1$; $p < 0.05$) in practicing quality and safety standards. The test ($F_{(2, 30)} = 41.383$, $p < 0.05$) confirmed that the standards of policies were rated significantly different from practices and services of quality/safety.

Communication and Patient Relation

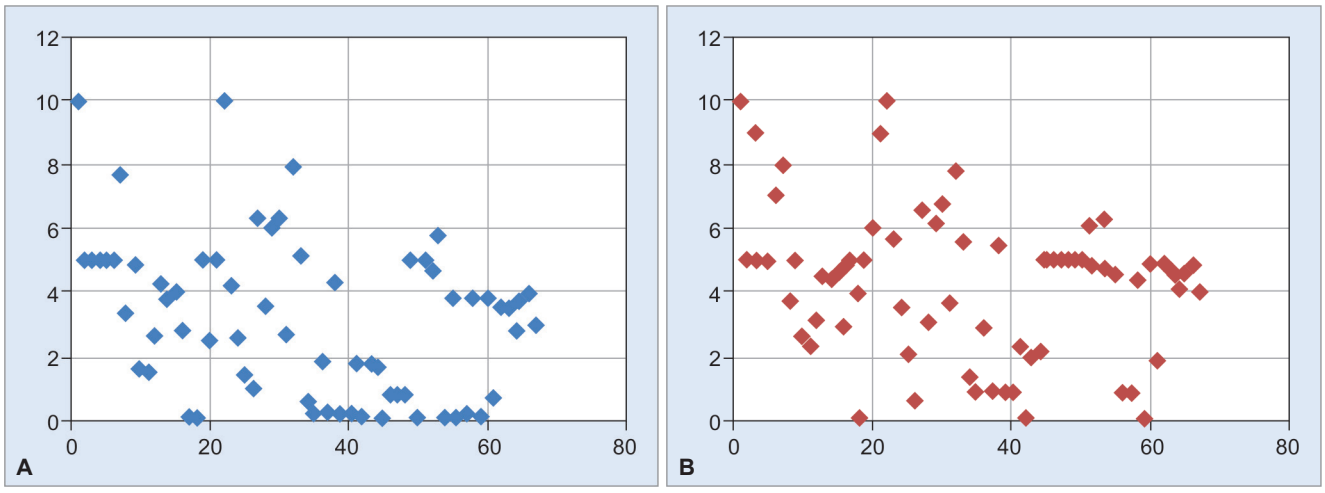
Table 5 shows the indicators and hospitals (H1, H2, …, H11). The mean scores of communication system for the policies, practices, and services are shown in last column and mean scores for each hospital are in the last row in Table 5. The statistical test confirmed that there was a significant gap among standards of practices and services.

There was a significant difference among hospitals in terms of compliance with communication policies ($F_{(10, 55)} = 10.455$; $p < 0.05$), especially between public and private hospitals ($t_{(10)} = 4.88$; $p < 0.05$). Graph 1 shows compliance with standards of HRM, quality, and communication in public and private hospitals respectively. The x-axis shows the number of standards and the y-axis shows the score (0, 5, and 10). The last 23 standards of communication can be seen near the baseline in public hospitals.

DISCUSSION

As per operational definition of the gap in standards in teaching hospitals, data were analyzed as follows:

- One or more standards were scored less than "5": Table 6 indicates the number of standards scored less



Graphs 1A and B: Standards for HRM, quality, and communication in public and private teaching hospitals

Table 6: Matrix (indicator-parameter) of standards received < 49% compliances

Parameters	*Human resource management*	*Quality/ safety*	*Communication*	*Total standards*	*Percent of standards <5*
Indicators					
Policy/documentation	0	3	5	8 out of 18	44.44
Knowledge/awareness/practices	6	6	2	14 out of 22	63.64
Services to the patients	3	11	13	27 out of 27	100
Total standards	9 out of 16	20 out of 28	20 out of 23	49/67	73.13
Percent of standards scored < 5	56.25	71.43	86.96		

than 5 in each of the three parameters, namely HRM, quality, and communication. The last row denotes the number/percentage of standards, which received less than score 5 overall.

- Aggregate score of one or more parameters of the study was less than "8": Average (including all indicators, policies, practices and services) was calculated for the parameter HRM, quality, and communication. In the current study, all these standards have scored 5, i.e., less than 49% compliance as per the global norms.

Significance Level

The gap is analyzed as per the operational definition. The test of significance shows that HRM ($t_{(15)} = 9.835$, $p < 0.05$), quality/safety ($t_{(27)} = 13.388$; $p < 0.05$), and communication ($t_{(22)} = 20.076$; $p < 0.05$). Therefore, it is accepted that there is a significant gap in the current HRM, quality/safety, and communication system of teaching hospitals with respect to international standards.

CONCLUSION

In this study of 11 teaching hospitals of Maharashtra, India, standards of patient care were analyzed as per global standards and existing gaps were assessed. Three parameters (as per JCIA and NABH), viz., human resource, quality/safety and communication, and three indicators (policies, practices, and services), were chosen. Data gathered were quantified, scored, and statistically analyzed. In all three parameters, significant gaps were found as compared with international standards. It was found that while most of the policies of the patient care are being maintained by all these hospitals as per global standards what they lacked was their strict and complete implementation. Since teaching hospitals are the places where our health care professionals are trained, they have to be the role model for rest of the hospitals in providing world-class health care. This can only happen if the administrative authorities of these hospitals translate policies into action not-withstanding our limited resources.

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ORIGINAL ARTICLE

Operative Management of Liver Injury in Polytrauma Patients: Experience of One Trauma Center

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ABSTRACT

Introduction: The liver is one of two most frequent abdominal parenchymal organs involved in trauma. Liver injury (LI) remains an important cause of trauma-related mortality. It is often accompanied by trauma to the other organs.

Materials, methods and results: During 9 years in the Provincial Trauma Center, out of 10,191 hospitalized patients, there were 1,702 trauma-related hospitalizations and 393 multiorgan traumas; 217 patients underwent surgery due to multiorgan trauma and coexisting LI. The most frequent coinvolved organs were spleen (83.9%), colon (33.6%), kidney (18.9%), small intestine (18.9%), pancreas (17.5%), gallbladder (16.6%), diaphragm (15.7%), and ileocecal valve (12.9%), with 33.2% of rib fractures and 31.3% of pneumothorax and pneumohemothorax. Grade of liver trauma was assessed according to American Association for the Surgery of Trauma—Organ Injury Scale (AAST-OIS). Fifty-two liver injuries (24,9%) were classified as AAST-OIS grade I, 54 (24.9%) as grade II, 46 (21.2%) as grade III, 41 (18.4%) as grade IV, and 25 (11.5%) as grade V. Patients received laparotomy (n = 205, 94.5%) or thoracolaparotomy (n = 12, 5.5%). Liver injuries were managed with electrocoagulation (n = 64, 29.5%), parenchymal sutures (n = 87, 40.1%), resectional debridement (n = 12, 5.5%), and perihepatic packing (n = 54, 24.9%).

Predominance of males and young patients with a mean age of 36 corresponds to accident statistics. Among patients receiving surgery, 88.9% had blunt trauma, with a high predominance of motor vehicle accidents.

Conclusion: Liver injuries predominantly follow a blunt abdominal injury. Despite good results of nonoperative management in hemodynamically stable patients with blunt trauma, surgery is still required due to complexity and seriousness of multiorgan injuries. Complex liver injuries require surgery in a well-equipped and active trauma center, since the mortality rate of surgical management of major liver injuries remains high.

Keywords: Liver injury, Multiorgan trauma, Polytrauma, Surgery.

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INTRODUCTION

The liver is the second most frequently injured intraperitoneal parenchymal organ, next to spleen.[1,2] Liver injuries constitute 5% of all traumas.[3-5] Liver injury may occur by blunt or penetrating force. Motor vehicle accidents along with sports-related injuries are the most common causes of blunt trauma. In blunt abdominal injuries, LI is the commonest cause of mortality.[6] In majority of cases, LI is accompanied by injury to the other organs.[7]

To asses a polytrauma patient, an effective, efficient, and rapid diagnostic protocol needs to be followed. Ultrasound, including a focused assessment with sonography for trauma (FAST), and computed tomography are used for diagnosis. The FAST is noninvasive, rapid, and repeatable, but operator-dependent and positive only when intraperitoneal fluid volume exceeds 400 mL.[1,4] An invasive diagnostic peritoneal lavage may be required if noninvasive diagnostic tools are not available.[8]

Liver injuries are classified in a 6-point organ injury scale proposed by the AAST, from the least severe (grade I) subscapular, nonexpanding hematoma <10 cm surface area or capsular laceration <1 cm of parenchymal depth, to the most severe (grade VI) hepatic avulsion (Table 1).[3,7,9-11]

The majority of LIs require a nonoperative management; 50 to 85% of blunt LIs can be treated conservatively. Hemodynamically stable patients with blunt LI can be managed nonoperatively.[2,4-6,12] Grade III or higher AAST-OIS of LI and hemodynamically unstable cases require surgery (perihepatic packing, parenchymal sutures, liver resections and resectional debridement, partial hepatectomy, lobectomy, or selective vessel ligation).[3-6,9,13]

In this retrospective study, we present a series of polytrauma patients receiving surgery due to severity of either liver or other organ injury. The trauma mechanism,

Table 1: Liver injury scale according to AAST-OIS[11]

AAST-OIS grade of LI	Type of injury		
	Hematoma	*Laceration*	*Vascular*
I	Subscapular, nonexpanding, < 10 cm surface area	Capsular tear < 1 cm parenchymal depth	
II	Subscapular, nonexpanding, 10–50% of surface area or intraparenchymal, nonexpanding, <10 cm in diameter	1–3 cm parenchymal depth, <10 cm in length	
III	Subcapsular >50% of surface area or expanding, ruptured subcapsular or parenchymal hematoma, intraparenchymal hematoma >10 cm in diameter	>3 cm parenchymal depth	
IV		Parenchymal disruption involving 25–75% of hepatic lobe	
V		Parenchymal disruption involving >75% of hepatic lobe	Juxtavenous hepatic injuries, i.e., retrohepatic vena cava or central major hepatic veins
VI			Hepatic avulsion

Table 2: Percentages of trauma-related hospitalizations, multiorgan and liver injuries among all hospitalized patients

	No. of patients	*% of all hospitalized*	*% of trauma-related hospitalizations*	*% of multiorgan traumas*
All hospitalized	10,191			
Trauma-related hospitalizations	1,702	16.7		
Multiorgan trauma	393	3,9	23.1	
Liver trauma	217	2,1	12.7	55.2

AAST-OIS score, operative procedures, and mortality are presented. Patients treated nonoperatively were excluded from this evaluation.

MATERIALS, METHODS, AND RESULTS

Out of a total of 10,191 patients treated in the Department of General and Vascular Surgery in the Provincial Trauma Center, Czestochowa, Poland, over a period of 9 years, 217 (2.13%) patients had sustained LI along with other thoracoabdominal injuries. A retrospective study was done in these 217 patients (Table 2). Of these, 137 (63.1%) were males and 80 were (36.9%) females. Their age ranged from 18 to 81 years with an average age of 34 years for males, 39 years for females, and 36 years for the combined group. In 193 patients (88.9%), cause was blunt trauma, majority (72.4%) due to motor vehicle accidents. In 24 patients (11.1%), injuries were caused by penetrating trauma.

Liver injuries were classified as per AAST-OIS scale: 52 (24%)—grade I, 54 (24.9%)—grade II, 46 (21.2%)—grade III, 41 (18.4%)—grade IV, and 25 (11.5%)—grade V (Table 3). Other organ injuries were spleen in 182 patients (83.9%), colon (33.6%), kidney (18.9%), small bowel (18.9%), pancreas (17.5%), gallbladder (16.6%), diaphragm (15.7%), and inferior vena cava (12.9%). Besides, 72 patients (33.2%) had associated rib fractures and 68 patients (31.3%) had pneumothorax/hemopneumothorax (Table 4).

Table 3: Grading of liver injuries based on AAST-OIS[11]

AAST-OIS LI scale	*n (%)*
I	52 (24.0)
II	54 (24.9)
III	46 (21.2)
IV	41 (18.4)
V	25 (11.5)

Table 4: Organs coaffected with LI in polytrauma patients

	n (%)	*AAST-OIS for organ-specific injuries*[11]
Spleen	182 (83.9)	I (n = 48); II (n = 56); III (n = 18); IV (n = 34); V (n = 26)
Colon	73 (33.6)	Ascending n = 7; transverse n = 34; descending and sigmoid n = 32
Rib fracture	72 (33.2)	
Pneumothorax and pneumohemothorax	68 (31.3)	
Kidney	41 (18.9)	I (n = 13); II (n = 9); III (n = 8); IV (n = 4); V (n = 7)
Small intestine	41 (18.9)	
Pancreas	38 (17.5)	I (n = 10); II (n = 15); III (n = 9); IV (n = 2); V (n = 2)
Gallbladder	36 (16.6)	
Diaphragm	34 (15.7)	
Inferior caval vein	28 (12.9)	
Pelvis fracture	27 (12.4)	
Bladder	23 (10.6)	
Stomach	12 (5.5)	
Esophagus	7 (3.2)	
Pericardial tamponade	4 (1.8)	
Ovary	3 (1.3)	

A total of 205 patients (94.5%) underwent laparotomy and in 12 patients (5.5%), laparotomy was combined with thoracotomy. Operative procedures carried out for liver injuries consisted of perihepatic packing, parenchymal sutures, resections (partial hepatectomy or lobectomy), and selective vessel ligation. Other organ injuries were treated as per general surgical principles; 23 patients (6%) died intraoperatively. Overall, in-hospital mortality was 16.6% (36 cases).

DISCUSSION

Liver injuries constitute an important component of multiorgan injuries. Motor vehicle accidents are the commonest cause of these injuries. Grading of liver injuries as per AAST-OIS is carried out by using three parameters: (i) extent and location of hematoma, (ii) length and depth of laceration, and (iii) severity and location of vascular trauma. These are shown in detail in Table 1. Higher the grade of injury, worse is the prognosis. Grade VI liver injuries rarely reach the hospital alive as in the present study.

Right lobe injuries are more common than left lob injuries in blunt trauma, as seen in this study (right lobe 74.6% *vs* left lobe 49.3%). Male preponderance (63.1%) as seen this study corresponds to accident statistics as expected. Majority of the injuries are caused by blunt trauma (88.9% in this study) and most of these are due to motor vehicle accidents. These figures correspond to data published in literature.[1,5,6] Incidence of gunshot injuries in our study was only 1.8%, which corresponds with the data of other countries where possession of firearms is illegal. Splenic injury was the commonest one associated with liver injuries in our series (83.9%). Similar incidence has been reported by other authors.[1,5,13]

Bleeding from major liver injuries remains an important cause of mortality. The trauma surgeon has to be familiar with all methods of controlling bleeding from liver. In our series, bleeding from liver injuries was controlled by electrocoagulation in 29.5% cases, parenchymal sutures in 40.1%, resectional debridement in 5.5% and perihepatic packing, followed by relook laparotomy. Procedure to be used depends upon hemodynamic status of the patient, severity of LI, presence of other organ injuries (which need to be treated simultaneously), and expertise of the trauma center.[3-6,9,13] Mortality rate of liver injuries remains high. Higher AAST-OIS grade, prolonged prothrombin time, and decreased platelet count are associated with higher mortality.[13]

CONCLUSION

Liver injuries predominantly occur due to blunt trauma. When associated with other organ injuries, surgery is required in all cases. Mortality of major liver injuries remains high. Trauma surgeons must be familiar with various modalities of management of liver injuries. The aim should be to stop bleeding as expeditiously as possible. They also must possess expertise to deal with other injured organs in a polytrauma patient.

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REVIEW ARTICLE

The ASPIRE-to-Excellence Initiative: Can We recognize Excellence in Student Engagement with the Curriculum?

[1]John Dent, [2]Catherine Kennedy

ABSTRACT

Research has demonstrated clear benefits of student engagement both in terms of student performance and for academic institutions. Policy guidelines from a variety of sources have advocated for student engagement on a variety of levels. Academic Support Program Inspiring Renaissance Educators (ASPIRE)-to-Excellence initiative represents a means for medical schools to gain recognition of their achievements in this area. We continually see examples of positive initiatives through our work with AMEE, an international association for medical education and the Essential Skills in Medical Education course for students (ESME-Student). We hope to encourage further debate and sharing of experiences to promote student engagement.

Keywords: Academic support program inspiring renaissance educators-to-excellence, Criteria, Curriculum development, Student engagement.

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INTRODUCTION

The question of how to enhance student engagement in their learning has long been a consideration in medical education. Approaches taken to student engagement in higher education have varied from those which have sought to identify student involvement, to gather feedback, increase representation, and assess approaches to learning.[1] In recent years, this concept of engagement has been extended to include a requirement for curricula to be focused on student-centered learning[2] and for the involvement of students in curriculum development. Whilst a variety of policy statements have been issued which outline this requirement, it is less clear how such requirements are to be assessed or evaluated. One initiative that has sought to do so has been the ASPIRE-to-Excellence Initiative,[3] launched in 2012 by AMEE. In this article, we will explore the context and issues relating to student engagement within the curriculum before exploring how the ASPIRE initiative can be used to identify examples in practice. In doing this, we will draw on a range of illustrative practice.

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DEFINING "STUDENT ENGAGEMENT"

Student engagement has increasingly become an expectation for medical education providers and is included within a variety of policy statements and guidance for practice.[1] It has traced its origin back to the 1980s to the work by Astin[4] on student involvement, and highlighted the common use of the terms in North America and Australasia in their large-scale student engagement surveys (National Survey of Student Engagement and Australasian Survey of Student Engagement). While the term has traditionally been less commonly used within Europe, it has increasingly been evident in a range of higher education policy directives and guidance, for example, within the Bologna Process.[5] However, definitions as to what social engagement is and includes varies greatly. As The Student Engagement Partnership (TSEP)[6] notes, "there is no single, fixed, universal definition or model of student engagement; it is something which is intrinsically linked to and shaped by the context of the higher education provider in which it is situated."

Kahu[7] identified four different approaches to student engagement:

1. Behavioral, which focuses on student behavior and effective teaching practice;
2. Psychological, which centers on internal individual processes of engagement, including behavior, cognition, emotion, and conation;
3. Sociocultural, which highlights the importance of the wider social, political, and cultural contexts; and
4. Holistic, which synthesizes the elements of the above approaches.

The TSEP has distinguished three different categories of student engagement:

1. Academic—engagement in and with learning;
2. Social—engagement in and with the wider learning community;
3. Enhancement—engagement in and with processes, such as quality, governance, etc.[6]

Student engagement is widely seen as having many benefits for institutions, such as increased student retention,[8] reputational and quality assurance,[9] and student engagement in academic research and teaching to the benefit of medical education in general.[10] The benefits for students were considered to be increased satisfaction with studies,[11] improvement in learning, cognitive development, and critical thinking studies;[11,12] improved grades,[13] and a greater sense of connectedness, affiliation, and belonging.[14] It has been argued that a sense of belonging aides learning.[15]

FRAMEWORKS FOR ENGAGEMENT

A number of frameworks for the inclusion of student engagement as a priority within higher education have been developed. At a European level, the European Higher Education Area (EHEA)[2] included student-centered learning as part of the Bologna Process in its Leuven/Louvain-la-Neuve Communiqué. This stated that "student-centred learning requires empowering individual learners, new approaches to teaching and learning, effective support and guidance structures and a curriculum focused more clearly on the learner in all three cycles."[2] It continued, "Academics, in close cooperation with students and employer representatives, will continue to develop learning outcomes and international reference points for a growing number of subject areas."[2] Student engagement was further put forward in the EHEA Bucharest Communiqué[5] which stated the need to "establish conditions that foster student learning, innovative teaching methods and a supportive and inspiring working and learning environment while continuing to involve students and staff in governance structures at all levels." As part of the European MEDINE2 initiative, research exploring future trends in medical education[16] identified a current trend in medical education as being "the empowerment of students to take responsibility for their own learning and student involvement in curriculum planning committees as major current trends that it was hoped would develop further in the future."[17]

In the UK, the Quality Assurance Agency[18] for Higher Education has emphasized the importance of student engagement in terms of their motivation for learning and independent learning, and also their participation in the quality assurance and enhancement of educational provision. In Scotland, Student Participation in Quality Scotland[19] in partnership with key higher agencies identified five key elements of student engagement:

1. Students feel a part of a supportive institution;
2. They are engaged in their own learning;
3. They work with the institution in shaping the direction of learning;
4. There are formal mechanisms for quality assessment and governance;
5. Influencing student experience at a national level.

More recently, and specific to the area of medical education, the General Medical Council in the UK in their guidance "Promoting excellence: Standards for medical education and training"[20] include the recommendation: "R5.2 The development of medical school curricula must be informed by medical students, doctors in training, educators, employers, and other health and social care professionals and patients, families and carers".

THE ASPIRE-TO-EXCELLENCE INITIATIVE

With the variety of policy frameworks and guidance clearly advocating student engagement, the logical next step is how to put this into practice and enable medical schools to demonstrate the ways in which it is being implemented. Further, at a time in which excellence in research is often prioritized over teaching, there is a clear need to highlight positive teaching initiatives.

The concept of recognizing and rewarding excellence in teaching and learning in medical schools was first proposed by Harden and Wilkinson.[21] Following on from this, the ASPIRE-to-Excellence initiative was launched by AMEE in 2012. It sought to provide international recognition of excellence in education, teaching and learning, alongside research, as the mission of a medical, dental, or veterinary school. It was envisaged as going beyond the traditional accreditation process, with which we are all familiar, by recognizing that the educational program in a school can be subjected to peer review against an agreed set of standards or benchmarks that identify world-class excellence in education. The ASPIRE Board first met in 2010 and agreed on the criteria and subcriteria against which submissions for consideration for the award were to be assessed. Initial Areas or Themes in which excellence could be displayed were Student Engagement, Assessment of Students, and the Social Accountability of the Medical School. Later, two further areas were added, Faculty Development, and Simulation. The ASPIRE Board was charged with oversight of the awards and included 22 members from 15 different countries. A truly international opinion on an application could therefore be given in reference to its local context. In addition, a panel of experts in each of the five Areas or Themes identified would assist in reviewing and giving feedback to each institution making a submission. The area panel for Student Engagement consists of 12 members from 11 countries.

Table 1: Academic support program inspiring renaissance educators criteria and subcriteria for student engagement with the curriculum[22]

Criterion 1—*Student engagement with management of the school, including matters of policy, mission, and vision of the school* (student engagement with the structures and processes)
1.1 Students have been involved in the development of the school's vision and mission.
1.2 Students are represented on school committees.
1.3 Students are involved in the establishment of policy statements or guidelines.
1.4 Students are involved in the accreditation process for the school.
1.5 Students have a management/leadership role in relation to elements of the curriculum.
1.6 Students' views are taken into account in decisions about faculty (teaching staff) promotion.
1.7 Students play an active part in faculty (staff) development activities.
Criterion 2—*Student engagement in the provision of school's education program* (student engagement with the delivery of teaching and assessment)
2.1 Students evaluate the curriculum and teaching and learning processes.
2.2 Feedback from the student body is taken into account in curriculum development.
2.3 Students participate as active learners with responsibility for their own learning.
2.4 Students are involved formally and/or informally in peer teaching.
2.5 Students are engaged in the development of learning resources for use by other students.
2.6 Students provide a supportive or mentor role for other students.
2.7 Students are encouraged to assess their own competence.
2.8 Students engage in peer assessment.
Criterion 3—*Students' engagement in the academic community* (student's engagement in the school's research program and participation in meetings)
3.1 Students are engaged in school research projects carried out by faculty members.
3.2 Students are supported in their participation at local, regional, or international medical, dental, veterinary, and health professions education meetings.
Criterion 4—*Student engagement in the local community and service delivery*
4.1 Students are involved in local community projects.
4.2 Students participate in the delivery of local health care services.
4.3 Students participate in health care delivery during electives/attachments overseas.
4.4 Students engage with arranged extracurricular activities.

Demonstrating Student Engagement

In seeking to identify examples of excellence in student engagement, the ASPIRE panel highlighted the need to demonstrate students' active contribution and consultation in their teaching and learning. Four broad criteria were identified:

1. Student engagement with the management of the school, including matters of policy and the mission and vision of the school (Student engagement with the structures and processes).
2. Student engagement in the provision of the school's education program (Student engagement with the delivery of teaching and assessment).
3. Student engagement in the academic community (Students' engagement in the school's research program and participation in meetings).
4. Student engagement in the local community and the service delivery.

These criteria and their subcriteria are listed in Table 1.

Examples of Excellence in Student Engagement

In the 6 years since its launch, the ASPIRE initiative has identified many examples of excellence in student engagement in medical schools, and a list of the institutions who have been successful in their applications can be found in Table 2.

Table 2: Academic support program inspiring renaissance educators-to-Excellence award winners[23]

2013	Southern Illinois, USA; Aga Khan University, Pakistan; Maribor University, Slovenia; International University, Malaysia; University of Western Australia; Minho University, Portugal
2014	Southampton University, UK
2015	Charitie Universidad, Germany; University of Leeds, UK; Utrecht University, Netherlands; Uppsala University, Sweden; Schulich University, Canada; Chulalongkorn University, Thailand
2016	School of Veterinary Medicine, UK
2017	Al Imam Mohammad Ibn Saud Islamic University, Saudi Arabia

In addition, through our work with AMEE and in the wider medical education community, there are other examples of medical school practice which may be considered as illustrating one of the aspects of student engagement with the curriculum, as defined by the criteria and subcriteria.

ESME-Student[24] Criteria 1

This 12-week program based on the successful ESME Online course,[25] provides a student-focused introduction to ESME. Its aim is to engender interest in medical education and to provide a vocabulary and awareness of key topics to enable students to participate more fully in dialogue with

their medical school. The course includes six key topics presented as webinars, followed by prescribed reading and discussion groups, and finishes with an assignment. Since its start in 2015, this annual course has attracted 216 participants from 33 countries; 90% of participating students found the course of great or considerable value, and 91% would recommend it to others. The pass rate for participants in the online course was 90%.

SPICES Approach[26] Criteria 2.1

As part of the ESME-Student course, medical students were asked to evaluate the curriculum of their medical school using the student-centered, problem-based, integrated, community-based, elective-oriented, and systematic (SPICES) model. The SPICES approach describes any curriculum as lying at some point on a spectrum between innovative and traditional (Table 3).

A review of the opinions of 100 students selected at random from the ESME-Student course found that 30% considered their curriculum to be student-centered while 30% thought it was largely teacher-centered. The remainder described a balanced curriculum between the two extremes.

Peer-assisted Learning Criteria 2.4[27]

Encouragingly, as part of the ESME-Student course, many students shared with us examples of direct experience of peer learning approaches. Some students had been involved in setting up their own initiatives. For example, senior students in the peer-assisted learning program for colleagues in the University of Health Sciences, Phnom Penh, Cambodia, have developed a course to teach other seniors how to be effective tutors to junior students. Their work was presented at the AMEE conference in 2017.

Engagement with the Academic Community Criteria 3

Since 2000, the number of students cited as coauthors of papers published in Medical Teacher has increased from 78 to 183. Two final-year medical students in Dundee devised a cadaver shoulder hemiarthroplasty program in a simulated operation theater to teach anatomy to third-year students. This provided purposeful exposure to anatomy, some insight into orthopedic surgery and created a memorable learning experience. Their work was subsequently published.[28] In addition, within AMEE, medical students are encouraged to take part in our annual conference, to represent student members on committees and the AMEE Executive and, through the award of bursaries, to present academic papers and posters.

Table 3: The SPICES model for curriculum development[26]

Characteristics of an innovative curriculum			*Characteristics of a traditional curriculum*
S	Student-centered	↔	Teacher-centered
P	Problem-based	↔	Information gathering
I	Integrated	↔	Discipline-based
C	Community-based	↔	Hospital-based
E	Elective-oriented	↔	Standard program
S	Systematic	↔	Apprenticeship-based/opportunistic

CONCLUSION

The recognition of excellence in teaching has long been overlooked as medical schools are more usually ranked on their academic and financial achievements in research. The idea proposed by the ASPIRE initiative is that it should be possible to subject a medical school to international peer review against an agreed set of standards that would identify world-class excellence in education. "Student engagement" represents one area which can be assessed for an ASPIRE award. Criteria and subcriteria agreed by the panel are used to assess the medical school's performance against benchmark standards irrespective of the school's ability to access expensive resources. The benefits to institutions and students of promoting student engagement have been recorded. Some examples of student engagement have been suggested.

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REVIEW ARTICLE

Over-the-counter Drug Market in India: A Study to understand the Current Regulatory Perspective and Industry Dynamics

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ABSTRACT

Self-medication is on the rise in India. This is due to various reasons that are connected to the environment, demographic factors, changing consumer lifestyles, government policies, and strategies of the pharmaceutical industry. There has been a significant increase in the number of over-the-counter (OTC) products introduced in the health care market in India. On the regulatory front, the government is trying to consider legal recognition to the OTC category of drugs which currently do not have any legal recognition. Over-the-counter drugs in India can be advertised in media unlike some categories of the prescription-only drugs which are totally prohibited. The OTC drugs require a sales license except some drugs in Schedule K, which are categorized as household remedies. However, *Ayurvedic* drugs in India do not require a sales license and therefore, can be sold freely. It is expected that the regulatory policies would undergo changes initiated by the government in the near future.

Keywords: Drug utilization, Over-the-counter, Pharmaceutical industry, Prescriptions, Regulatory policy.

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INTRODUCTION

Self-medication is not a new phenomenon for India, as historically it has been practiced through the use of home remedies for common illnesses in many Indian households. Compared with the United States, the incidence of self-medication in India is slightly less. Around 76% of the consumers in India self-medicate for minor ailments as compared with 81% in the United States.[1] Self-medication is effected primarily through the consumption of OTC and Otx (combination of prescription and OTC) drugs, which are an important constituent of the Indian Pharmaceutical Industry. Consumption of OTC drugs addresses the needs of the population for easy accessibility, availability, and affordability of drugs in the face of difficulties like inadequate health care infrastructure, inadequate physician coverage, high medical costs, and the burden of health care delivery. Proliferation of the digital media has also added to increasing trends of self-medication in India. There are reports that 1 in 20 searches on Google is related to health.[1] There is a need to have in place an appropriate regulatory framework to support and control such efforts of the consumers. Vitamins, minerals, analgesics, health tonics, cold and cough preparations, topical preparations, and gastrointestinal drugs are some of the drug categories consumed as OTC in India.[2] There are various prescription drugs that can be moved into the OTC category if there is a proper regulatory mechanism of the government in place to facilitate this movement. Currently, there is no formal recognition of the OTC drugs category in India. Countries like the United States, the United Kingdom, Canada, and the Netherlands have regulatory policies for OTC drugs.

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Current Regulatory Practices

Definition of OTC: In India, the manufacture, import, distribution, and sale of drugs are regulated by the Drugs and Cosmetics Act, 1940 (DCA) and Drugs and Cosmetic Rules, 1945 (DCR). The term "OTC" or nonprescription has no legal recognition in India and all drugs which are not included in the list of "Schedule H, H1, X" are considered to be nonprescription drugs (or OTC drugs), which can be sold without the prescription of a registered medical practitioner. Prescription category drugs are those drugs that are included in Schedules H and X of the DCR. Schedule G drugs require the following mandatory text on the label: "Caution: It is dangerous to take this preparation except under medical supervision" (Some examples of Schedule G drugs include antidiabetic, anticancer, immunosuppressant, and some antihistamine drugs). The OTC products have no legal recognition in

India, as there is no category of OTC drugs in the DCR. Due to this, all drugs which are not included in the list of "prescription only drugs" (Schedules H, H1, and X) category and the ones classified as "household remedies" that are listed in Schedule K are considered by default to be "OTC" drugs. Even nonpharmacists, i.e., stores without drug licenses, are allowed to sell a few drugs in villages with population less than 1,000 that are listed in Schedule K of the DCR.

Medicated dressings and bandages for first aid, oral rehydration salt, nicotine gum, and lozenges containing up to 2 mg of nicotine and substances intended to be used for destruction of vermin or insects that cause disease in humans or animals, i.e., insecticides and disinfectants, are legally permitted for sale without the requirement of a license to sell.[3]

The Government of India through the Central Drugs Standard Control Organization is planning to include an independent schedule for OTC drugs in India. A separate category for OTC drugs to treat minor illnesses like colds, fevers, contraceptive pills, and treatment for allergies is likely to be created.[4]

Ayurvedic Medicines

The OTC drugs that are registered as "Ayurvedic medicines," i.e., the medicines of the Indian traditional system containing herbal/natural ingredients, also come under the purview of the DCA, 1940 and the DCR, 1945. The manufacturing of Ayurvedic drugs comes under the manufacturing license issued by the state licensing authorities for Ayurvedic products. Ayurvedic drugs in India do not require a drug selling license and can be sold legally at all nonchemist outlets. Some of the highest selling OTC brands in India are registered as "Ayurvedic Medicines," as they contain active ingredients that are plant based. Examples: Pudin Hara, Itch Guard Cream, Vicks Cough Drops, Iodex Pain Balm, Moov Pain Cream, and Zandu Balm.[2]

Regulatory Authority for OTC Drugs in India

All OTC drugs in India come under the purview of the DCA, 1940 and the DCR, 1945. The other regulations that have a bearing on the OTC drugs in India are the Pharmacy Act, 1948, Drugs Prices Control Order, 2013, and Drugs Magic Remedies Objectionable Advertisement Act, 1964. All the categories of drugs, viz., Allopathic, Ayurvedic, Siddha, Unani, and Homeopathy, either manufactured and/or imported are covered by the above legislation. The Ministry of Health and Family Welfare and the Department of Pharmaceuticals under the Ministry of Chemicals and Fertilizers, Government of India, are responsible for the overall control of the domain. Approval of new drugs, molecules, dosage forms, clinical trials, introduction of new formulations, grant of export and import licenses, manufacturing, and import of medical devices are being controlled by the Drugs Controller General of India. Statutory authority to grant manufacturing and selling licenses of a drug is the responsibility of the state governments through the Food and Drug Administration.

Labeling for OTC Drugs

Rule 96 of DCR stipulates the labeling instructions. There are no specific labeling conditions or requirements for OTC drugs in India, whereas it is mandatory for all medicines except Ayurvedic, Siddha, and Unani medicines to put the following information on their labels:

- Generic name and brand name
- Contents of ingredients and total contents
- Details of the manufacturer including name, address, and manufacturing license number
- The batch details, dates of manufacturing, and expiry dates
- The maximum retail price

Rule 127 of DCR mentions the list of approved colors. Rule 161 states the labeling provisions of all Ayurvedic, Siddha, and Unani drugs while Rule 169 stipulates preservatives and coloring agents.

Distribution and Supply of OTC Drugs Online

For online sale of OTC drugs, there is no specific law till date to regulate online pharmacies in India. But all drug sales are governed indirectly by DCA, 1940 and Food Safety and Standards Act. To regulate online sale of drugs (including OTC drugs), Maharashtra government has directed that all manufacturers, wholesalers, distributors, and retailers who are interested in selling drugs and medicines online will have to register themselves on an e-portal which would be set up soon by the Central government. An e-enabled autonomous body under the supervision of Ministry of Health and Family Welfare will control this portal. Unless registered on the portal, the government would not allow any retailer, chemist, and e-pharmacist outlet to sell any medicine or drug to any consumer. It would be mandatory for all the retail pharmacy outlets also to enter details of all receipts, sales of medicines or drugs, medicines returned to the manufacturer, or disposed of in any other manner.[5] Drugs included in Schedules H, H1, and X of the DCA shall be sold online only on a prescription of a registered medical practitioner.

Advertisements of OTC Drugs

The promotion of all drugs is regulated through the Drug and Magic Remedies (Objectionable Advertisement) Act

and Rules, which mentions a list of ailments for which there is no advertising permissible in India. Recently, the government made an amendment to DCR 1945, vide a G.S.R. number 289 (E) dated April 15, 2015,[6] wherein the advertisements of all drugs in Schedule H, Schedule H1, and Schedule X are prohibited by law. Over-the-counter drugs are allowed to be advertised on various media.

Pricing of OTC Drugs

The Drugs Price Control Order is the one mechanism through which the government exercises control on the pricing of all the allopathic drugs in India. There are around 370 drugs under price control and those that are not under price control are under the nonscheduled category. Over-the-counter drugs do not come under price control except a few OTC actives, viz., acetylsalicylic acid, ephedrine, and its salts, etc., which are under price control.[7] All Ayurvedic drugs fall outside the ambit of price controls.

Indian Pharmaceutical Industry and OTC Drugs

The Indian Pharmaceutical Industry ranks third with respect to volumes and thirteenth with respect to value, on the global level. It contributes around 10% of the global production of pharmaceuticals by volume. It is growing at an annual growth rate of around 5.5%.[8] One of the major components of the Indian Pharmaceutical Industry is the business of OTC products.

Over-the-counter Drugs Market in India

The market for OTC products in India can be categorized which includes: (1) frank OTC products which are advertised on public media and construed as true OTC products, (2) prescription brands that are not advertised, but which are promoted to the physicians and also purchased by consumers without prescription called Otx brands.[9]

The value of the Indian OTC drugs market is estimated to be US$ 2.7 billion (Rs 188.6 billion) at a compounded annual growth rate of 9% to reach around $6.5 billion (Rs 441.1 billion).[10] The major players for OTC products in India are: Cipla, Abbott India Limited, Amrutanjan Health Care Limited, Boehringer Ingelheim Limited, Mankind, Dabur India Limited, Pfizer, Emami, GlaxoSmithKline, Sanofi, Himalaya Herbal Health care, Novartis, Marico, Merck, Piramal Enterprises, Procter & Gamble, and Lupin.[11]

Composition of the Indian OTC Drug Market

The OTC market in India comprises of the main product categories[12] listed in Table 1.

Table 1: Composition of the indian OTC drug market–main drug categories

Drug category	*% contribution*
Vitamins, minerals, and supplements	30
Gastrointestinal products	19
Cough, cold, and allergy products	18
Dermatology products	15
Analgesics products	15
Lifestyle-related products	3

Factors driving the Indian OTC Drug Market

India is the 11th largest market for OTC drugs in the world.[13] The growth in the OTC drugs market is a result of various socioeconomic factors impacting the various stakeholders in the health care industry. The factors driving OTC drug consumption in urban India are changing lifestyles which involve a fast and stress-oriented lifestyle where timely solutions become paramount in health care; changing food habits, increasing literacy rates, increasing awareness of health and illnesses through individual efforts and government promotion, prevalence of untreated common illnesses, high medical costs, proliferation of social media, increased promotion of newly shifted OTC drugs by manufacturers, and changing concept of good health from illness to wellness are some of the driving factors for increasing OTC drug consumption in India. With both the husband and wife employed in urban areas, there is an increase in the disposable incomes in the family which is reflected in the trend of the per capita income in India. The real per capita net national income at constant (2011–2012) prices is an important pointer for the well-being of the people of a nation. As per the Government of India's economic survey report for 2017 to 2018, it is expected to improve from Rs 77,803 in the year 2015 to 2016 to Rs 86,660 in the year 2017 to 2018 with an annual average growth rate of 5.5%. In nominal terms, it demonstrates an average growth rate of 9% per annum from Rs 94,130 in the year 2015 to 2016 to Rs 1,11,782 in the year 2017 to 2018.[14] There is a clear thinking among the consumers toward good health, fitness, and prevention of diseases that are responsible for driving the growth for OTC products in categories, such as nutraceuticals, antacids, vitamins and minerals, health drinks, dietary supplements, and dermatological preparations.

Since the cost of medical treatment is increasing due to increase in the consulting fees of physicians and other factors, more and more people today are driven toward the use of OTC drugs for self-medication. The power of internet can be effectively used by OTC drug manufacturers to promote their drugs. Moreover, decisions of consumers are also influenced by reviews posted by peers about certain OTC drugs on internet blogs. The OTC manufacturers should thus use internet as an effective platform for promotion and brand building of OTC drugs.

CONCLUSION

Unlike a product which is present in the prescription only category, the OTC products are used in health conditions that do not require the direct supervision of a registered medical practitioner. The parameters that are important determinants of a successful OTC treatment are safety of the drug, clarity in the indications and administration of the drug, and easy availability. With changing macroenvironmental factors, further increase in the consumption of OTC drugs can only be expected. The Government of India has taken cognizance of this fact and is working toward giving recognition to OTC drugs. In the future, we would see more and more health care organizations introducing newer OTC products in India and also newer organizations making an entry into the OTC segment in India. With these changes, it becomes imperative for the government to introduce strict regulatory policies that would help the government to meet national health care objectives in a satisfactory manner.

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CASE REPORT

Dermoid Cyst of Pancreas

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ABSTRACT

Pancreatic dermoid cyst is a rare clinical entity. We report the case of a 26-year-old female who presented with epigastric pain and weight loss for 1 month duration. Ultrasonography and computed tomography (CT) showed large solid cystic mass in the tail of pancreas. At surgery, the entire mass was excised. Histopathologic report revealed it to be a dermoid cyst.

Keywords: Computed tomography, Dermoid cyst, Mature cystic teratoma, Pancreas.

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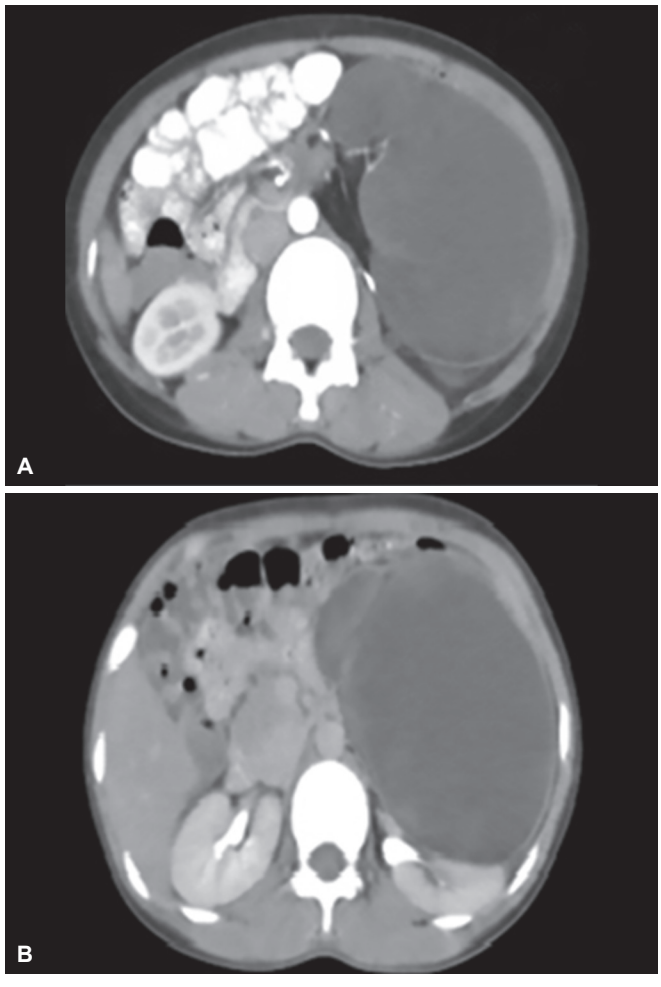
INTRODUCTION

Pancreatic dermoid cyst is a rare germ cell neoplasm with very few published case reports. World literature reports only 35 cases with complete data.[1] Dermoid cyst of the pancreas, also called cystic teratoma, was first described in 1918 by Kerr.[2] In 1922, it was included by Primrose[3] in the classification of cystic pancreatic lesions. Dermoid cysts occur in all ages, have no sex preference, and are commonly found in ovaries,[4] but may occur in any pathway of ectodermal cell migration. The pancreas is an extremely rare primary site of dermoid cyst with some predilection for the head region.[5] Clinical picture is nonspecific,[6] and the preoperative diagnosis is difficult.

CASE REPORT

- A 26-year-old woman was admitted in MGM Hospital, Aurangabad, Maharashtra, India, with epigastric pain, anorexia, weight loss, and backache of 1 month duration. The patient had no significant medical history. On examination, there was mild tenderness in the epigastrium. All laboratory investigations were normal.
- Ultrasonography of abdomen and pelvis showed a large cystic lesion (15 × 11 × 9 cm, approximately 880 cm^3) arising from the tail of pancreas and displacing left kidney posterolaterally.
- Computed tomography scan revealed lobulated cystic lesion of 12 × 9 × 14 cm in size, with dense foci of calcification and fat in left lumbar region along tail of pancreas, displacing left kidney posterolaterally and abutting spleen (Fig. 1). No definite lymphadenopathy was seen at the celiac axis origin or in peripancreatic area. The mass appeared to be a peritoneal dermoid cyst.

After preoperative workup, the patient underwent surgery. A large cystic mass of 25 × 10 × 17 cm was seen arising from the tail of pancreas (Fig. 2). It was adherent to transverse colon, omentum, left kidney, left renal vein, spleen, splenic vein, and inferior mesenteric vein (Fig. 3).



Figs 1A and B: Dermoid cyst along pancreatic tail region displacing left kidney posteriorly (A) and abutting spleen laterally (B)

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Fig. 2: Dermoid cyst arising from pancreatic tail region

Fig. 3: Dermoid cyst adhered to transverse colon

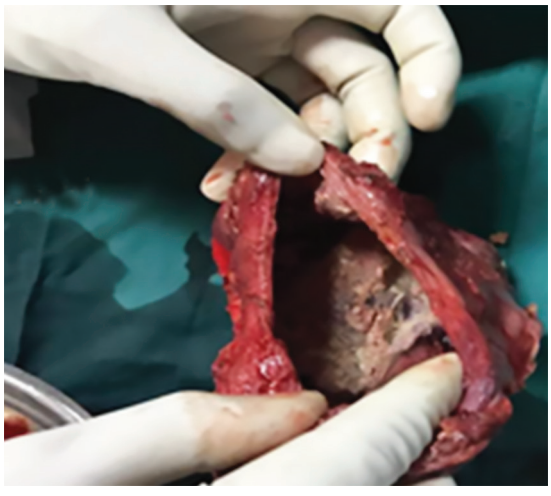

Fig. 4: Surgical specimen shows that the cyst is filled with finely granular, grayish white, keratinaceous, and sebaceous material

Fig. 5: Macroscopic view of the dermoid cyst

The mass was excised *in toto*. Its cut surface showed pultaceous material, hair, bone, and areas of hemorrhage (Figs 4 and 5). On microscopic examination, cyst wall was lined with stratified squamous epithelium with keratin flakes. Adipose tissue, cartilage, and bony trabuculae were also seen.

DISCUSSION

Teratomas are widely believed to arise from embryonic inclusions of skin at the time of neural groove closure, hence, their characteristic midline localization. Two subtypes of teratomas have been described: Mature and immature. Mature teratomas are further classified as either solid or cystic. Cystic teratomas are also known as "dermoid cysts." Although dermoid cysts most commonly develop within the ovaries, they have been shown to occur anywhere along the route of ectodermal cell migration, usually in the midline. Other reported sites are testis, cranium, brain, mediastinum, omentum, retroperitoneum, and sacrococcygeal region. Pancreatic dermoid cysts are extremely rare.[7] They may appear in any site in the pancreas, being more common in the head region. In this case, tumor was found in the pancreatic tail.

Dermoid cysts of the pancreas are true cysts. The cyst wall, which surrounds the lesion, is lined by a single layer of keratinizing stratified squamous epithelium, and the underlying connective tissue may contain adnexal tissue, sebaceous glands, lymphoid tissue, and even inflammatory cells. Dermoid cysts often contain thick, pasty, doughy sebaceous secretions. Fully differentiated tissues from one or more germ cell layers, most commonly the ectoderm, including hair, teeth, bone, cartilage, and dermal appendages, such as hair follicles, sweat glands, and sebaceous material, are also usually encountered.[8] The difficulty in preoperative diagnosis of pancreatic dermoid cysts is well emphasized in the literature. The presence of fat/fluid or hair/fluid levels is considered pathognomonic of dermoids in other locations, but they are found in only a minority of cases.[9]

In our case, the cyst showed pultaceous material, hair, and bone with areas of hemorrhage. Yu et al[10] reported a dermoid cyst of the pancreas in a 2-year-old child. The cystic wall contained smooth muscle, pancreatic tissue, lymphoid tissue, intestinal tissue, and glial tissue. The case report by Markovskyt and Russin[11] was diagnosed preoperatively as dermoid cyst with the use of fine-needle aspiration.

Computed tomography scan imaging is considered to be highly specific and virtually pathognomonic for diagnosis of dermoid cyst of pancreas. Computed tomography accurately estimates the density of all the included tissues, such as soft tissue, fluid, fat, calcification, and teeth.

Treatment of dermoid cysts is through surgical removal, as done in the present case. Being located in the tail region of the pancreas, technically surgery was easier than if it was located in head or body, which have a mortality rate of up to 2%.[12]

CONCLUSION

Pancreatic dermoid cysts are very rare benign neoplasms. To our knowledge, only 35 cases have been reported so far in world literature. Surgical resection remains the gold standard of treatment. It is recommended that surgical excision be undertaken for any symptomatic lesion as well as for any lesion larger than 2 to 3 cm in size. Excision of the lesion provides definitive diagnosis and is curative. Prognosis is excellent.

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10.5005/jp-journals-10036-1181

CASE REPORT

Wilson's Disease presenting as Resistant Depression

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ABSTRACT

Introduction: Wilson's disease (WD) is rare, but it commonly presents with a variety of psychiatric symptoms.

Case report: A 31-year-old male presented with depression as the earliest manifestation. The depressive symptoms showed limited response to conventional antidepressants and electroconvulsive therapy in spite of compliance. Gradually, the patient showed neurological symptoms like motor slowing, speech disturbances, and abnormal movements which gave a clue toward organic etiology. Laboratory and neuroimaging findings along with ophthalmological examination helped in confirmation of diagnosis of WD. Introduction of the chelating agent penicillamine led to improvement in nonpsychiatric as well as psychiatric symptoms.

Conclusion: Psychiatric manifestations are common in WD. Depression was the earliest manifestation in our patient, which was not responding to usual treatment. Workup for organicity helped to diagnose WD and patient's depressive symptoms responded to chelating therapy.

Keywords: Depression, Neuropsychiatric interface, Wilson's disease.

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INTRODUCTION

Wilson's disease, which is also known as hepatolenticular degeneration, is an autosomal recessive disorder characterized by multiple mutation of gene ATP7B on chromosome 13q14.3 which is critical for hepatic copper excretion. Disturbances in copper metabolism result in copper accumulation in many tissues (brain, liver, and cornea), affecting the function of these organs. Though copper accumulates in all brain regions, pathological changes are mainly localized in the basal ganglia in the brain. As a result of this, psychiatric and behavioral abnormalities are frequently seen in WD, and are often the initial manifestations of this disease. The estimates of psychiatric manifestation range from 30 to 100% of symptomatic patients. Various types of psychiatric morbidity are seen in patients with WD, of which depression is the commonest, affecting 30 to 60% of patients.[1]

One-third of patients with WD initially present with behavioral abnormalities, and failure to recognize these may lead to misdiagnosis and delay in starting specific treatment.[2] Nearly 20% of patients undergo psychiatric treatment before specific chelation therapy begins.[3]

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CASE REPORT

A 31-year-old male patient came with complaints of gradual onset of withdrawn behavior, irritability, sadness of mood, and fatigue since 1 year. Patient stopped going to work due to decreased interest and concentration in work. Also, there was a history of marital disharmony followed by separation due to his irritability and change in behavior. Patient was taken to a private psychiatrist where a diagnosis of major depressive disorder was made and the patient was started on antidepressants (combination of different classes of antidepressants in optimum doses). In view of nonimprovement of depressive symptoms, patient was administered 10 electro convulsive therapy. Still there was no improvement. So the patient discontinued medications due to side effects, such as excessive sedation. He was without medication for about 6 months when the symptoms gradually worsened and he presented to our institute for further management.

On detailed history taking, patient's mother said that she has observed tremulousness and leaning of body backward while sitting by her son for last few months. She also reported that he had started speaking slowly and his speech had become slurred.

On neurological examination, the patient was conscious with dystonic posturing of back and grimacing facial movements. His cranial nerves and fundoscopy were normal. There was hypertonia involving all four limbs, slurred speech, and bilateral brisk deep tendon reflexes.

On mental status examination, patient had psychomotor retardation, with grimacing and mannerisms. His mood was sad with restricted affect. Ideas of helplessness, hopelessness, and death wishes were expressed.

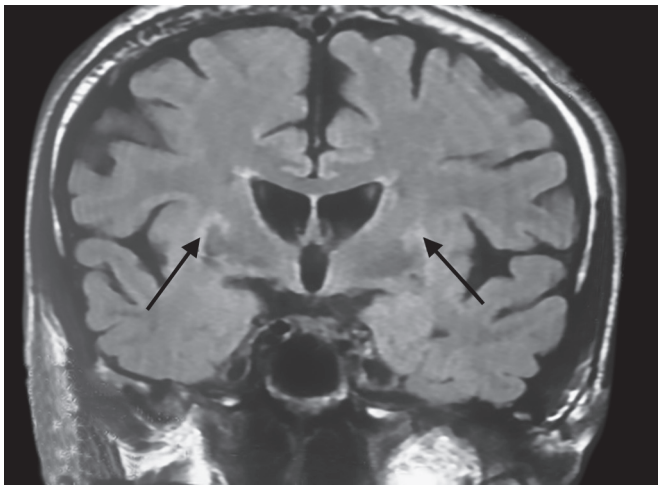


Fig. 1: Magnetic resonance imaging brain (plain) showing gliosis with calcification in bilateral basal ganglia

In view of his recently developed neurological symptoms, a neurological opinion was sought. Neurologist referred patient for laboratory and neuroimaging evaluation. Investigations revealed raised liver enzymes and high urine copper levels (48.30 µg/dL normal up to 40 µg/dL). Hemogram, thyroid function tests, renal function test, and serum B12 levels were normal. Magnetic resonance imaging (MRI) brain showed gliosis with calcification in bilateral basal ganglia (Fig. 1). Suspicion grew toward possibility of an organic movement disorder like WD. For confirmation of diagnosis, patient underwent ophthalmological examination which showed Kayser Fleischer ring (KF ring) in both eyes (Fig. 2).

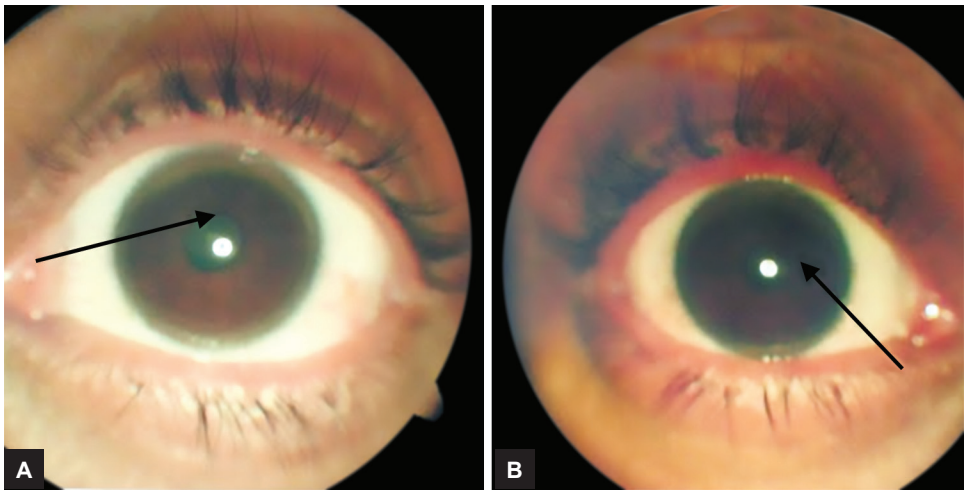
In view of depressive features not responding to the conventional antidepressants, gradual onset of neurological signs and symptoms and supportive laboratory, neuroimaging, and ophthalmological findings, patient was diagnosed as WD and started on penicillamine in a neurology inpatient setting. Patient's depressive symptoms responded to the chelation therapy gradually.

DISCUSSION

Neurology and psychiatry have evolved as two different specialties over a period of time, with neurology dealing with the structural aspect and psychiatry dealing with functions of the mind. However, in clinical practice, a significant overlap of symptoms in various neurodevelopmental and neurodegenerative conditions like multiple sclerosis, dementia, schizophrenia, and WD is seen. Clinical manifestations of WD are the result of gradual accumulation of free copper in the tissues, which may cause damage in many organs. Early manifestations are hepatic (40% of cases), neurological (35%), psychiatric (10%), and others (15%) like hematologic, renal, ocular.[4] Neuropsychiatric symptoms in WD occur due to copper accumulation in basal ganglia and prefrontal cortex. Proposed biological mechanisms are reduced striatal dopamine and tyrosine hydroxylase levels and reduced dopamine D2 receptor density.[5]

Epidemiologically, WD is a disease of young age with slightly high prevalence in males who are also more likely than females to have neuropsychiatric symptoms.[6] This can be attributed to difference in gender-related pathology in brain and may be explained by both estrogen neuroprotective effects and differences in brain iron metabolism. In the brain, estrogens act (1) as neurotrophins for dopaminergic neurons; (2) as antioxidants to protect cells against toxic metabolites; and (3) in dopamine synthesis, affecting uptake and dopamine receptor expression (decrease of D2 receptors and increase of the dopamine transporter density).[7] This "estrogen protective hypothesis" can explain low prevalence of neuropsychiatric symptoms in females as compared with males in various neurodegenerative disorders including WD.

Psychiatric and behavioral abnormalities are common in the 5 years prior to diagnosis. Clinical features include loss of emotional control (angry outbursts and bouts of



Figs 2A and B: Ophthalmological examination showing bilateral KF ring

crying), depression, hyperactivity, loss of sexual inhibitions, anxiety disorders, cognitive impairment, mental retardation, mania, behavioral abnormalities, personality changes, and alcohol abuse.[8] Most studies have shown that depression is predominant at the time of onset of the disease.[1,8]

Accompanying neurologic symptoms are usually subtle and include tremors, speech difficulties, and micrographia. Most common neurological manifestations include postural and intentional tremors, dysphagia and contractions of facial muscles, dysarthria, bradykinesia, muscle hypertonia and choreathetoid movement of limb.[9] Our patient presented with predominant mood and personality change and only on enquiry, his mother reported neurological symptoms—tremors, speech difficulty, and dystonic posturing of his back while sitting.

Diagnosis of WD is based on detailed evaluation and investigations. The laboratory findings show abnormal liver function tests (like raised liver enzymes), elevated urine copper (more than 40 µg/dL), high 24 hour urine copper (normal: 15–60 µg/24 hours), decreased blood ceruloplasmin levels, and increased copper levels on liver biopsy (>150 µg/gm). Similar findings were seen in our patient. In these patients, MRI of the brain shows hyperintensities in basal ganglia in the T2 setting. The KF ring is the single most important diagnostic sign in WD.[10]

In management, the mood disturbances show limited response to antidepressants in an optimum dosage and duration. Depressive symptoms in WD are probably due to the presence of both pre- and postsynaptic dopaminergic damage.[5] Introduction of the chelating agent has been observed to be useful in normalization of mood and improvement in nonpsychiatric symptoms.[11]

CONCLUSION

Wilson's disease commonly presents with psychiatric symptoms. Our case describes a patient presenting primarily with depressive features. Poor response to antidepressants, excessive sensitivity toward psychotropic medications with gradually evolving neurological symptoms, and signs supporting investigations pointed toward WD. This case is presented to highlight the fact that a psychiatrist needs to be vigilant about psychiatric illnesses caused by underlying neurological diseases.

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CASE REPORT

Cornual Placenta Percreta with Uterine Rupture

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ABSTRACT

A 25-year-old woman, gravida 2, para 1 reported with history of 27 weeks pregnancy with pain abdomen and bleeding per vaginum (PV) of 2 days duration. She had undergone lower segment cesarean section (LSCS), done 3 years back during previous pregnancy. On examination, patient had pallor, tachycardia, and hypotension. The uterus was corresponding to the period of gestation. There was tenderness over left side of uterus and fetal heart sounds were absent. Per speculum examination revealed amniotic fluid leak mixed with blood. Ultrasonography (USG) findings were suggestive of moderate hemoperitoneum. Uterine rupture at the site of the previous LSCS scar was suspected. Patient was taken for emergency laparotomy. Intraoperative, previous cesarean scar was intact with the fetus inside the uterine cavity. There was left cornual implantation of placenta with a rent of about 4 cm. The placenta was protruding outside the uterus at left cornual end. Per-operative diagnosis of placenta percreta leading to uterine rupture was made. Obstetric hysterectomy was performed. The diagnosis of placenta percreta was confirmed later by histopathological examination.

Keywords: Obstetric hysterectomy, Placenta percreta, Uterine rupture.

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INTRODUCTION

Placenta percreta comes under the classification of placenta accreta syndrome. Derivation of *accreta* comes from the Latin *ac-crescere*—to grow from adhesion or coalescence, to adhere, or to become attached to.[1] Placenta accreta syndrome is a general term used to describe the clinical condition when part of the placenta, or the entire placenta, invades and is inseparable from the uterine wall.[2]

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Three grades of abnormal placental attachment are defined according to the depth of invasion:

1. Accreta: Chorionic villi attach to the myometrium, rather than being restricted within the decidua basalis
2. Increta: Chorionic villi invade into the myometrium
3. Percreta: Chorionic villi invade through the uterine serosa

The incidence of placenta accreta syndrome is 1 in 533 deliveries for the period 1982 to 2002,[3] which has increased from the previous reports of 1 in 4,027 deliveries in 1970s and 1 in 2,500 deliveries in 1980s.[4,5] The highest risk of placenta accreta is in cases with myometrial damage caused by a previous cesarean delivery with either an anterior or posterior placenta previa overlying the uterine scar.[4] Other risk factors include advancing age, multiparity, advanced maternal age, myomectomy, severe endometrial damage seen in Asherman's syndrome, submucosal fibroid, and endometrial ablation. In addition to their significant contribution to maternal morbidity and mortality, accreta syndromes are one of the leading causes of intractable postpartum hemorrhage and emergency peripartum hysterectomy.[6-8] Maternal mortality with placenta accreta has been reported to be as high as 7%.[9]

CASE REPORT

A 25-year-old patient, gravida 2, para 1 reported with 27 weeks pregnancy, pain abdomen, and bleeding PV. She had undergone LSCS, done 3 years back during her previous pregnancy. On examination, her pulse was 140/min and blood pressure was 90/60 mm Hg, and she had marked pallor. On per abdominal examination, uterus was corresponding to the period of gestation, fetal presentation was beech, and fetal parts were felt. There was tenderness over the left side of uterus and the fetal heart sounds were absent. Per speculum examination revealed amniotic fluid leak mixed with blood. Investigations on admission were: hemoglobin: 6.6 gm%, total leukocyte cells: 36,000/mm^3, and blood group: O positive. An USG was done, which revealed moderate hemoperitoneum. A provisional diagnosis of uterine rupture at the site of previous LSCS was made.

The patient was taken up for an emergency laparotomy. A midline incision was taken and abdomen was opened in layers. Hemoperitoneum of approximately 1.5 to 2 L was noted. After clearing the blood and blood

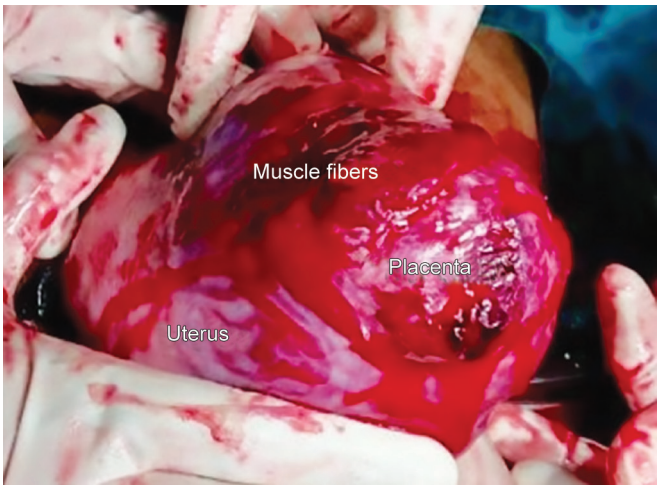

Fig. 1: Cornual implantation of the placenta invading the myometrium

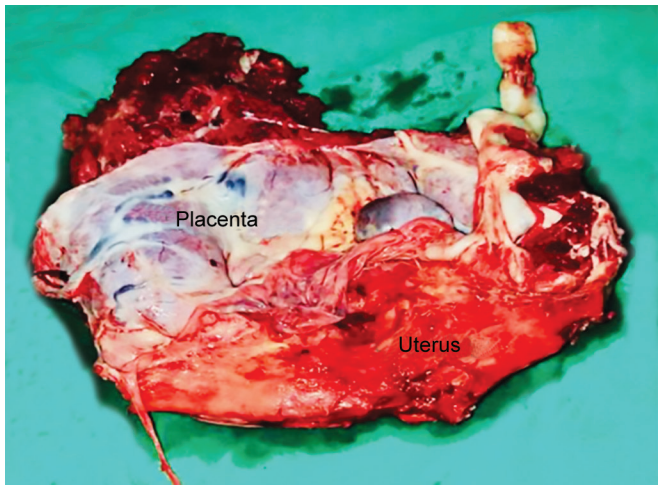

Fig. 2: Specimen of subtotal hysterectomy showing the placental invasion on cut section

clots, the uterus was examined for rupture. The previous LSCS scar was intact with fetus inside the uterine cavity. A transverse incision was made in lower segment and a stillborn baby was delivered. The uterus exteriorized, which revealed a cornual implantation of the placenta that had invaded through the myometrium and had led to a rent in the uterus of about 4 cm. The site had blood oozing from it. This was probably the cause of the hemoperitoneum (Fig. 1). The diagnosis of placenta percreta with uterine rupture was made. Obstetric hysterectomy was performed. After achieving complete hemostasis, abdomen was closed. The patient made an uneventful recovery. Since the patient had lost significant amounts of blood, four units of packed cells and four units of fresh frozen plasma were transfused. The hysterectomy specimen was sent for histopathological examination (Fig. 2), which confirmed the diagnosis of placenta percreta.

DISCUSSION

Placenta accreta syndromes are on a rising trend and this rise is associated with the increase in the rate of cesarean sections. Placenta previa with history of previous LSCS is at high risk of developing placenta accreta syndrome. On the contrary, rupture uterus is a rare entity and is generally seen with previous LSCS scar giving away.

In our case, although patient had history of previous LSCS the implantation of the placenta was at the left cornual end. Uterine rupture had occurred secondary to the placenta percreta and not the previous LSCS scar giving away.

The antenatal diagnosis of placenta accrete syndrome is extremely difficult but not impossible with the development in the field of radiology. Mainstay of prenatal diagnosis for abnormal placentation remains USG with magnetic resonance imaging (MRI) being used only as an adjunct in indeterminate cases. Although the predictive values for both MRI and Doppler are low, Doppler helps in visualization of numerous vessels, which show turbulent flow in the lacunae.[10]

In cases of placenta accreta-induced uterine rupture, conservative approach in its management can be applied. These include uterine curettage along with packing, adjuvant chemotherapy with selective arterial embolization, prophylactic uterine, or hypogastric artery ligation with wedge resection of the ruptured uterine wall.[11] These treatment modalities have higher rates of mortality compared with hysterectomy and hence, hysterectomy is preferred in cases of emergency where the patient presents with acute abdomen, like in our case.[12]

CONCLUSION

Uterine rupture with placenta percreta is an obstetrical catastrophe and every obstetrician's nightmare. The antenatal diagnosis by USG and MRI has low sensitivity and specificity. Yet, if diagnosed early and managed promptly it can be life saving for the mother and the fetus. However, in most cases diagnosis is made on operation table leading to severe maternal morbidity and mortality. As a general rule placenta accreta should be suspected in all the cases of previous LSCS and in cases of placenta previa.

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CASE REPORT

Subarachnoid Hemorrhage as a Complication of Cerebral Venous Thrombosis

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ABSTRACT

Cerebral venous sinus thrombosis (CVST) is an uncommon but important cause of stroke in young women. Subarachnoid hemorrhage (SAH) secondary to CVST is a rare presentation. We present a case of 40-year-old female who presented with hemicranial headache. Magnetic resonant imaging (MRI) showed CVST along with SAH and venous infarcts. The patient improved on anticoagulant therapy. This report highlights the value of early diagnosis of CVST through neuroimaging and the importance of immediate anticoagulation as a part of patient management.

Keywords: Anticoagulant therapy, Cerebral venous thrombosis, Neuroimaging, Subarachnoid hemorrhage.

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INTRODUCTION

Cerebral venous sinus thrombosis is a disease seen with increasing frequency in daily practice with a variety of nonspecific clinical symptoms. It most frequently presents as an acute onset throbbing type of headache which may or may not be associated with neurological deficit or seizures.[1] The acute stage of CVST may be associated with complications like venous infarction, SAH, and pulmonary embolism. The SAH is becoming more frequently recognized as a potential complication of CVST. The presentation of CVST sometimes greatly mimics SAH presenting as thunderclap headache in more than 10% of cases. Seizures and hemiparesis, possible manifestations of SAH, occur in about one-third of patients. However, CVST presenting with an associated SAH on computed tomography and MRI is infrequent.[2,3] Thus, it is important to establish whether SAH is due to CVST, as this requires a completely different treatment from SAH due to a leaking aneurysm.

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CASE REPORT

A 40-year-old female was admitted to our ward with complaints of sudden-onset severe right hemicranial throbbing type of headache and six to seven episodes of vomiting since 5 days. Patient also complained of heaviness on the right side of the body. She had no other complaints. She had no significant past medical history. On admission, she was afebrile with a pulse of 58 bpm and blood pressure of 140/80 mm Hg. Rest of physical and neurological examination was normal with no evidence of any focal neurological deficit or signs of meningism. Magnetic resonance imaging was done which showed venous infarcts in both parietal lobes, SAH over right parietal lobe, and thrombosis of posterior aspect of superior sagittal sinus, right transverse sinus, right sigmoid sinus, and proximal aspect of right internal jugular vein (Figs 1 and 2). The magnetic resonance angiography was normal with no evidence of any aneurysm (Fig. 3).

She had no history of irregular periods and no history of taking oral contraceptive pills. Routine lab investigations were normal. The patient underwent a complete coagulation profile testing including prothrombin time, activated prothrombin time, antiphospholipid, and anticardiolipin antibody titer, protein C, protein S, antithrombin III, and homocysteine levels. All the results were in the normal range except for high homocysteine level, which was 35 µmol/L (normal value <15 µmol/L). Treatment was started with analgesics, mannitol, and anticonvulsants. In addition, subcutaneous low-molecular-weight heparin 60 mg/day was started and later raised to 120 mg/day on 3rd day which was continued for 1 week. Patient was closely monitored. She was subsequently started on oral anticoagulation with warfarin, maintaining international normalized ratio between 2.0 and 3.0, after it was confirmed that there was no further SAH. Patient showed marked clinical improvement in 6 weeks. Repeat MRI done after 6 weeks also showed regression of SAH and resolving venous sinus thrombosis (Fig. 4). Subsequently, she was followed up in the outpatient department every 2 weeks for 12 months.

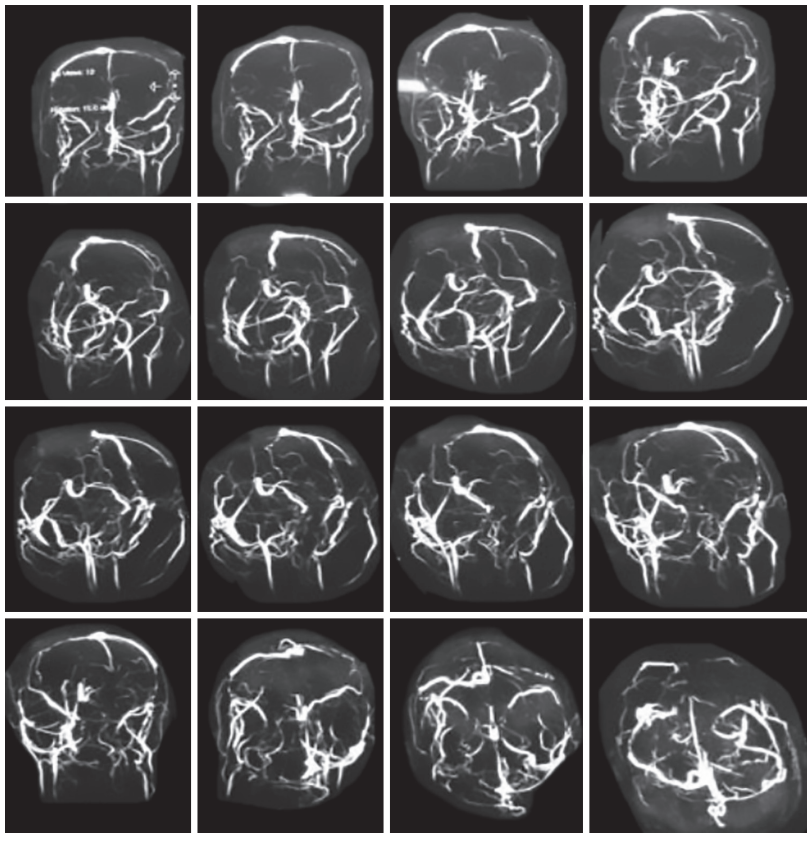


Fig. 1: MRI showing venous thrombosis involving posterior aspect of superior saggital sinus, right transverse sinus, right sigmoid sinus, and proximal aspect of right jugular vein

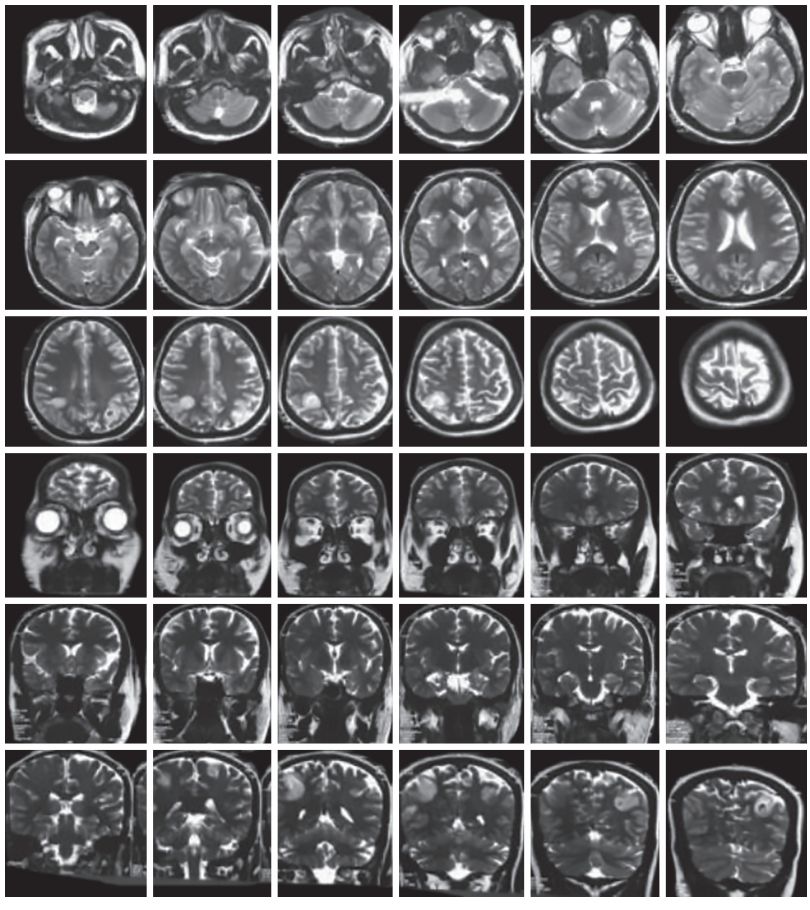


Fig. 2: MRI showing venous infarcts and SAH over right parietal lobe

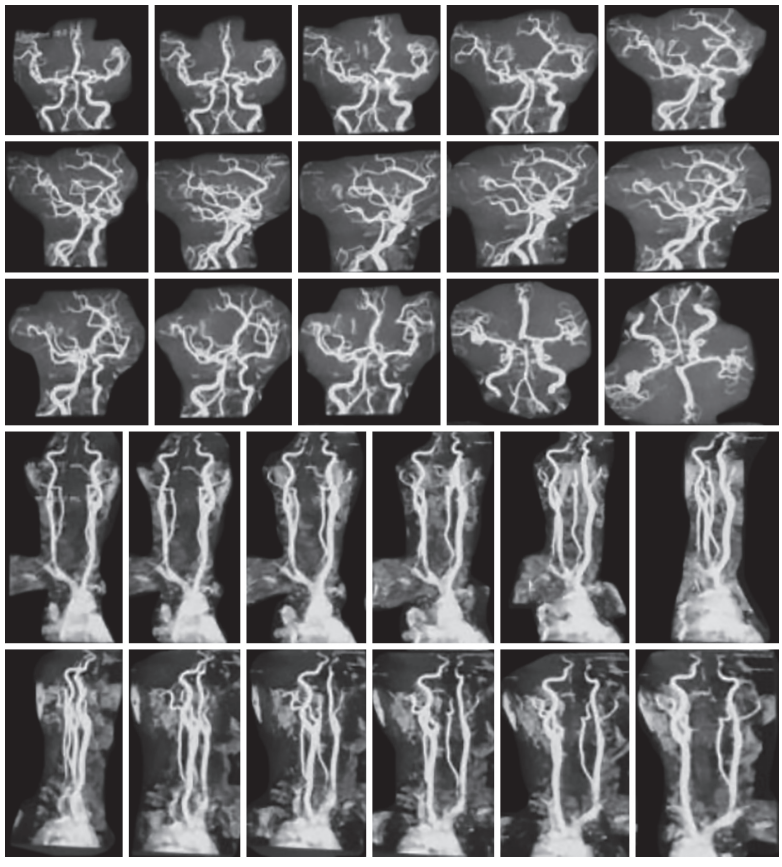


Fig. 3: MR angiogram shows no evidence of any aneurysm

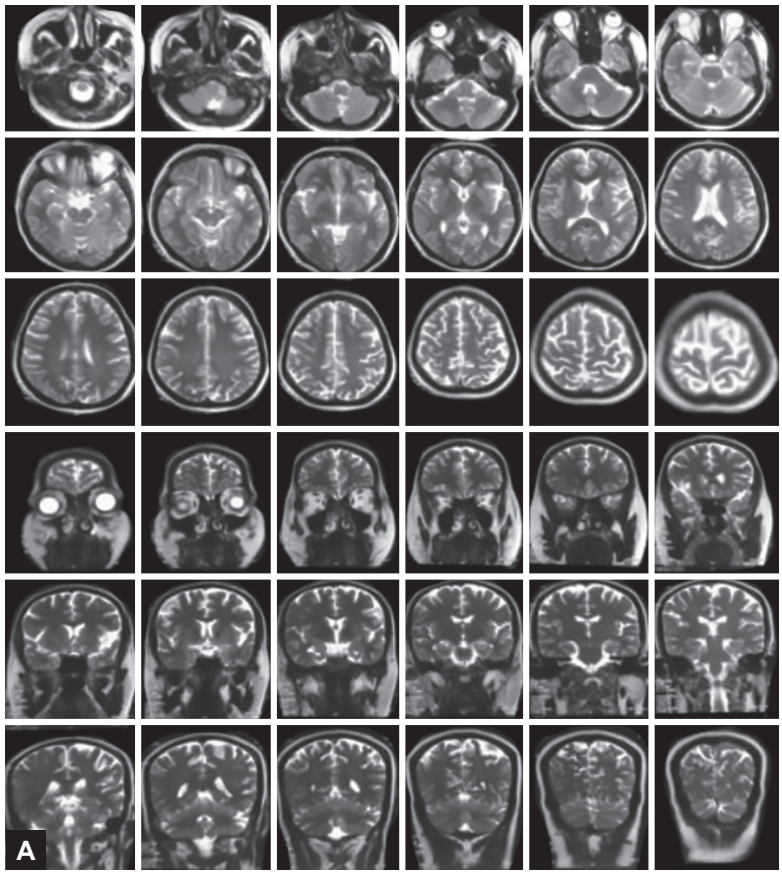
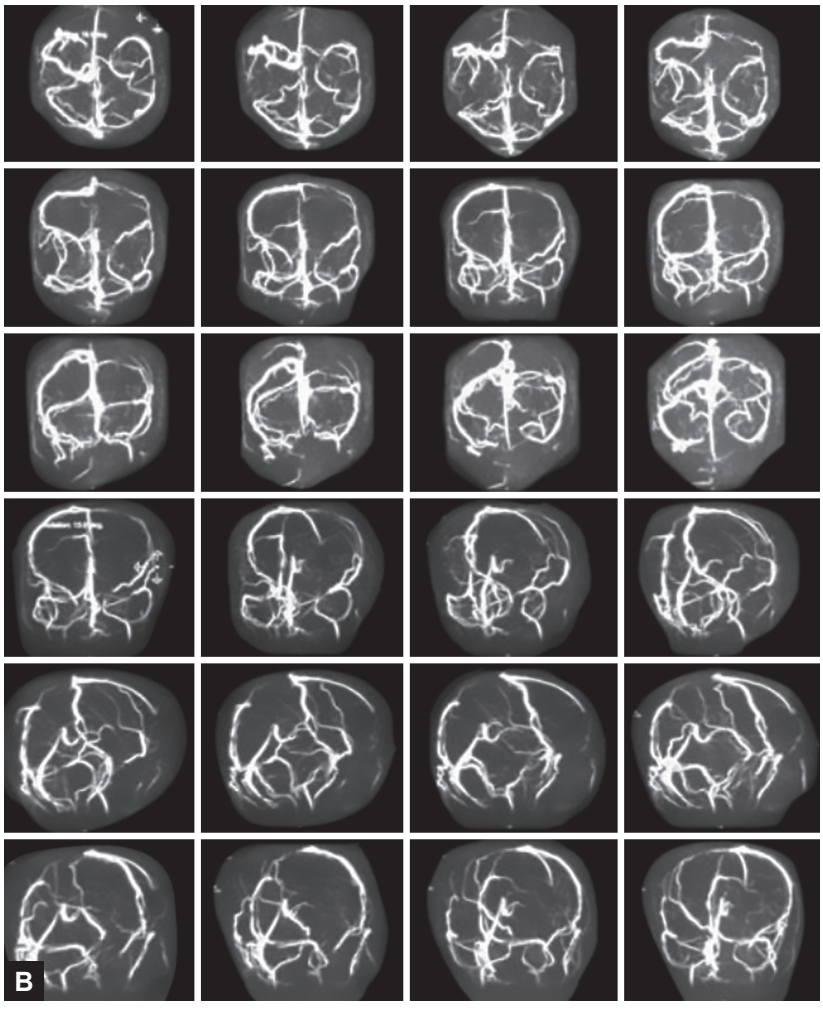


Fig. 4A:



Figs 4A and B: (A and B) Repeat MRI after 6 weeks of starting oral anticoagulants showing regression of SAH and resolving venous sinus thrombosis

DISCUSSION

Cerebral venous sinus thrombosis is a well-known cause of cortical SAH. The CVST is seen in 3 to 4% of all stokes in adults. Cortical SAH without the involvement of the basal cisterns may suggest underlying CVST. The distribution of SAH due to CVST is usually localized to the cerebral convexity and spares the skull base and basal cisterns.[4] The exact cause of mechanism of SAH secondary to CVST remains unknown. One possibility is rupture of venous parenchyma hemorrhagic infarcts into the subarachnoid space.[5,6] Our patient showed no signs of hemorrhagic venous infarction. Another possible mechanism is venous hypertension and subsequent rupture of dilated, valveless, thin-walled, bridging subarachnoid cortical veins which lack smooth muscle.[5] The third mechanism of SAH could be local inflammatory response caused by CVST, which would increase the vascular permeability, allowing for extravasation of blood into the subarachnoid space. This is the most likely cause in our patient, who, because of her altered metabolism of homocysteine, had a proinflammatory status.

Management of SAH secondary to CVST is quite different from that of arterial SAH. The usual treatment of sinus thrombosis is anticoagulation or local thrombolysis. Systemic anticoagulation is the first line of treatment for CVST, as it is safe, effective, and not too costly.[7] In our case, we preferred to initiate treatment with low doses of fractioned heparin, 60 mg once a day, which was increased to 120 mg/day on the 3rd day for 1 week and later followed by oral anticoagulants with effect from the 2nd week. During this period, we observed the patient carefully for any deterioration due to increase in SAH. We did not use intravenous heparinization, as we thought that it may cause more SAH. Review of literature shows that very early anticoagulation in SAH due to CVST is avoided due to fear of bleeding.[8] More studies like ours are required to find out the appropriate timing of starting anticoagulation safely in a case of SAH secondary to CVST.

CONCLUSION

Subarachnoid hemorrhage is a rarely seen complication of CVST. All patients with neurological symptoms, even a simple headache, should be carefully evaluated using neuroimaging to analyze the underlying cause and initiate treatment accordingly as early as possible. Furthermore,

in cases of CVST, a complete study of thrombophilia and procoagulative profile work-up should be done to identify the possible cause and appropriate treatment should be given. Though initiation of early anticoagulation with low-molecular-weight heparin has given good results in our case, more studies are required before we can say the final word.

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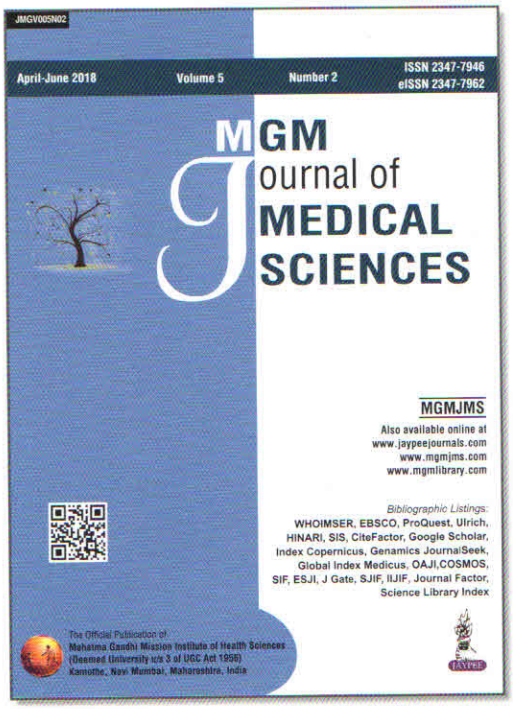

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