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Editor-in-Chief
Shibban K Kaul

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From the Editor's Desk

An important component of Community Health Services is taking care of Occupational Health issues and hazards in a comprehensive way. Whereas most governments have robust policies and programs for Occupational Health Services in the organized sector, lot remains to be done in the unorganized sector. One article in this issue describes health status of Auto Rickshaw drivers in a part of Navi Mumbai, Maharashtra, India. Auto Rickshaws are motorized 3-wheeler vehicles, which play very important role as a means of transport in urban, semi-urban and even rural areas. Their drivers are daily wage earners. They spend long hours every day, sitting in uncomfortable postures in their seats. They get exposed to pollution and noise on all their working days. Their food habits are irregular and erratic. Many of them start indulging in tobacco products and liquor. Long working hours and shift duties interfere with their healthy contact with family members and friends. Their earnings may not be adequate on all days, leading to stress. All these factors make their life-styles unhealthy. So they are prone to musculoskeletal disorders, hypertension, headache, digestive ailments, stress disorders and respiratory diseases, all of which have been brought out in the study published in this issue. So we need to look at what all can be done for preventing or at least reducing the incidence of their health issues. Just for an example, the driver's seat of the Auto Rickshaw may need to be re-designed to make it ergonomic and more comfortable for the driver's spine and lower limbs. Regular preventive health checkups could be introduced by the transport authorities of the state governments and necessary health education about substance-abuse and food habits given to them. Similar measures can be taken in respect of all other occupational health problems in the unorganized and semi-organized workforce of our country, which constitute over 90 percent of total workers.

We are pleased to bring the current issue (volume 4, issue no. 4) of MGM Journal of Medical Sciences (MGMJMS) to our esteemed readers with a variety of original and review articles and case reports, covering many disciplines of medical sciences. We are grateful to our readers who contribute articles for publishing in MGMJMS and also hope that we keep getting more and more papers regularly. Because of our stringent quality benchmarks, please bear with us if you are requested to give clarifications or to re-write an article which you have sent to us for publishing.

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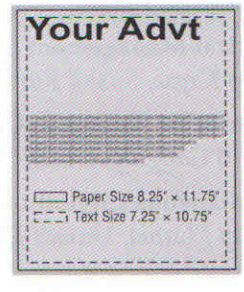

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ORIGINAL ARTICLE

Prevalence of Disability and Family Burden in Patients with Obsessive Compulsive Disorder: An Observational Study

[1]Arun V Marwale, [2]Sana A Quadri, [3]Aziz A Quadri

ABSTRACT

Introduction: Obsessive compulsive disorder (OCD) is a common psychiatric disorder with significant disability.

Aim: To study the prevalence and extent of family burden and disability in patients with OCD and its correlates.

Materials and methods: A cross-sectional study involving 75 consecutive patients with OCD was done. Family burden was assessed using the family burden schedule (FBS). Disability was calculated using the World Health Organization's (WHOs) disability assessment schedule (DAS). Various variables were analyzed and significance of correlation was assessed using chi-squared test of significance.

Results: Prevalence of family burden was 13.33% and that of disability was 42.67%. These were significantly associated with low socioeconomic status, single marital status, early age of onset, and severity of disease. There was significant association between severity of disability and family burden.

Conclusion: Patients with OCD have significant disability and burden on family.

Keywords: Disability, Family burden, Obsessive compulsive disorder.

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INTRODUCTION

Obsessive compulsive disorder is a chronic psychiatric disorder that often tends to run a chronic course. It is also one of the ten most disabling medical conditions worldwide.[1] The lifetime prevalence of OCD is estimated to be around 2.5 to 3.29%.[2-5] Diagnostic criteria for defining OCD according to both the Diagnostic and Statistical Manual of Mental Disorders 4th edition (text revision) (DSM-IV-TR) and the International Classification of Diseases, 10th edition (ICD-10) are: (a) Presence of marked distress from symptoms, (b) spending more than 1 hour per day on obsession or compulsive behaviors, and (c) significant interference with normal routine, occupational or academic functioning, and social relationships or activities.[6] World Health Organization ranked OCD as one of the most disabling disorders and estimated that in 2000, OCD was among the top 20 causes of illness-related disability in patients aged 15 to 44 years.[7]

The OCD has substantial effect on sufferer's quality-of-life (QoL). While severity of compulsions was associated with decreased ability to work, the strongest correlation was found between severity of obsessions and overall impaired QoL.[8] They suffer from disability in several areas particularly in marital, occupational, emotional, and social functioning. There is evidence that even the treatment responders continue to experience poor QoL.[9]

The families of OCD patients report considerable burden due to illness and reduce their social activities, leading to an increase in their feeling of isolation and distress.[10-14] They also report poor QoL in the domains of physical wellbeing, psychological wellbeing, and social relationships.[15] A study done in India comparing the family burden across various anxiety disorders reported that the degree of burden was essentially comparable across all the groups.[16]

Keeping in view all the above facts, the present study was conducted to measure the prevalence of family burden and disability in OCD patients.

MATERIALS AND METHODS

This is an observational cross-sectional study in a clinical setting without the use of any normal control group. The study was carried out in the outpatient department of the mental health center. Totally, 75 consecutive patients suffering from OCD, after fulfilling the inclusion criteria, were taken for the study.

Inclusion Criteria

Patients having primary axis I diagnosis of OCD as per DSM-IV-TR in the absence of other comorbid axis I and III

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disorders, of ages 18 through 60 years were included in the study. Patients having no reliable relative were excluded. Ethical and scientific approval was obtained from the Ethics and Scientific Committees of the parent institute.

A pilot study was undertaken to establish a semistructured pro forma, which was used for the final study. All 75 patients with their caregivers were approached and included in the study after their informed consent. All were evaluated by psychiatric history and mental status examination, and the final diagnosis of OCD was established by applying DSM-IV-TR diagnostic criteria for OCD.[17] Yale–Brown obsessive compulsive scale (Y-BOCS) was applied for assessment of severity of OCD.[18] The Y-BOCS is a 10-item clinician-administered scale designed to rate the symptom severity and not to establish the diagnosis of OCD. Each item is scored on a 4-point scale from 0 = no symptoms to 4 = extreme symptoms. Total score is translated into overall severity as: 0 to 7 = subclinical, 8 to 15 = mild, 16 to 23 = moderate, 24 to 31 = severe, and 32 to 40 = extreme.

The FBS was applied to assess burden perceived by family members of patients suffering from OCD.[19] It assesses burden in following areas: financial burden, disruption of routine in family activities, disruption of family leisure, disruption of family interactions, effect of physical health on others, effect of mental health on others, and other areas. Each item is scored on "no burden = 0, moderate burden = 1, and severe burden = 2." Total score is calculated, and a score of 0 to 25 is taken as mild burden and score of 26 and above is taken as high burden.

The WHO-DAS-2 was applied to assess the disability that the patient has due to OCD.[20] This scale was devised by the WHO in 1988 to assess the disability in patients with mental disorders. This instrument has been extensively studied across the world and found to be suitable for use across different cultures and social classes, irrespective of literacy. We used the 12-item version, which was interviewer-administered. In "simple scoring," the scores assigned to each of the items—"none" (1), "mild" (2), "moderate" (3), "severe" (4), and "extreme" (5)—are summed. Total score of 23 or less is considered as mild disability, while the score 24 and above is considered as moderate-to-severe disability. All the collected data were appropriately tabulated and analyzed to find out the statistical significance with the help of chi-squared test. Probability value less than 0.05 was taken as statistically significant.

RESULTS

Sociodemographic Profile of Studied Sample

Out of 75 patients, there were 21 (28%) females and 54 (72%) males. Age ranged from 18 to 60 years. Maximum number of patients, 29 (38.67%), were in the age group of <25 years, while 28 (37.33%) in 26 to 35 years, and 18 (24%) in >35 years. 43 (57.33%) patients were from the urban domicile, while 32 (42.67%) from the rural area. 46 (61.33%) patients were Hindus, whereas 28 (37.33%) were Muslims. One patient was illiterate, 4 had primary education, 28 had secondary education, 24 had higher secondary education, and 16 had graduate/diploma education, while 2 had postgraduate education. 18 patients were self-employed, 14 unskilled workers, 14 students, 12 household workers, 6 professionals, 9 clerical/skilled/semiskilled workers, and 2 were unemployed. 34 patients were married, 32 were never married, while the rest were single/separated/divorced/widow/widower. 68 patients had caregivers residing with them. Two patients had monthly income below Rs. 635, 27 between Rs. 635 and 1,904, 22 between Rs. 1,905 and 3,809, and 24 had a monthly income of Rs. 3,810, or more.

We found a significant correlation between age ≤25 years and moderate–extreme disability. Also, significant correlation was found between single marital status and moderate-to-extreme disability. Per capita monthly income of ≤Rs. 3,809 (i.e., low) was found to have significant correlation with moderate–extreme disability (Table 1). In illness-related variables (Table 2), statistically significant correlation was seen between age of onset ≤25 and moderate–extreme disability. Also, significant correlation was found between ≥5 hours spent in obsessions and compulsions daily and moderate–extreme disability.

Patients who had moderate–extreme severity of OCD (Table 3) had statistically significant higher rates of disability. However, correlation between severity of OCD and family burden was not significant ($p = 0.07$). Higher disability was associated with significantly higher family burden ($p < 0.001$; Table 4).

DISCUSSION

In this study of 75 patients suffering from OCD, prevalence of family burden was low in 65 (86.67%) and high in 10 (13.33%). Mean family burden score was 13.42 ± 1.10. Gururaj et al[21] found much higher family burden in their study, because most of the patients in their study had moderate-to-severe cases of OCD. Prevalence of disability was 57.33% (43) in mild OCD cases and 42.67% (32) in moderate–extreme cases. Bobes et al[22] found significantly greater disability in the patients with OCD in the areas of self-care, interpersonal activities, communication and understanding, and in work and global disability scores in age- and duration-matched schizophrenia patients, which was not supported by Mohan et al.[23] Other studies

Table 1: Correlation of sociodemographic variables with family burden and disability

		Family burden (FBS score)			*Disability (WHO-DAS-2 score)*		
Sociodemographic variable		*Low (1–25)*	*High (26–50)*	*Significance*	*Mild (≤24)*	*Moderate–extreme (>24)*	*Significance*
Age (years)	≤25	24 (82.76%)	5 (17.24%)	$\chi^2 = 0.625$, df = 1, p = 0.429	10 (34.48%)	19 (65.52%)	$\chi^2 = 10.1$, df = 1, p = 0.001
	>25	41 (89.29%)	5 (10.71%)		33 (71.43%)	13 (28.57%)	
Gender	Male	46 (85.19%)	8 (14.81%)	$\chi^2 = 0.366$, df = 1, p = 0.545	31 (57.41%)	23 (42.59%)	$\chi^2 = 0.433$, df = 1, p = 0.983
	Female	19 (90.48%)	2 (9.52%)		12 (57.14%)	9 (42.86%0	
Domicile	Urban	38 (88.37%)	5 (11.63%)	$\chi^2 = 0.254$, df = 1, p = 0.615	26 (60.47%)	17 (39.53%)	$\chi^2 = 0.404$, df = 1, p = 0.525
	Rural	27 (84.38%)	5 (15.63%)		17 (53.13%)	15 (46.88%)	
Religion	Hindu	40 (86.96%)	6 (13.04%)	$\chi^2 = 0.865$, df = 1, p = 0.926	28 (60.87%)	18 (39.13%)	$\chi^2 = 0.375$, df = 1, p = 0.846
	Muslim and Christian	25 (85.71%)	4 (14.29%)		17 (57.14%)	12 (42.86%)	
Education	Up to secondary	28 (84.85%)	5 (15.15%0	$\chi^2 = 0.169$, df = 1, p = 0.681	22 (64.29%)	11 (35.71%)	$\chi^2 = 2.10$, df = 1, p = 0.147
	Higher secondary and above	37 (88.10%)	5 (11.90%)		21 (45.83%)	21 (54.97%)	
Occupation	Working	64 (87.67%)	9 (12.33%)	$\chi^2 = 2.39$, df = 1, p = 0.122	43	30	$\chi^2 = 2.76$, df = 1, p = 0.097
	Nonworking	1 (50%)	1 (50%)		0	2	
Marital status	Married	34 (97.14%)	1 (2.86%)	$\chi^2 = 6.23$, df = 1, p = 0.013	26 (76.47%)	8 (23.53%)	$\chi^2 = 9.31$, df = 1, p = 0.002
	Single	31 (77.50%)	9 (22.50%)		17 (40.63%)	24 (59.38%)	
Caregiver residing with patient	Yes	60 (88.24%)	8 (11.76%)	$\chi^2 = 1.55$, df = 1, p = 0.213	41 (60.29%)	27 (39.71%)	$\chi^2 = 2.61$, df = 1, p = 0.106
	No	5 (71.43%)	2 (28.57%)		2 (28.57%)	5 (71.43%)	
Family type	Nuclear	33 (82.5%)	7 (17.5%)	$\chi^2 = 1.29$, df = 1, p = 0.256	22 (55%)	18 (45%)	$\chi^2 = 0.191$, df = 1, p = 0.662
	joint	32 (91.43%)	3 (8.57%)		21 (60%)	14 (40%)	
Per capita monthly family income (Rs)	≤3,809	41 (79.31%)	10 (20.69%)	$\chi^2 = 5.43$, df = 1, p = 0.020	24 (0%)	27 (100%)	$\chi^2 = 5.17$, df = 1, p = 0.023
	≥3,810	24 (91.30%)	0 (8.70%)		18 (51.85%)	6 (48.15%)	

Table 2: Correlation of illness-related variables with severity of family burden and disability

		Family burden (FBS score)			*Disability (WHO-DAS-2 score)*		
OCD-related variable		*Low (1–25)*	*High (26–50)*	*Significance*	*Mild (<24)*	*Moderate–extreme (>24)*	*Significance*
Duration in years	<1	16 (94.12%)	1 (5.88%)	$\chi^2 = 1.06$, df = 1, p = 0.304	30 (58.82%)	19 (41.18%)	$\chi^2 = 0.317$, df = 1, p = 0.955
	≥1	49 (83.33%)	9 (16.67%)		20 (83.33%)	13 (50%)	
Age of onset (years)	≤25	34 (87.18%)	5 (12.82%)	$\chi^2 = 0.185$, df = 1, p = 0.892	16 (41.03%)	23 (58.97%)	$\chi^2 = 8.83$, df = 1, p = 0.003
	>25	31 (86.11%)	5 (13.89%)		27 (75%)	9 (25%)	
Regular treatment	Present	38 (92.68%)	3 (7.32%)	$\chi^2 = 2.83$, df = 1, p = 0.092	27 (65.85%)	14 (34.15%)	$\chi^2 = 2.68$, df = 1, p = 0.101
	Absent	27 (76.41%)	7 (20.59%)		16 (47.06%)	18 (52.94%)	
Daily in behavior	<5	26 (96.30%)	1 (3.70%)	$\chi^2 = 3.39$, df = 1, p = 0.066	24 (88.89%)	3 (11.11%)	$\chi^2 = 17.2$, df = 1, p < 0.001
	≥5	39 (85.19%)	9 (14.81%)		19 (55.56%)	29 (44.44%)	
Insight	Present	57 (85.07%)	10 (14.93%)	$\chi^2 = 1.38$, df = 1, p = 0.420	37 (55.22%)	30 (44.78%)	$\chi^2 = 1.14$, df = 1, p = 0.285
	Absent	8 (100%)	0 (0%)		6 (75%)	2 (25%)	
Family history of OCD	Absent	61 (85.92%)	10 (14.08%)	$\chi^2 = 0.650$, df = 1, p = 0.420	2 (50%)	2 (50%)	$\chi^2 = 0.929$, df = 1, p = 0.761
	Present	4 (100%)	0 (0%)		41 (57.75%)	30 (42.25%)	

Table 3: Correlation of severity of OCD with family burden and disability

Severity of OCD	*Family burden (FBS score)*				*Disability (WHO-DAS-2 score)*			
(Y-BOCS score)	*Low (1–25)*	*High (26–50)*	*Total*	*Significance*	*Low (1–25)*	*High (26–50)*	*Total*	*Significance*
Subclinical–mild (0–15)	21 (100)	0 (0)	21 (100%)	*$\chi^2 = 3.28$, p = 0.07	20 (95.24)	1 (4.76)	21 (100%)	*$\chi^2 = 17.130$, p = 0.00001803
Moderate–extreme (16–40)	44 (100)	10 (0)	54 (100%)		23 (71.43)	31 (28.5)	54 (100%)	
Total	65	10	75		43	32	75 (100%)	

*χ^2 is corrected Fisher-exact

Table 4: Relationship of disability due to OCD with family burden

Disability (WHO-DAS-2 score)	Family burden (FBS score)		Total	χ^2 (corrected Fisher-exact)
	Low (1–25)	High (26–50)		
<24	43 (100)	0	43	$\chi^2 = 12.91$,
>24	22	10	32	$p < 0.001$
Total	65	10	75	

reported that patients with OCD had greater disruption in their careers and relationships with family and friends.[24,25]

In our study, we found a statistically significant correlation between single status and moderate–extreme disability, a finding consistent with study by Steketee.[11] The family burden was more in nuclear families compared with joint families and in nonworking class compared with working class. These were found to be statistically not significant. Our study did not show significant correlation in other socio-demographic characteristics like gender, domicile, and religion, which is consistent with most studies. There was statistically significant correlation between lower per capita income (social class IV and V)[26] and moderate-to-extreme disability. Family burden was found more in those living in a nuclear family than those living in a joint family (17.5 *vs* 8.57%) but, this was not statistically significant. High family burden was more in those who were nonworking than in those working (50%), but this was also not statistically significant. Similar findings were reported in other studies.[8,10,13,21,23,27]

In our study, patients with moderate–extreme OCD and a Y-BOCS score (16–40) had statistically significant higher rates of family burden (76.19 *vs* 29.11%) than those who had low scores (0–15). These findings are consistent with other studies.[21,22,27] The disability due to OCD and the family burden is much more pronounced than imagined. Social consequences, professional problems, and family troubles linked to hospitalizations lead to low QoL for patients and high cost for society. Severe OCD is associated with significant disability, poor QoL, and high family burden, often comparable with schizophrenia. All these correlations of disability in OCD are consistent with existing literature.[8,10,13,21,23,27]

Indian families of patients with OCD experience burden comparable with that of families of patients with schizophrenia. There is a need to develop local needs-based support programs for families of patients with psychiatric disorders in India.[27] Therefore, there is an urgent need to increase the sensitivity among health care professionals to recognize and treat OCD.[21] Early recognition of the disorder facilitates early intervention. This reduces the distress, disability, and burden of the illness.[27]

CONCLUSION

Patients with OCD experience significant disability and high burden on family. Young age of onset (≤25 years), single marital status, and low socioeconomic status have significant correlation with disability and/or family burden. There is also a positive correlation between disability and family burden. Higher the disability, greater is the family burden.

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ORIGINAL ARTICLE

Diagnostic Value of Fine Needle Aspiration Cytology in Enlarged Cervical Lymph Nodes in a Tertiary Care Hospital in Navi Mumbai, Maharashtra, India

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ABSTRACT

A retrospective study of 362 patients with cervical lymphadenopathy, who underwent fine needle aspiration cytology (FNAC) at Mahatma Gandhi Mission (MGM) Medical College & Hospital, Navi Mumbai, Maharashtra, India, is presented. Tuberculosis was the commonest pathology (42%). Other causes were reactive lymphadenitis, granulomatous lymphadenitis, metastases, chronic nonspecific lymphadenitis, acute suppurative lymphadenitis, and lymphoma. Histopathological examination of lymph node biopsy specimens was carried out in 26 cases.

Keywords: Cervical lymph node, Fine needle aspiration cytology, Tuberculous lymphadenitis.

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INTRODUCTION

Lymphadenopathy is one of the commonest clinical presentations of patients attending outpatient departments. The etiology varies from an inflammatory process to a malignant condition. Fine needle aspiration cytology is a reliable and quick method to sample superficial cervical lymph nodes and has been successfully adopted as a routine in most of the centers.[1-3] The present study was undertaken with the aim to investigate pattern of cervical lymphadenopathy among the patients visiting MGM Hospital—a tertiary care center attached to the MGM University of Health Sciences, Navi Mumbai, Maharashtra, India, to evaluate the diagnostic efficacy of FNAC and analyze the different cytomorphological patterns associated with various lymphadenopathies.

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MATERIALS AND METHODS

A total of 362 cases of FNAC of cervical lymphadenopathy and its histopathological correlation (wherever available) was conducted and studied over a period of 3 years (October 2011 to September 2014) at the Department of Pathology, MGM Medical College & Hospital, Navi Mumbai, Maharashtra, India.

All the referred patients were clinically examined. The procedure of FNAC was explained to the patients including its limitations and complications. An informed consent was taken from each patient.

Under aseptic precautions, the lymph node was fixed between the index finger and the thumb of nondominant hand, and a sterile 23-gauge needle fitted to a 10 mL syringe was introduced into the lymph node. The plunger was withdrawn, and negative pressure was created in syringe after entering the lymph node. The needle was moved back and forth several times with a constant suction. The negative pressure was released and needle removed from the mass. The needle containing aspirated material was detached and air was drawn into the syringe. The needle was reattached and the material collected in needle hub was aspirated out on the clean, dry, and grease-free glass slides. Smears were prepared with another glass slide sliding over the slide length exerting a little pressure. Smears were immediately fixed in 95% ethyl alcohol, and these smears were stained by Papanicolaou (Pap) stain. Air-dried smears were prepared and stained with May–Grünwald–Giemsa stain. Ziehl–Neelsen stain was done for all the cases in which necrotic material was aspirated and in clinically suspected tuberculosis cases. Smears were examined, and cytological diagnosis was given. Lymph nodes of the patients who underwent subsequent surgical biopsy were fixed in 10% buffered formalin. Biopsy specimens were processed to obtain 3 to 5 µm paraffin sections, which were stained with hematoxylin and eosin stain. Histopathological study was done separately. The results of cytological and histopathological study were correlated to evaluate the efficacy of the procedure.

Inclusion Criteria

- All age groups and both sexes
- Enlarged cervical lymph nodes >2 cm in size

Exclusion Criteria

- Enlarged cervical lymph nodes <2 cm in size

RESULTS

Among 362 cases, the age group varied from 3 months to 87 years with maximum number of cases in age group of 21 to 30 years. A total of 209 (57.5%) were females and 153 (42.3%) were males (Table 1). The most common cause of cervical lymphadenopathy was tuberculous lymphadenitis with 152 cases (42%) followed by 79 cases (21.8%) of reactive lymphadenitis, 69 cases (19.1%) of granulomatous lymphadenitis, 30 cases (8.3%) of metastatic malignancy, 20 cases (5.5%) of chronic nonspecific lymphadenitis, 9 cases (2.5%) of acute suppurative lymphadenitis, and 3 cases (0.8%) of lymphoma. Tuberculous lesions were divided in three groups based on their cytomorphological features as described by Singh et al.[4] Caseous necrosis with or without polymorphonuclear cells and epithelial cells was commonest type accounting for 89.4% cases. Total acid-fast bacilli (AFB) positivity was 66.4%. Cytohistopathological correlation was available in 26 cases. Among 17 cytologically diagnosed cases of non-neoplastic lesions, discordance was observed in 6 cases including 4 cases of reactive lymphadenitis and 2 cases of granulomatous lymphadenitis.

DISCUSSION

The incidence of cervical lymphadenopathy was found to be highest in the age group of 21 to 30 years, which was comparable with other studies.[3,5] Similar incidence was observed by Shakya et al[6] and Khan et al[7] in their studies. Among 362 patients, age ranged from 3 months to 87 years, with mean age of 30.75 years. The study revealed female predominance, with 209 females (57.7%) and 153 males (42.3%) (Table 1) which was similar to other studies.[7,8]

Seventy-nine (21.8%) cases of reactive lymphadenitis were reported. Aspirate showed various stages of maturing lymphocytes, as seen in a reactive lymphoid follicle (Fig. 1). Out of eight cases diagnosed as reactive lymphadenitis (Table 2) on FNAC, four cases were consistent with reactive lymphadenitis, whereas two cases were diagnosed as tuberculous lymphadenitis and two cases as non-Hodgkin's lymphoma (NHL) on histopathological examination. Pandav et al[3] and Giri and Singh[9] observed similar discordance where cytodiagnosis of reactive hyperplasia turned out to be tuberculosis on histopathology. The discrepancy could be due to nonrepresentative sampling or because a node other than the aspirated one was biopsied.[9] Another possible cause of discrepancy could be due to partial effacement of nodal architecture by disease process. About 20 (5.5%) of our cases were reported as chronic nonspecific lymphadenitis. These showed lymphocytes, plasma cells, and immunoblasts. Similar incidence was observed by Babu et al.[10]

Out of 362 cases, there were 69 (19.1%) cases of granulomatous lymphadenitis. The study conducted by Kumar et al[11] and Shakya et al[6] showed an incidence of 0.94 and 10% respectively. The maximum number of cases was seen in the age group of 11 to 20 years. When the cytological smears showed epithelioid granulomas with or without giant cells, without caseation necrosis, or AFB, a diagnosis of granulomatous lymphadenitis was offered. Cytohistopathological correlation was available in seven cases. Of these, five cases were consistent with the diagnosis, one case was diagnosed as follicular lymphoma and the other as Castleman's disease (Table 2). The presence of granulomata in an aspirate may indicate the presence of a neoplastic process. The background cell population needs to be scrutinized if a malignant lymphoma is suspected.[12] The discordance in the study was mainly because of presence of granulomas on smears which was reported as

Table 1: Age and gender distribution of 362 cases of cervical lymphadenopathy

Age group (years)	*Female*	*Male*	*Total*	*Percentage*
0–10	11	19	30	8.3
11–20	57	24	81	22.4
21–30	60	40	100	27.6
31–40	40	25	65	17.9
41–50	23	15	38	10.5
51–60	09	13	22	6.1
61–70	08	11	19	5.2
71–80	01	04	05	1.4
81–90	00	02	02	0.6
Total	209 (57.7%)	153 (42.3%)	362	100

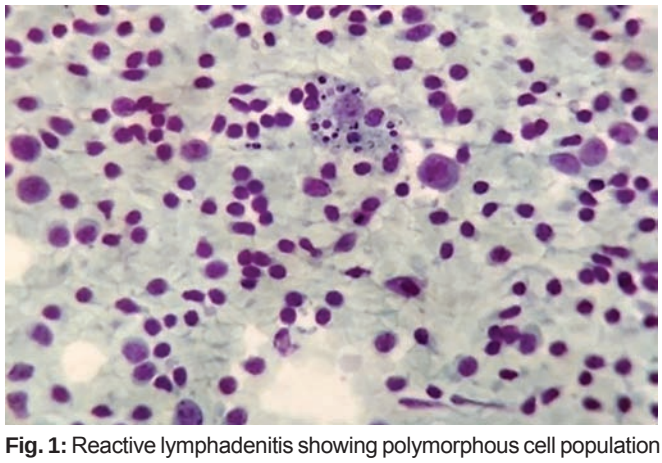

Fig. 1: Reactive lymphadenitis showing polymorphous cell population of lymphoid cells along with tangible body macrophage (Pap 40×)

Table 2: Cytohistopathological correlation of 26 cases

Cervical lymph node lesions	*Number of cases diagnosed on FNAC*	*Number of cases diagnosed on histopathology*	
Non-neoplastic (17)		*Cordance*	*Discordance*
Tuberculous lymphadenitis	2	2	–
Reactive lymphadenitis	8	4	Tuberculous lymphadenitis (2 cases) NHL (2 cases)
Granulomatous lymphadenitis	7	5	Follicular lymphoma (1 case) Castleman's disease (1 case)
Neoplastic (9)			
Metastasis	8	8	–
Lymphoma	1	1	–
Total	26	20	6

Table 3: Incidence of various cervical lymph node lesions

Lesions	*Number of cases*	*Percentage*
Reactive lymphadenitis	79	21.8
Acute suppurative lymphadenitis	9	2.5
Chronic nonspecific lymphadenitis	20	5.5
Granulomatous lymphadenitis	69	19.1
Tuberculous lymphadenitis	152	42.0
Metastasis	30	8.3
Lymphoma	3	0.8
Total	362	100

Table 4: Cytomorphological features of tuberculous lymphadenitis and its correlation with AFB positivity

Cytomorphological features	*Number of cases*	*AFB positivity*	*Percentage of AFB positivity*
Epithelioid cell granulomas without caseous necrosis	30	0	0
Epithelioid cell granulomas with caseous necrosis	56	42	75
Caseous necrosis with or without polymorphonuclear cells and epithelioid cells	66	59	89.4
Total	152	101	164.4

granulomatous lymphadenitis. One case of granulomatous lymphadenitis was diagnosed as Castleman's disease on histopathology. Castleman's disease should be considered in the differential diagnosis with lymph node tuberculosis, lymphadenitis, sarcoidosis, and granuloma.[13]

Tuberculous lymphadenitis constituted the most common lesion (152/362 cases) accounting for 42% of all cases (Table 3). Similar incidence of tuberculosis has been observed in other studies.[3,5,7,11] The aspirates from cervical lymph node were diagnosed as tubercular lymphadenitis based on the presence of epithelioid cell granulomas and caseous necrosis with or without Langhan's giant cells in a milieu of parent lymphoid cells. In all these cases Ziehl–Neelsen stain for AFB was done.

About 101 cases (66.4%) showed AFB positivity (Table 4 and Fig. 2). The frequency of AFB positivity in FNAC smears in various studies ranges from 10 to 70%.[11] The AFB positivity was higher in smears containing necrotic material, which is consistent with findings in other studies.[9,14,15] On cytohistopathological correlation, two cases diagnosed as tuberculous lymphadenitis on FNAC were consistent with histopathological diagnosis (Table 2).

Thirty cases (8.3%) were diagnosed as metastatic lymph nodes. Other studies[5,7,11] showed an incidence of 13.9, 6, and 2.8% respectively. The aspirates revealed small to large groups of anaplastic cells having pleomorphic nuclei with irregular chromatin and prominent nucleoli, with a background of lymphoid cells (Fig. 3). Eight cases were biopsied and the cytodiagnosis was consistent with histopathological diagnosis. Out of eight cases, seven cases were of squamous cell carcinoma and one case of adenocarcinoma. Cervical group is the most common group of lymph nodes to be involved and the primary is most often from the oral cavity with squamous cell carcinoma being the common histopathological type.[16]

Three (0.8%) cases of lymphoma were diagnosed (Table 3 and Fig. 4). These findings correlate well with results reported in other studies.[3-7] The maximum number of cases was seen in the age group of 41 to 50 years, which was similar to the findings observed by Baji et al.[5] A definite diagnosis of Hodgkin's disease on FNAC can be made in the presence of typical Reed–Sternberg cells

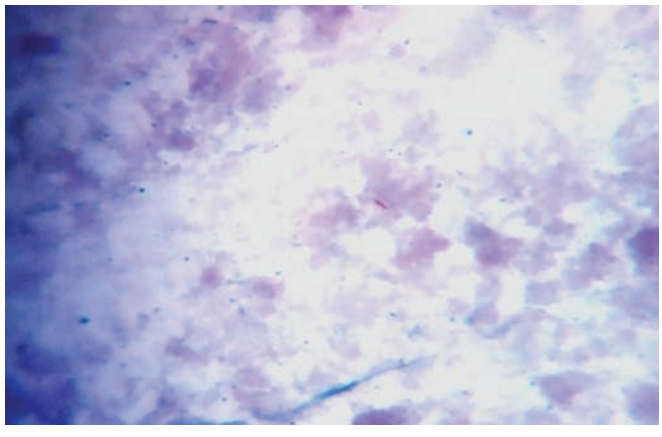

Fig. 2: Ziehl–Neelsen stain: AFB in aspirate for tuberculous lymphadenitis (oil immersion field)

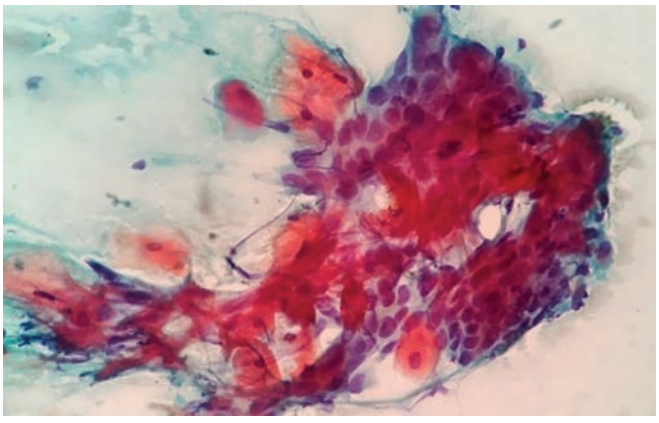

Fig. 3: Metastasis of squamous cell carcinoma (Pap 40×)

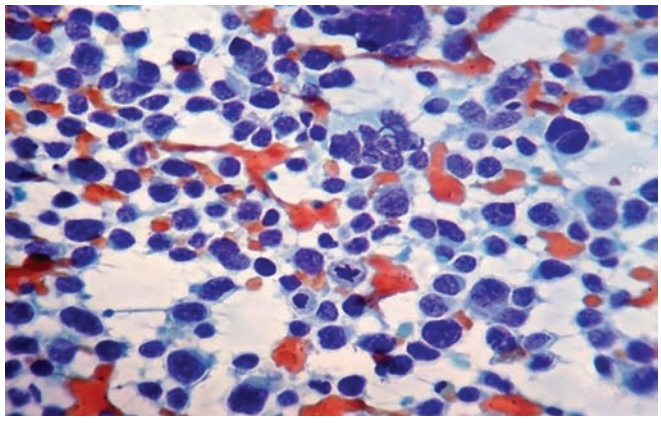

Fig. 4: Aspiration smear from lymphoma showing monomorphic population of lymphoid cells. Atypical mitosis seen (Pap 40×)

in a background of lymphocytes and reactive cells. The FNAC provides a good method to diagnose lymphomas; however, evaluation of lymphomas is best done on lymph node biopsy and immunohistochemistry for confirmation and final classification.[11]

The sensitivity in this study was 75%, similar to the study conducted by Rakhshan and Rakhshan.[17] Specificity was 75%, with 100% positive and 82.3% negative predictive value.

CONCLUSION

Fine needle aspiration cytology is a very simple and inexpensive method in diagnosing lesions of cervical lymph nodes. Quick diagnosis can be made within short duration of time and early treatment can be started. The FNAC can be helpful in diagnosing metastatic lesions as well as to detect occult primary malignancies. In lymphomas, preliminary diagnosis can be given. Further evaluation by histopathology and immunohistochemistry can be done for confirmation.

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ORIGINAL ARTICLE

Cross-sectional Study of Health Status of Auto Rickshaw Drivers in Vashi, Navi Mumbai, India

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ABSTRACT

Introduction: It is observed that auto rickshaw drivers are prone to musculoskeletal, respiratory, and gastrointestinal disorders and also to injuries and substance abuse.

Objective: To study the health status, disease profile, and substance abuse among auto rickshaw drivers in Navi Mumbai, Maharashtra, India.

Materials and methods: Participants in this cross-sectional observational study were drivers plying rickshaws registered at Regional Transport Office (RTO), Vashi, Navi Mumbai, India. Considering 1,500 registered auto rickshaws, a 10% random sample was planned. Questionnaire was designed to collect data by trained doctors including sociodemographic factors, occupational details, perceived stress scale, Nordic Musculoskeletal Questionnaire (NMSQ), addiction details, current symptoms, and significant history of past illness as well as general and systemic examination findings. Bone mass density (BMD) testing and random blood glucose levels were done. Data were analyzed using Microsoft Excel and Epi Info.

Results: Totally, 159 drivers participated. Majority [82 (51.6%)] belonged to socioeconomic class III, 37 (23.3%) to class IV, while 40 (25.1%) to class II. Among those, 54 (33.9%) drivers were in the profession for 10 to 19 years, while 36 (22.7%) were driving for 20 years or more. Only 19 (11.9%) drivers were asymptomatic, while 140 (88.1%) had one or more complaints. The commonest complaint was musculoskeletal pain in 95 (59.9%) of the study participants. Generalized fatigue, acidity, and headache were other common complaints. Ninety seven (61.1%) drivers had osteopenia. This had significant association with age and the number of years in profession. Substance abuse was found in 95 (59.7%) of the study participants.

Conclusion: Auto rickshaw drivers are very susceptible to health-related problems and there is need for monitoring on an ongoing basis and institutionalization of measures to prevent it.

Keywords: Addiction, Morbidity, Occupational health, Osteopenia, Rickshaw driver.

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INTRODUCTION

Auto rickshaw driving involves prolonged sitting in a fixed posture and also exposes the driver to a number of harmful elements such as vibrations, noise, glare and which over the period of time may lead to one or more of the occupational disorders. They are also exposed to significant amounts of air pollutants in their work like carbon monoxide, sulfur dioxide, diesel fuels with carcinogenic properties, etc., which can damage the respiratory tract leading to morbidity and mortality due to diseases like chronic obstructive pulmonary diseases, asthma, bronchitis,[1-4] headache, sore eyes, and ear problems. Prolonged hours of work result in insufficient sleep,[5,6] less time spent with family members and friends, insufficient leisure time, less physical activity, and less time for preparation of food.[6] It is also observed that transport-related sitting is one domain of sedentary behavior that has been linked to increased risks of chronic diseases.[6]

Several studies have shown that lengthy commuting perpetuates conditions that compromise individual's health, like stress caused by traffic congestion, searching for parking, interacting with other drivers, and safety concerns (phenomena characterized as "travel impedance").[6]

Navi Mumbai is an urban conglomerate which has come up in the last 30 years where auto rickshaws constitute major means of private transport, unlike neighboring metro city of Mumbai where taxis are the main mode of private transport. Currently, approximately 1,500 drivers plying rickshaws are registered with RTO of Vashi in Navi Mumbai.

This study was conducted with the aim to examine the health status, disease profile, and substance abuse among auto rickshaw drivers in Navi Mumbai.

MATERIALS AND METHODS

A cross-sectional study was conducted among auto rickshaw drivers working in Navi Mumbai in the year 2014 in January and June at two sites. The first site was at the auto rickshaw parking place near Vashi railway station where they stop to pick passengers and also use it as a resting place. Most of the auto rickshaws of city come to Vashi railway station daily. The second site was

the testing ground near RTO at Vashi where they gather for vehicle testing and driving tests and wait for variable period for their turn for the test. So this sample size was well representative of the whole city of Navi Mumbai.

Two hundred and seven auto rickshaw drivers were approached randomly. No specific sampling technique was used. In order to eliminate impact of association of age with the occurrence of chronic diseases and chronic conditions, those of the age of 55 years and above were excluded. All were males and were plying auto rickshaw for more than 1 year with a valid driving license. Their willingness to participate in the study was confirmed.

A questionnaire was designed to collect the data regarding the sociodemographic factors, occupational details, perceived stress scale, addiction details if any, current symptoms, and significant history of past illness. Nordic Musculoskeletal Questionnaire[7] was used to identify musculoskeletal disorders (MSDs). The prestructured questionnaire was tested on 20 auto rickshaw drivers to rule out interpretational errors. After taking an informed consent, each participant was interviewed and the data were collected using this pretested and prestructured questionnaire.

A detailed clinical examination was done including measurement of weight, height, and blood pressure. Significant general and systemic examination findings were recorded. All participants were subjected to random capillary blood glucose (RCBG) estimation using Optium Xceed Meter of Abbott Diabetes Care Ltd, Witney, UK. As per the recommendation of Madras Diabetes Research Foundation,[8] the cut-off value of RCBG of <110 mg/dL was considered normal and those in excess of cut-off value were recommended to undergo further diagnostic evaluation. Quantitative ultrasound (QUS), which is a reliable and cost-effective method[9-10] to check the BMD, was performed using calcaneal QUS (BMD SONOST 3000) machine. To calculate BMD, QUS of calcaneus (right heel) was used. Machine converted the BMD values into T-score.[9]

All those who needed medical interventions, based on history and examination findings, were treated at the data collection points immediately and those who required specialty care were referred to Mahatma Gandhi Mission Medical College & Hospital for further management.

Data were entered in Microsoft Excel and analyzed using Excel and Epi Info (a public domain statistical software for epidemiology). The proportions and medians were calculated to describe respondent's characteristics. For categorical variables, proportions were compared using Chi-square tests; t-test was used for quantitative data. Correlation and regression analysis was done to identify the independent effects of associated factors.

Approval from the Institutional Ethical Committee and Deputy Regional Transport Officer, Vashi, Navi Mumbai, India, was obtained before commencing the study.

RESULTS

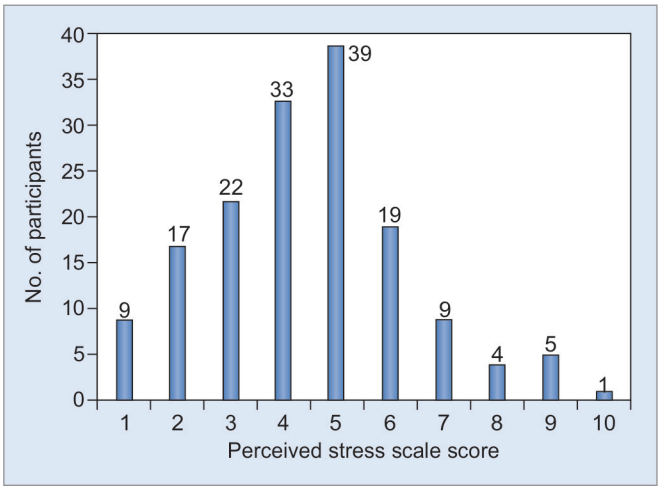
Sociodemographic Profile

The study subjects were in the range of 19 to 54 years of age. The mean age was 36.3 [standard deviation (SD) ± 8.7] years and median age was 36 years. Out of total 159 participants, 13 (8.2%) were below the age of 25 years, 58 (36.5%) between 25 and 34 years, 55 (34.6%) between 35 and 44 years, and 33 (20.7%) were between 45 and 54 years. Among the participants, 131 (82.4%) were married; 146 (91.8%) were Hindus, while 13 (8.2%) were Muslims. Among the 159 drivers, 114 (71.7%) belonged to Maharashtra state, 39 (24.5%) were from Northern states, and 6 (3.8%) were from Southern states; 135 (84.9%) were from urban community, while 24 (15.1%) were from rural community. The 129 (81.1%) drivers were staying in pucca houses, while 30 (18.9%) had kutcha houses. Eight (5.0%) drivers had not received any formal education, while 18 (11.3%), 123 (77.4%), and 10 (6.3%) drivers had received primary, secondary, and graduation level of education respectively. Fifty four (33.9%) participants had joint family. Maximum number of family members was 15, with average family size of 4.26 (Median: 4).

In 126 (79.3%) families, the participant was the sole earning member while in 26 (16.3%) families there were two earning members and in 7 (4.4%) families there were three earning members. Total monthly family income ranged from Rs. 5,000 to Rs. 60,000 (mean Rs. 1,538.79, median Rs. 15,000, Q3 Rs. 20,000). The mean per capita income was Rs. 4,473.10 (median Rs. 3333.33, Q3 Rs. 5,000). As per Kuppuswamy scale for socioeconomic class (SEC)[11] based on education, occupation, and income (scoring range updated for Consumer Price Index 2014), the majority [82 (51.6%)] belonged to Class III, 37 (23.3%) to Class IV, and 40 (25.1%) to Class II.

Occupational Details

All the drivers were driving compressed natural gas-based rickshaws. Mean age to start driving auto rickshaw was 23.5 years with range of 18 to 41 years (median 22 years). Age-group wise the mean age to get into the profession was 18.6 years in the age group below 25 years, 22.8 years in the age group of 25 to 34 years, 24.3 years in the age group of 35 to 44 years, and 24.5 years in the age group of above 45 years. Majority of the drivers, [54 (33.9%)] were in the profession for 10 to 19 years, while 36 (22.7%) were driving for 20 years or more. Moreover, 37 (23.3%) drivers were plying rickshaw for 5 to 9 years



Graph 1: Perceived occupational stress scoring done by auto rickshaw drivers

and 32 (20.1%) for less than 5 years. The working hours ranged from 4 to 16 hours. The mean working hours were 10.3 (median 10 hours, Q3 12 hours). About 90 (56.4%) drivers ply rickshaw daily on an average for 10 hours or less, and 69 (43.6%) for more than 10 hours.

All except one stated that they feel occupationally stressed. On the scale of 1 to 10, the mean perceived stress was 4.4 (median 4, Q3 5). Out of 158, 81 (51.6%) had felt stress up to scoring level of 4, while 77 (48.4%) felt stress level score of 5 or more (Graph 1). The stress score is significantly associated with socioeconomic class (Table 1).

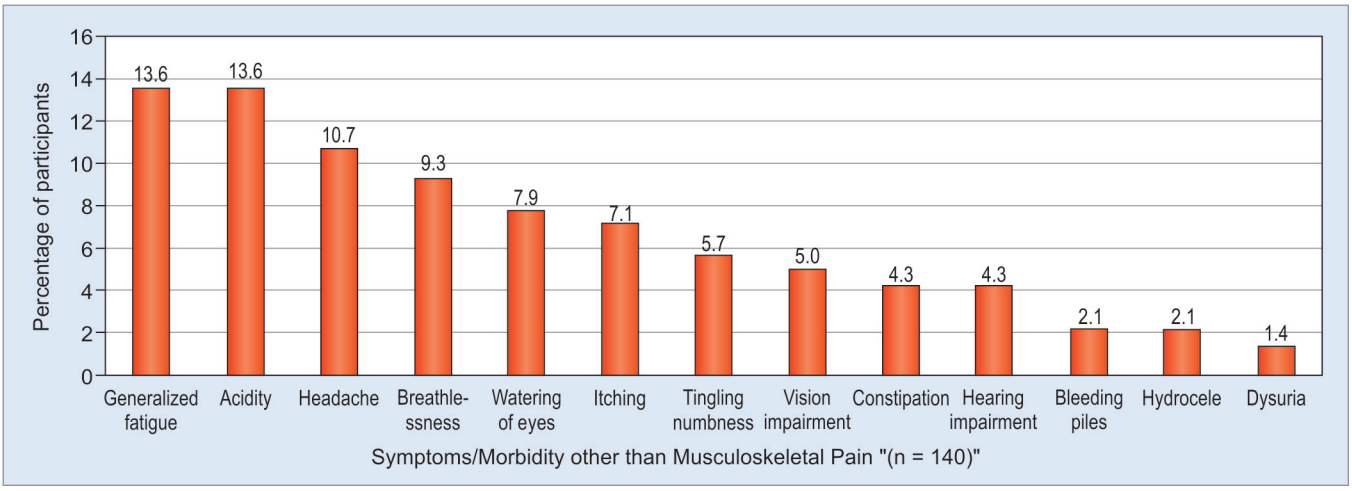
Morbidity Profile

Among the 159 study participants, 19 (11.9%) were asymptomatic, while 140 participants (88.1%) had one or more complaints. The commonest complaint was musculoskeletal pain in 95 (59.74%). Generalized fatigue, acidity, and headache were the common complaints other than musculoskeletal pain (Graph 2). The musculoskeletal pain assessed by NMSQ has shown low back pain in 80 (50.3%) auto drivers followed by knee pain in 36 (22.6%). However, medical care was sought by only 5% for lower back pain and only 14% for knee pain. Treatment-seeking behavior varies as per site of pain (Graph 3). There was significant relationship found between presence of musculoskeletal pain and working for more than 10 hours daily (Table 1).

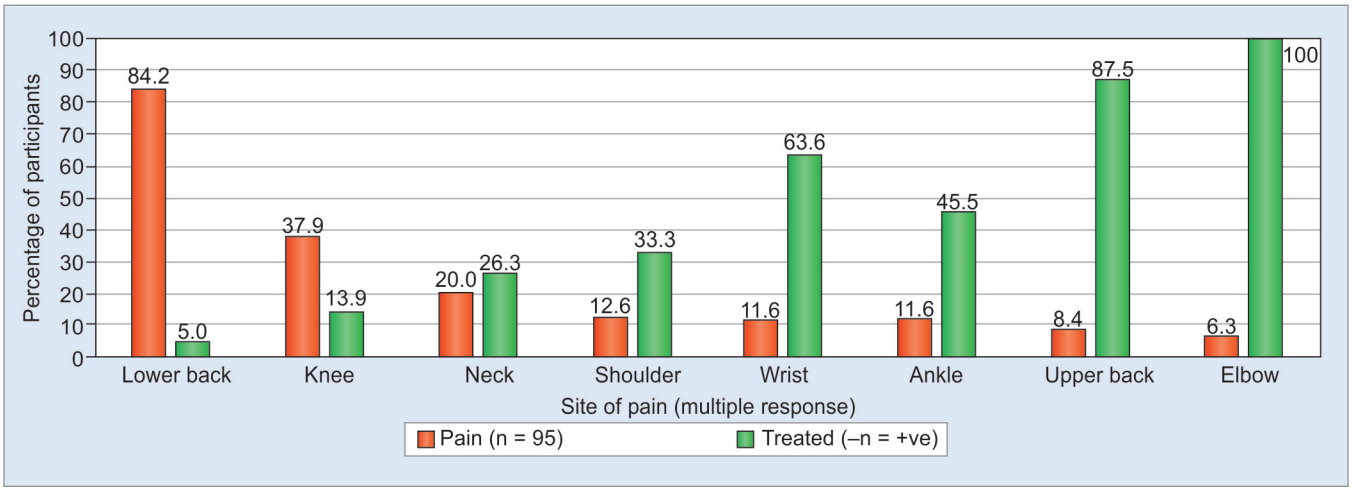
In the past, 22 (13.4%) had visual impairment, 10 (6.3%) were suffering from diabetes, 7(4.4%) from hypertension, 6(3.8%) from impaired hearing, and 1 (0.6%) had asthma. All of them were under treatment either from government or from private sources. Mean body mass index (BMI) of the study participants was 25.4 (SD ± 4.11). Preobesity (BMI 25–29.99) was seen in 66 (41.5%) auto drivers, 15 (10.1%) were in Class I obesity (BMI 30–34.99) and 3 (1.9%) were in Class II obesity (BMI 35–39.99) category. Body mass index was normal (18.5–24.99) in 75 (47.1%) of the auto drivers. The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) were 124.27 (SD ± 12.01) mm Hg and 78.90 (SD ± 7.39) mm Hg

Table 1: Risk factors of musculoskeletal pain, osteopenia, and stress

	Group characteristics		*Musculoskeletal pain +ve*		*Osteopenia +ve*		*Perceived stress score >4*	
Chi-square test result	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Age (years)	df = 3		p > 0.05		p < 0.05		p > 0.05	
<25	13	8.2	8	61.5	6	46.1	7	58.3
25–34	58	36.5	36	62.1	28	48.3	33	56.9
35–44	55	34.6	31	56.4	40	72.7	23	41.8
45–54	33	20.7	20	60.6	23	69.7	14	42.4
Years in profession (years)	df = 3		p > 0.05		p < 0.05		p > 0.05	
1–4	32	20.1	15	46.9	14	43.8	18	58.1
5–9	37	23.3	28	75.7	19	51.4	20	54.1
10–19	52	32.7	32	61.5	34	65.4	26	50.0
20 and above	38	23.9	20	52.6	30	78.9	13	34.2
Daily working hours	df = 1		p < 0.05		p > 0.05		p > 0.05	
10 or less	90	56.6	47	52.2	57	63.3	41	46.0
More than 10	69	43.4	48	69.5	40	57.9	36	52.2
Kuppuswamy SEC	df = 2		p > 0.05		p > 0.05		p < 0.05	
Class II	40	25.1	22	55.0	24	60.0	13	32.5
Class III	82	51.6	49	59.7	49	59.8	46	56.8
Class IV	37	23.3	24	64.9	24	64.8	18	48.6
BMI	df = 2		p > 0.05		p > 0.05		p > 0.05	
24.99 or less	75	47.2	41	54.7	46	61.3	40	54.1
25.00–29.99	66	41.5	42	63.6	42	63.6	27	40.9
30.00 or more	18	11.3	12	66.6	9	50.0	10	55.6



Graph 2: Symptoms mentioned by auto rickshaw drivers



Graph 3: Musculoskeletal pain and treatment taken by auto rickshaw drivers

respectively, except in 7 known hypertensives. Blood pressure was normal (<120 SBP/<80 DBP mm Hg) in 37 (24.3%) of the 152 study subjects. Prehypertension (120–139 mm Hg SBP or 80–90 mm Hg DBP) was seen in 90 (59.2%) auto drivers, hypertension stage I (140–159 SBP or 90–99 DBP mm Hg) in 23 (15.1%), and hypertension stage II (>160 SBP or >100 DBP mm Hg) in 2 (1.3%). The overall occurrence of hypertension in the study group was 20.1% (7 + 23 + 2 = 32/159).

The mean RCBG value among the 149 nondiabetic drivers was 95.86 mg/dL. Among them, 116 (77.8%) drivers had normal blood sugar (RCBG <110 mg/dL). Among those who were suspected to be diabetic based on RCBG cut-off value, 24 (16.1%) had RCBG in the range of 110 to 140 mg/dL, while 9 (6%) had RCBG >140 mg/dL.

When examined for BMD, it was found that 97 (61.1%) drivers had osteopenia and 1 (0.6%) had frank osteoporosis. This has significant association with age and number of years in profession (Table 1).

Personal Habits

Mean sleeping hours were 7.4 (median 8 hours). Only 18 (11.3%) were vegetarian, while remaining 141 (88.7%) use to take mixed diet. Substance abuse was found in 95 (59.7%) of the study participants. Current tobacco users were 78 (49.05%) and 2 were past tobacco users. The pattern of type of tobacco consumption was chewing [61 (78.20%)], cigarette smoking [21 (26.92%)], Mishri and Gutka [12 (15.38%)], and bidi smoking [4 (5.12%)]. Overall smokeless consumption was found in 53 (67.94%) participants, smoking in 13 (16.66%), and both forms in 12 (15.38%). History of alcohol consumption was found in 61 (38.36%). Among them, only 9 (14.75%) take alcohol every day, 15 (24.59%) once a week, and the rest 37 (60.66%) occasionally (Table 2).

DISCUSSION

Sociodemographic Profile

The subjects in this present study were in the range of 19 to 54 years of age. The majority 82 (51.6%) belonged to

Table 2: Addictions in auto rickshaw drivers

	Age of onset	*Duration*	*Frequency*	*Quantity*
Tobacco chewing (n = 61)				
Mean	24.26 years ± 1.11	11.61 years ± 1.14	4.5 times/day ± 0.39	9.09 gm/day ± 0.60
Median	23 years	10 years	4 times/day	10 gm/day
Mode	23 years	10 years	Once a day	10 gm/day
Gutka (n = 6)				
Mean	20.16 years ± 1.42	6.33 years ± 1.20	5.5 times/day ± 1.83	25 gm/day ± 7.18
Median	21 years	5 years	4 times/day	20 gm/day
Mode	21 years	4 years	–	20 gm/day
Mishri (n = 6)				
Mean	17.33 years ± 2.8	24.5 years ± 5.61	1.33 times/day ± 0.21	16.16 gm/day ± 5.16
Median	15.5 years	30 years	Once a day	11.5 gm/day
Mode	–	30 years	Once a day	7 gm/day
Cigarette smoking (n = 21)				
Mean	26.57 years ± 1.26	7.28 years ± 1.62	2.9 times/day ± 0.53	2.9/day ± 0.53
Median	26	5 years	2 times/day	2/day
Mode	22	4 years	Once a day	1/day
Bidi smoking (n = 4)				
Mean	24.21 years ± 6.9	9.3 years ± 6.9	6.2 times/day ± 1.3	6.2/day ± 1.3
Median	18 years	3.5 years	5.5 times/day	5.5/day
Mode	18 years	–	–	–
Alcohol consumption(n = 61)				
Mean	25.11 years ± 0.75	9.39 years ± 1.38	6.16 times/month	531.31 mL per instance ± 81.09
Median	25 years	1 year	Once a month	300 mL per instance
Mode	25 years	1 year	Once a month	650 mL per instance

Class III. Similar sociodemographic profile was reported by Singh et al[12] in the auto rickshaw drivers of Agra city.

Occupational Details

The mean age to start driving was 23.5 years. Majority of the drivers in the study [90 (56.6%)] were in the profession for more than 10 years. The working hours ranged from 4 to 16 hours with the mean working hours of 10.3. Out of 158, 81 (51.6%) had felt stress up to scoring level of 4, while 77 (48.4%) had felt it 5 or more. The stress score was significantly associated with socioeconomic class. Sinha and Shasikala[13] from the study in Bengaluru reported that 412 (85.8%) of the auto rickshaw drivers work for more than 10 hours and stress was significantly associated with number of years in profession but not with the socioeconomic class.

Morbidity Profile

In the present study, only 19 (11.9%) auto drivers did not have any complaint at the time of examination, while the rest all had complained either MSD or some other systemic symptoms. Kartikeyan et al[14] showed 13.9% tempo drivers were asymptomatic, while Singh et al[12] reported that 42.0% auto rickshaw drivers in Agra were asymptomatic. It shows that majority of professional drivers seem to have had at least one or more health complaints consistently in the studies referred.

Musculoskeletal pain was the major complaint in 95 (59.74%) auto rickshaw drivers. Majority (50.3%) had lower back pain followed by knee pain (22.6%). A study among urban taxi drivers in Ghana[15] reported a prevalence of MSDs as 70.5%, with low back pain in 34.3% and knee pain in 10.0%. In a study at Guntur city,[16] low backache was the main complaint in 63.66%, followed by knee pain in 52.33% of the auto rickshaw drivers. Several studies have reported objective evidence of vertebral pathology related to an occupation as a professional driver. Whole body vibration and posture adopted in driving like sitting in driving position over a long period of time exert considerable forces on the spine and can cause backaches, neck problems, pulled muscles, and general stiffness.[17,18] In the present study, more than 10 working hours a day has been found to be significantly associated with musculoskeletal pain. Drivers are exposed to constant noise and vibration from their own vehicles and also other vehicles in their vicinity, which may impair their hearing and also contribute to disorders of the cardiovascular, nervous, and digestive systems and reduce their productivity which is compounded by MSDs. Noise also has an adverse effect on the nervous system leading to stress and increased blood pressure. A study in India has reported association between high noise levels to which drivers are exposed and high abnormal audiograms.[19] Present study of morbidity profile reaffirms this.

Based on T-score of BMD study, it was found that the 61.1% auto drivers were having osteopenia in this study. Sridhar et al[20] have reported that 6% of apparently healthy Indians <50 years have osteopenia. Rao et al[21] found that in the age group of 31 to 40 years, 29.16% males were having osteopenia, while 3.63% males were osteoporotic. Though the role of genetics and nutrition was emphasized in the above studies mentioned, the high proportion of osteopenia significantly associated with duration of profession needs further evaluation.

The overall prevalence of hypertension in the present study group was 20.1%, similar to the reported pooled prevalence of about 16 to 20% in India.[22] Lakshman et al[23] reported that 41.3% bus drivers were found to be hypertensive and 41.9% had BP in prehypertensive range. Another study on transit vehicle operators in India deals with hypertension among auto rickshaw drivers of Nagpur,[24] among whom the reported prevalence was 35.1%. The alarmingly high proportion of prehypertensives (59.2%) found in this study is a matter of concern and indicates need of advocacy of preventive measures.

Personal Habits

Tobacco use was reported in 78 (49.05%) of the present study subjects and was predominantly smokeless, chewing and Mishri. Rahaman et al[25] showed that the overall prevalence of smoking was 75.9% and concluded that the prevalence of smoking among rickshaw pullers is very high compared with that of the general population. Sudhir et al[26] found that 87.2% auto rickshaw drivers in Jaipur were using tobacco products in one form or the other, and only 12.8% never used tobacco products. Smokeless tobacco is more common in auto drivers (81.7%). Chaudhary et al[24] reported that 71.28% auto rickshaw drivers consume some form of tobacco, while 28.7% did not.

The prevalence of alcohol consumption in the present study was 61 (38.36%), which is slightly lower than the prevalence of 43.6% reported by Girish et al[27] from the study conducted among the auto rickshaw drivers in Kannur, Kerala. A multicentric study conducted by Thankappan et al[28] also reported a prevalence of alcohol use to be 40 to 50% in urban men.

LIMITATIONS OF THE STUDY

Time given by auto rickshaw drivers for the health examination and interview was variable and at times inadequate in view of their preoccupation. There is need for more engagement to combine knowledge, attitude, and practice with health examination for auto rickshaw drivers.

CONCLUSION

Auto rickshaw drivers are susceptible to various health-related problems and there is need of monitoring on an ongoing basis. Many perceive high occupational stress. Musculoskeletal pain is very common. However, the treatment-seeking behavior has gaps, for which long daily working hours over many years is a contributory factor. The presence of osteopenia at an early age is also alarming. There is a need of institutionalization of health monitoring of this relatively unorganized sector to address these issues.

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ORIGINAL ARTICLE

Cognitive Decline due to Impaired Homocysteine Metabolism in Adults on Antiepileptic Monotherapy: A Prospective Study

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ABSTRACT

Aim: Long-term antiepileptic therapy is associated with hyperhomocysteinemia (HHcy), causing cardiovascular risk and subsequent cerebrovascular and cognitive disorders. Objective of our study is to assess the effects of old and new generation drugs on homocysteine (Hcy), folate, and B12 levels in serum and to relate HHcy with cognitive decline.

Materials and methods: Drug-naïve patients recently diagnosed with epilepsy in the age group 18 to 40 years (n = 124) were recruited and grouped according to the drug prescribed: conventional drugs, like phenytoin, carbamazepine, valproate, and newer drugs, like oxcarbazepine and levetiracetam. A pretreatment analysis of Hcy, folate, and B12 was done. Mini-Mental State Examination (MMSE) was used to assess cognitive impairment, if any. After 6 months of continuous monotherapy, the analyses were repeated.

Results: Homocysteine levels were raised significantly in all the groups ($p < 0.05$ in all groups) after 6 months of therapy. Hyperhomocysteinemia (>15.1 µmoles/L) was found in 64 out of 124 patients, of which 42 were on conventional drugs. Folate and B12 registered a significant decrease in patients on phenytoin, carbamazepine, and oxcarbazepine. Cognitive decline was evaluated as drop of a point or more in MMSE score after 6 months of therapy. A significant positive relation between Hcy and cognitive decline was seen in groups on monotherapy of phenytoin [relative risk (RR) = 4.667; confidence interval (CI) = 0.7663, 28.42], carbamazepine (RR = 2.778; CI = 1.042, 7.403), and oxcarbazepine (RR = 3.316; CI = 0.9483, 11.59). An insignificant positive correlation was observed in sodium valproate and levetiracetam groups.

Conclusion: Both conventional and newer antiepileptic drugs (AEDs) may cause HHcy, leading to cardiovascular complications and cognitive decline. Subjects on sodium valproate and levetiracetam are less likely to show a decline in cognition, regardless of a rise in Hcy levels.

Clinical significance: Folate and B12 deficiency causes HHcy, which correlates positively with cognitive decline.

Keywords: Antiepileptic drugs, Cognitive decline, Hepatic enzyme inducers, Mini-Mental State Examination.

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INTRODUCTION

Homocysteine is a sulfur-containing nonessential amino acid derived from an essential amino acid methionine. Hyperhomocysteinemia in blood is indicative of atherosclerotic risk and cardiovascular disorders[1] and is observed in patients treated with AEDs.[2-8] Both atherosclerosis and cardiovascular disease have been found to be associated with cognitive impairment and dementia.[9,10] Association of HHcy with cognitive decline maybe through direct neurotoxicity[11] or through thrombosis.[12] Accumulation of Hcy is mainly due to deficiency of cofactors B12 and folate required by enzymes involved in remethylation of Hcy to methionine. Methionine is a potent donor of methyl group, which is required for synthesis of myelin, neurotransmitters, and membrane phospholipids.[13] Oral supplementation of folate, B12, and activated methionine S-adenosyl methionine lowers plasma concentrations of Hcy and reduces depressive symptoms.[14] Homocysteine in middle age is also an independent risk factor for progression of dementia and Alzheimer's later in life.[15] A positive correlation between the rate of cognitive decline and Hcy concentration has been observed in patients of Alzheimer's disease.[16] Hyperhomocysteinemia has been reported to be associated with cognitive dysfunction measured through several neuropsychological tests.[17,18]

Older AEDs like phenytoin (PHT), carbamazepine (CBZ), valproate (VPA) may affect folate and B12

metabolism but they are still prescribed due to lower costs, easy availability, and long practical experience. Comparatively newer AEDs like oxcarbazepine (OXC), levetiracetam (LEV), lamotrigine, and topiramate are less likely to affect adversely, reducing the risk of HHcy.[19] The risk of cardiovascular disease increases in epilepsy but the association with AEDs is inconclusive.[20,21] Studies on efficacy of newer AEDs over old AEDs in Indian population are few and the present study investigates changes in serum levels of Hcy, B12, and folate as an effect of AED therapy and correlation of HHcy with cognitive dysfunction in such patients.

MATERIALS AND METHODS

The study includes 124 drug-naïve patients, recently diagnosed with epilepsy, visiting the outpatient clinic at Department of Neurology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh, India. The Institutional Ethics Committee had approved final protocol of the study, which was in accordance with the guidelines of Helsinki Declaration. Written informed consent was obtained from subjects or their parents or caregivers.

Inclusion Criteria

Patients newly diagnosed with epilepsy within 18 to 40 years of age were recruited for the study. A baseline assessment of markers was done and treatment with AEDs was initiated thereafter.

Exclusion Criteria

Patients with history of ischemic stroke, hypertension, coronary artery disease, peripheral vascular disease, diabetes mellitus, pregnancy, renal and thyroid disorders, and chronic tobacco users were excluded from the study. Subjects on regular consumption of vitamins or drugs other than AEDs, like levodopa, fibrates, statins, metformin, methotrexate, and sulfasalazine, were also excluded.

Measurement of Hcy, Folate, Vitamin B12 Concentration

Following an overnight fasting period, blood was drawn between 8 and 10 AM, from the antecubital vein in sitting position. Serum was immediately separated by centrifugation and assayed for Hcy, B12, and folate. Serum total levels of Hcy folate and B12 concentrations were measured through chemiluminescent immunoassay, using kits available for Advia centaur autoanalyzer (Siemens). Normal reference ranges in fasting conditions were 5 to 15 µM/L for total homocysteine (tHcy), 3 to 17 ng/mL for serum folate, and 178 to 800 pg/mL for vitamin B12. Monotherapy with PHT, CBZ, VPA, OXC, or LEV was initiated and all assessments were repeated after 6 months. Serum Hcy levels ≥15.1 µM/L were indicative of HHcy.

Mini-Mental State Examination

Cognitive impairment was assessed using the MMSE.[19] Cognitive function was assessed with the 30-point MMSE, both at baseline and at follow-up.[22] The MMSE tests the patient with questions on orientation to time and place, registration, attention and calculation, recall, language, and visual construction. If less than four items (out of 20) were not answered by the patient, they were considered as errors.[23] If a subject did not answer four or more individual items, the total MMSE score was considered missing. A score of <26 points on the MMSE at baseline indicated cognitive impairment.[24] Cognitive decline was defined as a decrease in the MMSE score from baseline to follow-up of 1 point or more.[25]

Statistical Analysis

Data were analyzed using statistical software Prism Version 5 program (GraphPad). There were five groups of patients in accordance with the type of drug used for therapy. Discrete variables (gender, seizure type) were compared by the Pearson's Chi-square test. Continuous data (baseline and follow-up values of tHcy, B12, folate, and MMSE scores) in each group were compared using the paired t-test for normally distributed or log transformed data and the Wilcoxon signed-rank test for skewed data, which failed to exhibit normal distribution after log transformation. We used one-way analysis of variance (ANOVA) for normally distributed data and Kruskal–Wallis test for skewed data followed by Bonferroni correction, to study variation in different markers and MMSE scores between groups. Estimation of RR and 95% CI assessed the association between cognitive decline and HHcy.

RESULTS

Drug naïve subjects (n = 124) were included for the study and divided into five groups according to the drug prescribed: PHT (n = 24), CBZ (n = 22), VPA (n = 34), OXC (n = 28), and LEV (n = 16). Table 1 summarizes the demographic details of the five groups. No significant differences are observed in age ($p = 0.1042$) and gender ($\chi^2 = 4.592$, df = 4, $p = 0.3318$). There was a significant difference in seizure type among the five drug groups ($\chi^2 = 22.81$, df = 4, $p = 0.0001$).

All monotherapy groups registered an increase in tHcy levels after 6 months of continuous treatment ($p < 0.05$ in all the groups). A decrease in B12 levels was observed in PHT ($p = 0.0084$), CBZ ($p < 0.0001$), and OXC

Table 1: Demographic distribution of patients with epilepsy

	PHT (n = 24)	*CBZ (n = 22)*	*VPA (n = 34)*	*OXC (n = 28)*	*LEV (n = 16)*	*p-value between groups*
Age (years)	23.5 (1.525)	20.91 (1.347)	23.12 (1.131)	21.18 (1.069)	26.00 (1.917)	0.1042
Gender (male:female)	12:12	14:8	24:10	20:8	8:8	0.3318
Type of seizure (partial:generalized)	3:21	9:13	0:34	4:24	0:16	0.0001
AED dose (mg/day)	187.5 (13.54) (100–300)	540.9 (16.98) (400–600)	682.4 (29.39) (400–1000)	600 (8.909) (450–650)	968.8 (67.99) (500–1,500)	

Values are expressed as mean and standard error (SE); level of significance at $p < 0.05$

($p = 0.0261$) groups; similarly serum folate exhibited significant decrease with therapy of PHT ($p < 0.0001$), CBZ ($p < 0.0001$), and OXC ($p = 0.0205$) drugs. Drop of a point or more in MMSE scores was seen in groups on therapy of both conventional and newer drugs, PHT ($p < 0.0001$), CBZ ($p = 0.0009$), VPA ($p = 0.0308$), and OXC ($p = 0.0011$). Subjects on LEV registered no significant decrease in MMSE scores. One-way ANOVA revealed variation in all parameters among different groups of therapy (Tables 2 and 3).

About 51.6% (64/124) patients had Hcy levels above 15.1 µM/L, out of which 65.6% (42/64) were on therapy of conventional drugs. All drug groups, except LEV exhibited a significant drop in MMSE scores. To assess risk of cognitive decline associated with increased Hcy levels, RR along with CI (95%) was calculated. A significant positive correlation between HHcy and cognitive decline was recorded in the groups on PHT (RR = 4.667; CI = 0.7663, 28.42), CBZ (RR = 2.778; CI = 1.042, 7.403), and OXC (RR = 3.316; CI = 0.9483, 11.59), whereas subjects on VPA and LEV revealed a nonsignificant positive association (Table 4).

DISCUSSION

In accordance with previous studies, the present study shows HHcy along with decrease in vitamin levels in epileptic patients started on AED monotherapy.[2,4,5,26] Hyperhomocysteinemia is a major independent risk factor for atherosclerosis, cardiovascular, cerebrovascular, and cognitive disorders.[27-29] Our study demonstrates significant rise in Hcy levels with therapy of both conventional as well as newer AEDs. This is in accordance with previous studies conducted by Belcastro et al[4] and Kim et al.[30] In our study, vitamin B12 and folate levels show a decrease in patients on PHT, CBZ, and OXC, whereas VPA and LEV treatment shows no significant decrease in folate and B12 levels, which is in accordance with the results demonstrated in earlier studies.[31,32] Some studies have shown that adults on VPA treatment do not show a substantial decrease in folate levels,[33] while children on VPA show a decrease in folate levels.[34] In a mouse model, PHT directly decreases the activity of enzyme methyl tetra hydrofolate reductase, which is required to remethylate Hcy.[35] More studies reveal that P450 enzyme inducers like PHT and CBZ may lower folate concentrations through enhanced catabolism.[36] Antiepileptic drugs impair folic acid absorption and gastrointestinal transport and folate may serve as a cofactor in AED catabolism. In pregnant Wistar rats, VPA directly affects the activity of methionine synthase, which remethylates Hcy to methionine.[37] Hence, there are several mechanisms by which AEDs interfere with vitamin B and Hcy metabolism. A study on a transgenic mouse model of Alzheimer's disease revealed that a diet rich in methionine lowers Hcy, resulting in reduced brain amyloidosis and improved cognition,[38] though they were not confirmed in trials conducted on human patients.[39]

We observed that a higher percentage of subjects with HHcy were on enzyme inducers like PHT, CBZ, and OXC. Likewise, cognitive decline positively correlated with Hcy levels in patients on enzyme-inducing drugs.

The current study is the first to correlate HHcy with cognitive decline in newly diagnosed, drug-naïve patients started on antiepileptic treatment. Previous investigations have associated HHcy with a heightened risk of stroke and other cardiovascular conditions,[40] which are related to cognitive disturbances and dementia.[9,10,41] A study on more than 11,000 patients revealed 26% increase of depressive symptoms, with elevation in Hcy levels.[42] We observed a significant correlation between HHcy and cognitive decline in patients on monotherapy of conventional drugs like PHT and CBZ as well as those on newer drugs like OXC. The reliability of cognitive change over a time of 6 months was assessed as suggested in a study conducted by Hensel et al.[43]

This study is a prospective study, investigating the effect of five AEDs, both conventional and newer, on Hcy levels, folate and vitamin B12 levels, and subsequent cognitive decline. All these factors, we believe, are its major strengths. To our knowledge, this is the first study that correlates Hcy levels to cognitive decline as an effect of AED monotherapy.

Table 2: Total homocysteine, B12, folate levels, and MMSE scores at baseline and after 6 months of antiepileptic therapy

	PHT		*CBZ*		*VPA*		*OXC*		*LEV*	
	Baseline	*Follow-up*	*Baseline*	*Follow-up*	*Baseline*	*Follow-up*	*Baseline*	*Follow-up*	*Baseline*	*Follow-up*
tHcy (µM/L)	9.14 (0.843)	18.81 (1.78)	9.01 (0.651)	20.10 (1.27)	7.53 (0.21)	11.76 (0.62)	7.60 (2.080)	16.13 (3.203)	7.53 (0.24)	11.16 (0.64)
B12 (pg/mL)	293.40 (14.7)	267.80 (13.0)	645.6 (84.86)	359.7 (27.56)	298.1 (10.23)	277.5 (12.41)	327 (11.83)	304.40 (13.4)	315.00 (4.49)	306.30 (6.74)
Folate (ng/mL)	15.42 (0.69)	6.99 (0.39)	11.77 (2.06)	3.72 (0.06)	5.02 (0.47)	4.67 (0.27)	6.18 (0.39)	5.23 (0.13)	11.91 (2.20)	5.34 (0.27)
MMSE score	26.13 (0.26)	25.13 (0.33)	26.68 (0.20)	25.64 (0.16)	24.97 (0.32)	24.68 (0.35)	24.46 (0.41)	23.39 (0.38)	25.50 (0.44)	25.38 (0.54)

Values are expressed as mean and standard error (SE); reference ranges: 5–15 µM/L for tHcy, 3–17 ng/mL for serum folate, and 178–800 pg/mL for vitamin B12; MMSE is a 30-point score

Table 3: Variation in parameters after 6 months of monotherapy

	PHT		*CBZ*		*VPA*		*OXC*		*LEV*		
Measured variable	*Change in variable*	*p-value (within group)*	*Change in variable*	*p-value (within group)*	*Change in variable*	*p-value (within group)*	*Change in variable*	*p-value (within group)*	*Change in variable*	*p-value (within group)*	*p-value (between group)*
tHcy (µM/L)	9.6 (1.3)	0.0001*	11.1 (1.1)	<0.0001*	4.7 (0.6)	<0.0001*	8.5 (0.5)	0.0001*	4.4 (0.7)	0.0006*	0.0001*
B12 (pg/mL)	–25.6 (8.8)	0.0084*	–285.8 (63.7)	<0.0001*	–20.5 (14.4)	0.1621	–22.8 (11.4)	0.0261*	–8.7 (6.2)	0.1790	<0.0001*
Folate (ng/mL)	–8.4 (0.7)	0.0001*	–8.1 (2.0)	<0.0001*	–0.3 (0.4)	0.9318	–0.9 (0.4)	0.0205*	–6.6 (2.1)	0.0721	0.0001*
MMSE score	–1.0 (0.19)	0.0001*	–1.04 (0.20)	0.0009*	–0.29 (0.10)	0.0308*	–1.07 (0.28)	0.0011*	–0.1 (0.20)	0.5877	0.0004*

*Level of significance at $p < 0.05$; values are expressed as mean and standard error (SE)

Table 4: Relative risk and 95% CI for longitudinal cognitive decline according to presence or absence of HHcy

	PHT CBZ		*CBZ*		*VPA*		*OXC*		*LEV*	
	THcy (µmol/L)		*THcy (µmol/L)*		*THcy (µmol/L)*		*THcy (µmol/L)*		*THcy (µmol/L)*	
	<15.1	*>15.1*	*<15.1*	*>15.1*	*<15.1*	*>15.1*	*<15.1*	*>15.1*	*<15.1*	*>15.1*
% cases	25	75	45.5	54.5	64.8	35.2	32.2	67.8	81.3	18.7
% cases with cognitive decline[a]	16.7	77.7	33.3	66.7	13.6	25	22.2	73.7	15.3	66.7
RR (95% CI)	4.667 (0.7663–28.42)		2.778 (1.042–7.403)		1.833 (0.4353–7.721)		3.316 (0.9483–11.59)		4.3333 (0.9616–19.53)	
p-value	0.0147[b]		0.0274[b]		0.641		0.0166[b]		0.1357	

[a]Cases with a drop of at least 1 point in MMSE score after 6 months of AED therapy
[b]Level of significance at $p < 0.05$

Vitamins involved as cofactors in remethylation of Hcy show a decrease in concentration as a result of anti-epileptic therapy, resulting in elevated levels of Hcy in serum, though there are studies that confirm that Hcy might affect cognition independently of vitamin B status. Hyperhomocysteinemia may increase risk of cerebral micro- and macroangiopathy through pathological changes in arterial walls and blood coagulation systems.[44] A direct neuronal damage through activation of *N*-methyl-D-aspartate receptors[13] or apoptosis triggered by deoxyribonucleic acid damage has also been related with HHcy.[45]

CONCLUSION

Our study is a prospective cohort design, which shows that AEDs, both conventional and newer, are capable of causing HHcy, which may lead to decline in cognitive abilities. A dip in folate and B12 levels is observed with drugs that induce the P450 enzymes. A positive correlation between Hcy levels and cognitive decline is significant in subjects on these enzyme inducers. Subjects on VPA and LEV are less likely to show a drop in cognitive ability, regardless of a rise in Hcy levels in such individuals.

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REVIEW ARTICLE

Pancreatic Lipase Inhibitors from Plant Sources for Possible use as Antiobesity Drugs

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ABSTRACT

Pancreatic lipase inhibitors prevent the breakdown of dietary fat into fatty acids, thereby reducing their absorption in the gut. This action makes them attractive for use as antiobesity drugs. Currently, a few drugs have been approved by the Food and Drug Administration (FDA) for long-term use in the management of obesity. Over the last decades, studies have shown that many plants exhibit pancreatic lipase inhibitor activity in their extracts. The present review highlights the current status of our knowledge about lipase inhibitory activity in molecules derived from plant sources. We could possibly have a range of natural products derived from plants that could be of use in the treatment of obesity.

Keywords: Aquatic plants, Edible plants, Medicinal plants, Pancreatic lipase inhibitors.

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INTRODUCTION

Obesity is recognized as a major public health concern at the global level by the World Health Organization. It is related to a number of serious and potentially fatal diseases (Fig. 1).[1,2] A number of drugs for the treatment of obesity have been tried with varying results and adverse side effects (Table 1). Inhibition of dietary triglyceride absorption by inhibiting pancreatic lipase is an effective approach for the management of obesity (Fig. 2). Tetrahydrolipstatin (orlistat), a saturated derivative of lipstatin, which is a potent inhibitor of gastrointestinal lipase, has been approved by the FDA. However, it has severe side effects. So, discovery of other lipase inhibitors from natural sources, namely plants, which could have minimal side effects, is an attractive area of research. A number of plants have been reported as sources of pancreatic lipase inhibitory molecules (Fig. 3). Our present knowledge about plants as sources of lipase inhibitors, which could be used as antiobesity agents after proper clinical trials, is summarized in the following paragraphs.

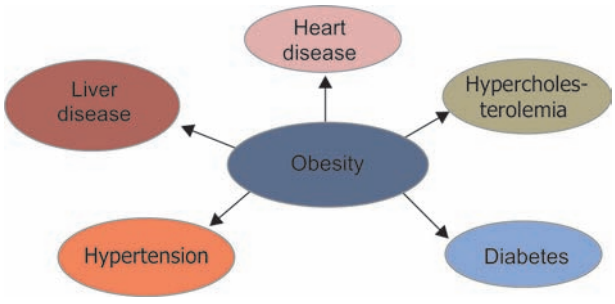

Fig. 1: Obesity and related complications (Adapted and derived from)[1,2]

Table 1: Name of drugs for obesity management and their side effects[3,4]

Name of medicine	*Side effects*
Dinitrophenol	High blood pressure, faster heart rate, palpitations, closed angle glaucoma, drug additions, restlessness, agitations, insomnia
Orlistat	Oily spotting bowel movement, oily stools
Sibutramine	Increase blood pressure, dry mouth, constipation, headache, insomnia
Rimonabant	Cause psychiatric problems
Phentermine/topiramate	Long-term effect on heart and blood vessels, mental health, cognitive side effects
Redux	Abnormal Heart rhythm, heart valve damage
Exenatide/Liraglutide	Severe nausea

GENERAL PLANTS

Various herbs and plants have been reported as having pancreatic lipase inhibitory activity (Fig. 4). Ado et al[5]

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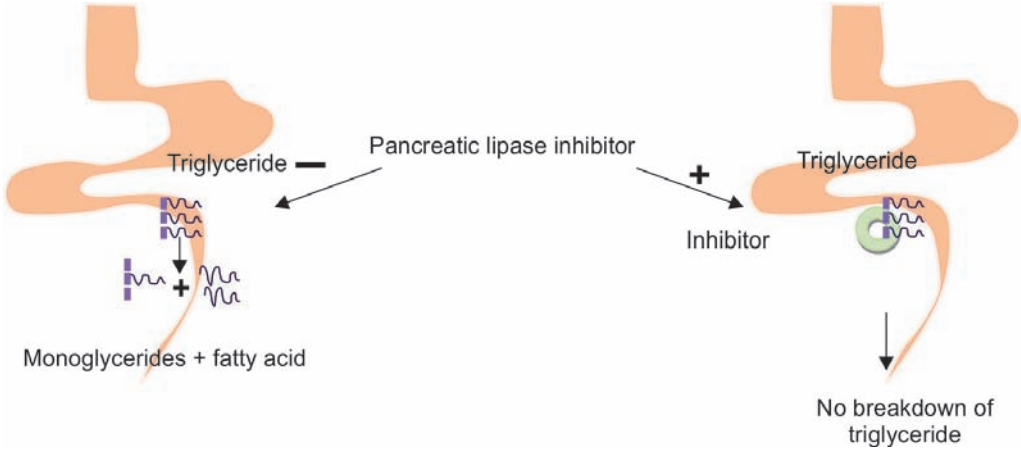


Fig. 2: Pancreatic lipase inhibition

evaluated the antilipase activity of the crude methanolic extract of different parts, such as leaves, stem, roots flower, and fruits of 98 plants collected from Malaysia. They concluded that 19.4% of extract exhibited antilipase activity more than 80%. Kim et al[6] screened 115 herbal ethanolic extracts for porcine pancreatic lipase inhibitory activity *in vitro*. Among the 115 plant extracts, 18 extracts showed an half maximal inhibitory concentration (IC_{50}) value <50 µg/mL. *Cudrania tricuspidata* showed an IC_{50} value of 9.91 µg/mL. *Cudrania tricuspidata* decreased the plasma triglycerol levels; however, these effects were weaker than that of orlistat (positive control). Teixeira et al[7]

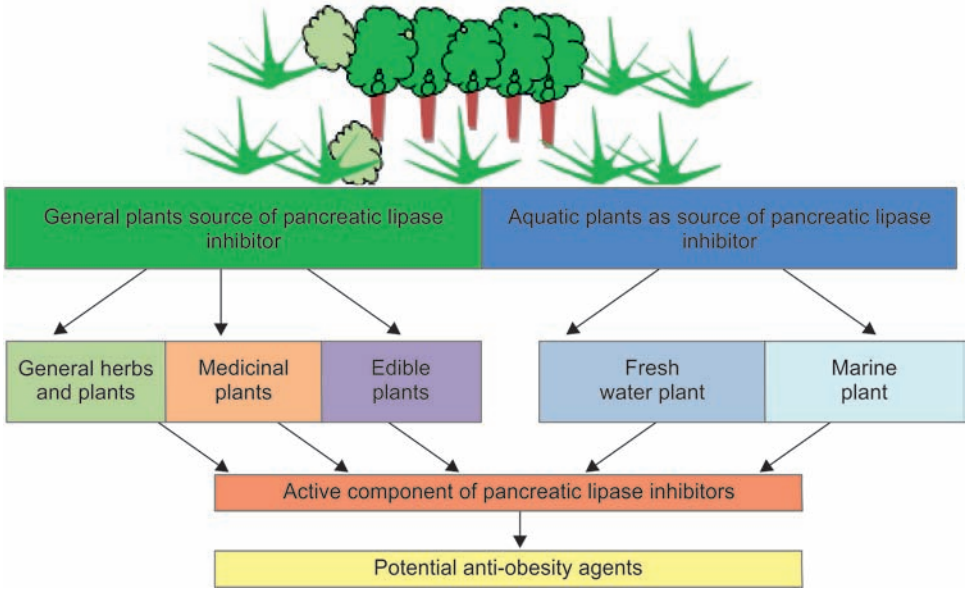
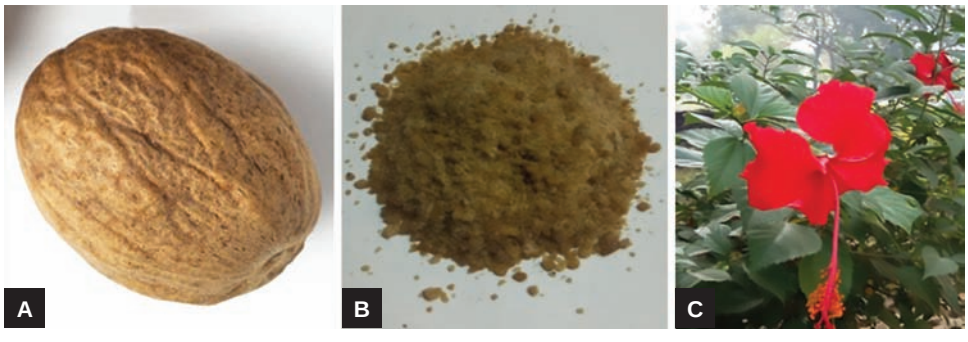


Fig. 3: Plant as source of inhibitor of pancreatic lipase



Figs 4A to C: (A) *Myristica seed*, (B) *Ferula asafoetida resin*, (C) *Hibiscus rosa-sinensis*

studied the effects of *Passiflora nitida Kunth* leaf extract on digestive enzymes and high caloric diet in rats on pancreatic lipase by using a spectrophotometric assay. The *Passiflora nitida* extract at a high concentration showed the inhibition against pancreatic lipase. Ekanem et al[8] found the inhibition activity of the pancreatic lipase of ethanolic extract of *Aframomum melegueta* (seeds) and *Spilanthes acmella* (flower buds) using the *in vitro* assay.

Roh and Jung[9] screened 400 crude plant extracts for their antiobesity activity. Among 400 plants examined, 44 extracts from plants showed a high antilipase activity using 2,4-dinitrophenylbutyrate as a substrate in porcine pancreatic lipase assay. Among 44 extracts, *Salicis radicis* cortex had the highest lipase inhibitory activity. Chompoo et al[10] screened the antiatherogenic properties of acetone extract of *Alpinia zerumbet* seeds. In this, they studied several methods to find the ability of acetone extract from pericarps, leaves, rhizomes, flowers, stem, and seed of *A. zerumbet*. Only seed showed the highest activity against the pancreatic lipase. Moreno et al[11] studied the effect of peanut shell extract on obesity. The plant extract exhibited inhibitory activity in pancreatic lipase. The concentration of 1 mg/mL showed the inhibitory effect against the pancreatic lipase. These plant extracts could prevent weight gain induced by feeding a high-fat diet to rats. Adnyana et al[12] studied the ethanolic extract of pomegranate (*Punica granatum*) leaves and found that they inhibited pancreatic lipase activity significantly. Habtemariam[13] investigated the inhibitory activity of ethanolic extract of *Cassia auriculata* (aerial part) on pancreatic lipase. The extract showed the lipase inhibitory activity which was dose-dependent. Kurihara et al[14] studied the inhibitory effect of *Cyclocarya paliurus* water extract of leaves against pancreatic lipase activity. These extracts reduced the plasma triacylglycerol level in mice when fed with lard and olive oil.

Kim and Kang[15] studied the inhibition of pancreatic lipase activity in aqueous and ethanol extract of 19 selected plants from Korea. Of these, *Illicium religiosum* (wood) and *juniperus communis* (bark) showed the highest pancreatic lipase inhibitory activity. Gholamhoseinian et al[16] measured the antilipase activity of methanolic extract of 100 plants. Among them, several plants showed an inhibitory activity between 25 and 50% on pancreatic lipase. Kwon et al[17] focused on the inhibitory activity of *Dioscorea nipponica* methanol extract on pancreatic lipase. Sahib et al[18] concluded that their pancreatic lipase inhibitory activity could be used for developing antiobesity agents. The antipancreatic lipase activity of ethanolic extract of *Centella asiatica, Morinda citrifolia,* and *Momordica charantia* was studied using different concentrations, using orlistat and epicatechin as synthetic and natural substrate as control respectively. Zhang et al[19] showed that 95% ethanol extract of *Taraxacum officinale* inhibited porcine pancreatic lipase activity. A single oral dose of this extract significantly inhibited an increase in plasma triglyceride levels.

Prashith Kekuda et al[20] studied the pancreatic lipase inhibitory study of *Artocarpus lakoocha* Roxb pericarp. These plants showed the pancreatic lipase inhibition in a dose-dependent manner. de Souza et al[21] investigated the effect of *Baccharis trimera.* They observed that aqueous and infused extract did not exhibit the effect on pancreatic lipase, whereas methanolic extract showed the inhibition activity. Oliveira et al[22] studied the chemical composition and inhibitory activity of pancreatic lipase from Brazilian Savannah *Oxalis cordata A*. leaves. The crude extract, ethyl acetate extract, and water extract of *O. cordata A.* showed an inhibitory activity. Wu et al[23] studied the inhibitory effects of Litchi flower–water extract containing phenolic acids, flavonoids, condensed tannins, anthocyanins, and proanthocyanidins, and found inhibitory effect on lipase *(in vitro).* Morikawa et al[24] studied the pancreatic lipase inhibitory activity in the flowers of *Bellis perennis.* The methanolic extract of the flowers of *B. perennis* displayed the pancreatic-lipase inhibitory activity. Griffiths[25] studied the inhibitory effects of digestive enzyme extracted from field bean (*Vicia faba*) and found that water extracts of testa of *V. faba* (colored-flower variety) were able to inhibit the activity of α-amylase, lipase, and trypsin, whereas no inhibitory activity was observed in similar extracts from white flower. Yoshikawa et al[26] studied the inhibitory activity from the flower bud of Chinese tea plant. The MeOH extract of flower buds of Chinese tea plant (*Camellia sinensis* L.) showed inhibitory effects against pancreatic lipase. Some of the compounds showed promoting effects on gastrointestinal transit in mice and inhibitory effects against porcine pancreatic lipase. Lee et al[27] studied the inhibitory effects of *Gardenia jasminoides* extract on pancreatic lipase and found that it inhibited lipase at a concentration of 2.1 mg/mL. Marrelli et al[28] investigated the potential health benefits of Mediterranean dietary plants as antiobesity agents. The formulation obtained from *Capparis sicula* showed the highest inhibitory effect on pancreatic lipase. Won et al[29] found lipase inhibitor from the roots of *Glycyrrhiza uralensis*.

MEDICINAL PLANTS

Several medicinal plants have been found to possess pancreatic lipase inhibitory activity. Bustanji et al[30] screened the methanolic extract of 23 traditional medicinal plants as antipancreatic lipase activity. These plants were collected from an area in Jordan. The inhibition of pancreatic lipase activity of the plant extract and orlistat was measured using a spectrophotometric assay. Thirteen plant extracts showed the inhibition of pancreatic lipase with an IC_{50}

ranging between 108 and 938 µg/mL. The positive control, orlistat, exhibited an IC_{50} value of 0.65 µg/mL. Ong et al[31] screened the lipase inhibitory activity of methanolic extract of different parts of 32 selected medicinal plants using porcine pancreatic lipase and p-nitrophenyl butyrate and *in vitro* assay. Out of these, a total of 4 crude extracts showed *in vitro* inhibitory activity against the porcine pancreatic lipase. Zheng et al[32] screened 37 traditional Chinese medicinal herbs. Among these, six extracts showed a moderate-to-strong antilipase activity.

Kumar et al[33] screened the lipase activity of different parts of 33 medicinal plants from India *in vitro*. The ethanolic extract of *Cassia siamea* roots showed the highest pancreatic lipase inhibition. Kaewpiboon et al[34] studied the lipase inhibitory activity of 52 plant species of Thai medicinal plant *in vitro*. Compared with all extracts, only the ethanol extract of *Coscinium fenestratum* stem showed a weak lipase inhibitory activity. Sharma et al[35] studied the antilipase activity of different parts of 75 medicinal plants. Among these, only three plants of methanolic extracts showed high antilipase activity above 80%, which were *Setaria italica (L.)* Palib., *Orixa japonica* Thunb., and *Eriochloa villosa* (Thunb.) Kunth. Lee et al[36] screened the inhibitory activity of pancreatic lipase and phosphodiesterase from Korean medicinal plant extracts. Sixty-one plants were screened for their antilipase activity. The lipase activity was determined by measuring the hydrolysis of p-nitrophenyl butyrate to p-nitrophenol and also the inhibitory effects were measured on phosphodiesterase. *Sorbus commixta* (stem, leaf) and *Viscum album* (whole plant) showed antilipase activity with an IC_{50} value of 29.6 and 33.3 µg/mL respectively. Yoshikawa et al[37] investigated some components against the pancreatic lipase and lipoprotein lipase from *Salacia reticulata* adipose tissue *in vitro* and *in vivo*. Soluble extract inhibited pancreatic lipase from the adipose tissue. Chen et al[38] showed various pancreatic lipase inhibitors in *Forsythia suspense* leaves. Sridhar et al[39] have highlighted the pancreatic lipase inhibitory activity of alkaloid-rich *Tabernaemontana divaricata L.* Kasabri et al[40] studied the antiobesity effects of *Adiantum capillus-veneris* extracts *in vivo* and *in vitro. Adiantum capillus-veneris* and its phytoconstituents inhibited the pancreatic lipase activity *in vitro. Adiantum capillus-veneris* showed pancreatic lipase inhibition. Uzun et al[41] studied the antiobesity activity of *Sempervivum davisii. Sempervivum davisii* showed a moderate pancreatic lipase inhibitory activity. Afifi et al[42] studied the biological evaluation of *Arum hygrophilum Boiss.* (Araceae). *Arum hygrophilum* exhibited pancreatic lipase inhibition in a dose-dependent manner.

Jaradat et al[43] evaluated the antilipase potential of ten traditional and medicinal plants of Palestine using organic and aqueous extracts. The inhibitory activity of aqueous extracts of *Vitis vinifera* and *Rhus coriaria* showed against pancreatic lipase. Buchholz and Melzig[44] studied 23 medicinal plants for the treatment of obesity. Methanolic and water extracts of plants were prepared for an *in vitro* study. The methanolic extracts of *Hibiscus sabdariffa L.* showed pancreatic lipase inhibitory activity with IC_{50} of 35.8 ± 0.8 µg/mL, whereas methanolic extracts of *Tamarindus indica L.* showed pancreatic lipase inhibition with the IC_{50} value of 152.0 ± 7.0 µg/mL.

EDIBLE PLANTS

Edible plants are known to be a source of pancreatic lipase inhibitor (Fig. 5). Adisakwattana et al[45] studied the inhibitory activity of aqueous extract of nine edible plants against the pancreatic lipase using orlistat as the positive control. They concluded that the *Ginkgo biloba* (ginkgo) and *Morus alba* (mulberry) have activity against the pancreatic lipase. Conforti et al[46] studied the pancreatic lipase inhibitory activity of 18 species of edible plants by monitoring the hydrolysis of p-nitrophenyl caprylate, which releases the yellow chromogen, p-nitrophenol. The aqueous extracts of *Silene vulgaris* leaves and *Portulaca oleracea* leaves showed highest pancreatic lipase inhibition. Senapaty et al[47] studied three extracts, namely petroleum ether, chloroform, and ethanolic extracts of fenugreek seeds, which were inhibitory against the porcine pancreatic lipase enzyme using *in vitro* assay. The ethanolic extract showed the highest activity compared with petroleum ether and chloroform extracts. The study showed that ethanolic extract of fenugreek seeds can be used as an antiobesity agent. Marrelli et al[48] screened the lipase inhibitory activity of hydro-alcoholic extracts of five edible plants. *Clematis vitalba L.* and *Lepidium sativum L.* showed the highest IC_{50} value of 0.99 ± 0.18 and 1.28 ± 0.29 mg/mL respectively. Moreno et al[49] assayed the inhibitory effect of grape seed on lipase. The ethanolic plant extract inhibited the pancreatic lipase activity. Han et al[50] studied the pancreatic lipase inhibitory activity of water extract of *Juglans mandshurica* fruit. This extract strongly inhibited pancreatic lipase in a dose-dependent manner. Moreno et al[51] investigated the inhibitory effect of ethanolic extract of *Mangifera indica* on pancreatic lipase. The plant extract showed inhibition against pancreatic lipase. The plant extract reduced the isoproterenol-stimulated lipolysis in 3T3-L1 adipocytes. Deshpande et al[52] investigated the antiobesity activity of *Ziziphus mauritiana Lam* bark powder (ZMBP) on high-fat-diet-induced obesity in a study done on rats. The dual-energy X-ray absorptiometry analysis was carried out for 90 days; at the end of this treatment, it showed a reduction in body weight over the standard drug treatment; it was due to the polyphenolic compound of ZMBP. Morikawa et al[53] investigated the antihyperlipidemic constituents from the

Figs 5A to E: (A) *Cinnamomum zelyanicum (bark)*, (B) *Syzygium aromaticum (bud)*, (C) *Trigonella foenum-graecum (Fenugreek) seeds*, (D) *Mangifera indica,* (E) *Moringa sp. (leaves)*

bark of *Shorea roxburghii*. They were found to suppress the plasma triglyceride elevation in olive oil-treated mice and also inhibited pancreatic lipase activity.

Tsujita et al[54] examined the lipase inhibition activity of citrus pectin. Lower molecular weight pectin strongly inhibited lipase activities. At acidic pH, i.e., below pH 7.0, a strong lipase inhibition was observed in pectin. Mhatre et al[55] studied the *in vitro* pancreatic lipase activity of some edible spices. A number of extracts showed pancreatic lipase inhibitory activity. *Zanthoxylum armatum* extract showed the lowest IC_{50} value of 9.0 µg/mL. Isaksson et al[56] have reported the effects of pH and duodenal juice viscosity on the inhibition of lipase and amylase enzymes. They found that pectin of high methylic etherification and guar gum reduces the lipase and amylase activity by lowering the duodenal juice pH, making it viscous. Lee et al[57] prepared methanolic and ethanolic extracts of *Phellinus linteus*. The methanol extracts of *P. linteus* showed a lipase-inhibiting activity. Toma et al[58] investigated the inhibitory activity of ethanolic extract of leaf *Moringa stenopetala* on pancreatic lipase. These plants showed a slight inhibition against pancreatic lipase. Kaisoon et al[59] studied the edible flowers of Thailand. *Tagetes erecta*, *Cosmos sulphureus,* and *Bougainvillea glabra* extracts inhibited the activity of pancreatic lipase.

AQUATIC PLANTS

Liu et al[60] studied the inhibition of pancreatic lipase in *Nelumbo nucifera* leaves. *In vitro* biochemistry study of *N. nucifera* leaves showed the highest pancreatic lipase inhibitory activity against porcine pancreatic lipase. Ono et al[61] assessed the effects of aqueous and ethanol extracts of *N. nucifera* leaves on pancreatic lipase. The extract showed a lipase inhibition activity and it also promoted lipolysis in 3T3-L1 adipocytes. The *in vivo* results showed the decrease of plasma triacylglycerol level at 1 hour after the oral administration of lipid emulsion in the group treated with the plant extract. Kim et al[62] studied the biological activities of *Lythrum salicaria.* They concluded that ethanolic and water extract of *L. salicaria L* exhibited the antiobesity activity.

ACTIVE COMPONENT AND POTENTIAL ANTIOBESITY AGENTS

A wide range of plants have been reported for pancreatic lipase inhibitory activity and, in some cases, active components have been identified (Table 2). Nakai et al[63]

Table 2: Some active components of plants for pancreatic lipase inhibition

Active components		
Polyphenols	Flavan-3-ol	Phenol
Saponin	Flavonol	Anthocyanidins
Ellagitannins	Flavonoids	Hydroxycinnamic acid
Hydroxybenzonic acids	Ligans	Proanthocyanidins
Alkaloids	Triterpenoidal saponin	Sessiloside saponin
Chiisanoside saponin	Benzylisoquinoline	Procyanidin

studied the inhibitory effects of oolong tea polyphenols on pancreatic lipase *in vitro. Epigallocatechin 3-O-gallate*, one of the major polyphenols in green tea, showed lipase inhibition with an IC_{50} 0.349 µM, whereas *flavan-3-ol digallate* esters showed higher activities of lipase inhibition with an IC_{50} of 0.098 µM. Sugiyama et al[64] studied the oligomeric procyanidins in apple polyphenol. The oligomeric procyanidins contained in apple polyphenols inhibited the triglyceride level by inhibiting the pancreatic lipase in both mice and humans. Buchholz and Melzig[65] showed the pancreatic lipase inhibitory activity in polyphenolic compounds. The class of polyphenols is an important source for the pancreatic lipase inhibitors. Phenols, saponin, flavonols, anthocyanidins, ellagitannins, flavonoids, hydroxycinnamic acids, hydroxybenzoic acids, lignans, and proanthocyanidins were different phytochemicals, which have been found as components of pancreatic lipase inhibition. Karu et al[66] isolated saponins from *ginseng* root powder and studied their inhibitory activity on the absorption of dietary fat in mice. Consumption of *ginseng* saponins suppressed the expected increase of body weight and plasma triglyceride level. *Ginseng* saponin inhibited the pancreatic lipase activity. Lee et al[67] studied the pancreatic lipase inhibition by c-glycosidic flavones isolated from methanolic extract from the leaves of *Eremochloa ophiuroides*. It showed potent inhibitory effects on pancreatic lipase with an IC_{50} value ranging from 18.5 ± 2.6 to 50.5 ± 3.9 µM.

Ivanov et al[68] isolated the novel catechin from *Bergenia rhizomes* that has pronounced lipase-inhibition activity. An aqueous ethanol extract of *Bergenia crassifolia* rhizomes strongly inhibited the pancreatic lipase *in vitro*. The hydrolysable tannins (+)-catechin 3, 5-di-O-gallate compound strongly inhibited HPL. Birari et al[69] found pancreatic lipase inhibitory alkaloids from *Murraya koenigii* leaves. Twenty-one different plants were screened against pancreatic lipase inhibition. Only *M. koenigii* leaves showed antilipase activity greater than 80%. Four different alkaloids were isolated from the ethanolic extracts of *M. koenigii.* Xu et al[70] studied the *in vitro* inhibitory effects of triterpenoidal saponin on pancreatic lipase. The water extracts of *Platycodi radix* were prepared. All fractions of saponin showed a pancreatic lipase inhibitory activity *in vitro.* Based on further purification of active compound triterpenoid saponin showed the highest pancreatic lipase inhibitory activity. Yoshizumi et al[71] studied the pancreatic lipase inhibitory activity of *Acanthopanax sessiliflorus* leaves. Using a hot water extract of *A. sessiliflorus* leaves, saponins were isolated. From these saponins, only sessiloside and chiisanoside inhibited the pancreatic lipase activity *in vitro.* The lupane-type saponins from *A. sessiliflorus* can be used for the treatment of obesity. Upadhyay et al[72] studied the inhibitory activity of *Moringa* seed protein and found that it inhibited the pancreatic lipase activity.

CONCLUSION

An overview of current literature about the plant sources of pancreatic lipase inhibitors has been presented. So far, the results have been very encouraging. In due course of time, lot of new antiobesity drugs derived from plant sources, which are potent and safe pancreatic lipase inhibitors, are likely to be found and after due clinical trials, these will be put into clinical practice. Hopefully, they will be effective and free of serious side effects.

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CASE REPORT

Medical Management of Cervical Ectopic Pregnancy

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ABSTRACT

A 27-year-old woman, primigravida, presented with a history of 8 weeks of amenorrhea and painless vaginal bleeding. Pelvic examination revealed ballooned-up cervix smeared with blood. The urine pregnancy test was positive. Ultrasonography showed a gestational sac of approximately 0.6 cm implanted in the anterior wall of cervix but the uterus was empty. The patient was diagnosed as a case of cervical ectopic pregnancy based on clinical and sonographic findings. As this was her first pregnancy, it was decided to follow a conservative approach. She was treated with methotrexate (MTX) six doses on alternate days with folinic acid, administered intramuscularly. The patient made a remarkable recovery. She stopped bleeding after 1 week of MTX therapy, the gestational sac was not seen after 30 days, and the beta human chorionic gonadotropin (hCG) level decreased continuously and was undetectable after 55 days of MTX therapy.

Keywords: Cervical pregnancy, Ectopic pregnancy, Methotrexate.

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INTRODUCTION

Following fertilization and fallopian tube transit, the embryo normally implants in the endometrial lining of the uterine cavity. The implantation of embryo other than uterine cavity is considered ectopic pregnancy. Ectopic pregnancies comprise of 2% of all first-trimester pregnancies, but accounts for 6% of all pregnancy-related deaths. Among the ectopic pregnancies, cervical pregnancy is a rare entity and the one which is difficult to diagnose and treat. The incidence of cervical pregnancy varies from 1 in 2,400 to 1 in 50,000 pregnancies. The diagnosis of cervical pregnancy is often confused with incomplete abortion.[1] The patients generally report with severe degree of painless vaginal bleeding. Hysterectomy is often required as life-saving measure. However, over the last decade, medical management with systemic MTX has been used for cervical pregnancy with considerable success.

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CASE REPORT

A 27-year-old patient presented with the complaint of bleeding per vagina for past 15 days. On examination, pulse of 90/min, blood pressure of 110/70 mm Hg, no pallor, or pedal edema were observed. On per vaginal examination, a healthy vagina with cervix ballooned up and smeared with blood was observed, and uterus was of 8 weeks' size. Initial investigations revealed hemoglobin (Hb) of 8.7 gm%, total leukocyte count (TLC) of 8,200/mm^3, platelet count of 3.2 lac/mm^3, and beta hCG value of 2,282 mIU/mL. Following day, the patient reported with heavier bleeding. Ultrasonography was advised. Transvaginal sonography findings suggested a gestational sac of 0.6 cm diameter attached to anterior wall of cervix, fetal pole was seen with no cardiac activity. Uterus was normal in size and shape with decidual reaction of 8.8 mm. Both ovaries were normal. Correlating all the findings, the diagnosis of cervical pregnancy was made. The patient wanted to conserve fertility, therefore medical management was preferred. It was decided to put the patient on MTX and folinic acid regimen.

The following treatment schedule was followed: injection MTX [64 mg intramuscular (IM), 1 mg/kg body weight], 6 doses were given every alternate day, alternating with injection leucovorin (folinic acid) (7 mg IM, 6 doses). Keeping in mind that cervical pregnancy may give rise to sudden catastrophic hemorrhage, the patient was kept in hospital for 15 days for observation. However, during the chemotherapy, bleeding decreased considerably. Pelvic examination done on 30th day of chemotherapy showed normal cervix, uterus, and adenexa. Also, there was no evidence of gestational sac on ultrasound scan. The other lab investigations done on same day revealed Hb at 10.7 gm/dL, TLC of 5.24/mm^3, platelet count of 2.2 lac/mm^3. She was followed up with serum beta hCG values. The beta hCG values after initiation of chemotherapy were 858.5 mIU/mL on 15th day, 550 mIU/mL on 22nd day, 200 mIU/mL on 30th day, and negative after 55 days.

With normal clinical and ultrasound findings and negative serum beta hCG levels, the patient was considered cured after 55 days of initiation of chemotherapy. She was advised contraception for 6 months in the form of oral contraceptives in view of use of MTX.

DISCUSSION

The cervical pregnancies constitute less than 1% of all ectopic pregnancies. Unlike intrauterine pregnancy, the evacuation of the pregnancy by curettage does not always stop the bleeding because there is little contractile muscle in the cervix. There are two main treatment options for cervical pregnancy: Surgical and medical. The surgical interventions include cervical cerclage, intracervical balloon tamponade of the cervix, vaginal packing, local hemostatic sutures, curettage, ligation of the descending branches of the uterine arteries, and bilateral hypogastric artery ligation.[2,3] Often uncontrolled bleeding necessitates emergency hysterectomy.[4] Among the medical treatment options, the most common is systemic or local administration of MTX.[5,6] The presence of fetal cardiac activity or advanced gestational age is associated with higher rates of treatment failure.[6] During MTX administration, an increase in bleeding pattern or the reappearance of vaginal bleeding may require additional intervention. Any profuse bleeding during therapeutic measures with consequent hemodynamic instability also necessitates emergency surgical intervention.

In our case, in an attempt to preserve fertility, we chose a conservative approach. Six doses of MTX alternating with folinic acid were given to the patient. Bleeding per vagina stopped after 1 week of initiation of treatment. Ultrasound was negative for cervical pregnancy after 30 days. The serum beta hCG became negative after 55 days of treatment. Although the resolution of ectopic pregnancy in our case was slow, it helped in conserving the uterus.

CONCLUSION

The use of MTX for cervical pregnancy is safe and effective in selected patients. It is simple to administer and it also preserves fertility.

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CASE REPORT

Attitude of Parents to Carrier Screening for Genetically Transmitted Diseases in India

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ABSTRACT

Carrier screening plays a pivotal role in controlling transmission of genetic abnormalities through generations. Irreparable genetic aberrations are preventable by understanding the nature of alterations and nurturing prenatal/pre-implantation diagnosis. Retrospective carrier screening of blood-linked relatives not only prevents transmission to future generations but also helps in understanding the impact on future health. However, lack of cooperation of the parents/family members posts barriers for carrier screening, and thus, abnormalities occur in recurrent pregnancies. Parental attitude toward carrier screening has been discussed in this paper based on a case having unbalanced karyotypic abnormality with a chimeric extra chromosome (47,XX,+mar). This female baby was born with choanal atresia (CA), anteposed anus, and atrial septal defect to nonconsanguineous parents as second child. Owing to common problem of difficulty in breathing in father and the elder son, it could have been speculated that the father was the carrier of some genetic condition, which contributed to clinical expression; however, the parents were reluctant to undergo screening. Since there was aneuploidy with a rearranged chromosome, the possibility of normal karyotype in the parents cannot be expected, and thus, karyotyping was essential for the other child too. That was also refused. Refusal of screening by the family will necessarily put future generations of the family at risk of inheriting CA.

Keywords: Carrier screening, Choanal atresia, Chromosome aberration, Genetic testing, Prevention of genetic defects.

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INTRODUCTION

The balanced rearrangements resulting in alterations in sequence/structure of genes/chromosomes may not pose serious phenotypic or clinical expression. However, likelihood of four types of genetic combinations in gametes of carriers might lead to severe to fatal outcome in the offspring.[1-3] When a child is born with congenital deformities or grows with delayed milestones and/or mental retardation, and is diagnostically detected to have chromosomal anomaly, parental genetic testing is considered essential to exclude or confirm their carrier status.[2,3] A carrier is otherwise a healthy individual not affected with clinical expression; however, he/she may transmit one copy of recessive mutation or a complete balanced chromosomal translocation. When both partners are identified carriers of a similar recessive mutation, they have 1 in 4 (25%) risk in each pregnancy of having a child with disease manifestation. In case of X-linked disorders, half of the male offspring of a carrier mother will be affected clinically, whereas girls will be asymptomatic carriers. Therefore, the primary objective of carrier screening is to create alertness in the family for preventing possible health risks in offspring of present and future generations as a result of clinical expression of prevailing genetic mutation, and, thus, should be compulsory for families having an affected member.[4] However, carrier screening is optional for people who do not have any prior knowledge/history about risk of recessive or suspected genetic disorders.

We report a child born with CA who was found to have unbalanced chromosomal rearrangement and whose parents were not willing for carrier screening.

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CASE HISTORY

Parental attitude toward carrier screening is the focus of analysis in the present report, based on the history of a female child born to nonconsanguineous parents with a 7-year-old sibling. Antenatally, oligohydramnios was the only history of this conception. The 2.8 kg baby was born uneventfully and cried immediately after birth but developed respiratory distress and needed O_2 shortly afterward. Nasogastric tube could not be passed through both the nostrils leading to a presumptive diagnosis of bilateral CA (Box 1). With help of ear, nose, and throat surgeon, the nasogastric tube could be placed through left nostril with difficulty. Distress then gradually decreased. The baby was given phototherapy for neonatal hyperbilirubinemia on 3rd day. Two other

Box 1: Genetics of CA

Choanal atresia (OMIM # 608911) is a congenital defect with 2:1 female:male ratio, exhibited by obstruction in the posterior nasal apertures with bilateral or unilateral presentation wherein bilateral CA requires medical emergency at birth. It is occasionally associated with coloboma/heart defects/mental retardation and growth impairment. Infants with bilateral CA are at an increased risk of having cerebral abnormalities, developmental delay, laryngeal tracheomalacia, and subglottic stenosis, and also with life-long nasal complications, nasal stuffiness, sleep apnea, and rhinorrhea, which may require repeat correction surgeries. Phenotypically, affected infants with either unilateral or bilateral CA can have depressed nasal bridge or mid-face retraction, craniosynostosis, and more similarities with CHARGE (coloboma, heart defects, atresia choanae, retarded growth and development, genital anomalies, ear anomalies) syndrome,[5-7] which is linked to an autosomal dominant mutation in the chromodomain helicase DNA binding protein 7 (CHD7) gene at chromosome 8q12.1.[7-10]

A candidate gene for CA has been described in the coding region of CHD7 of 9003 bp, corresponding to a translated amino acid sequence of 3000 aa.[11,12] The present case with ASD and CA may display mutations in the CDH7 gene, and the unbalanced marker chromosome could be a recombinant product of chromosome 8 (which was described with a microdeletion in CHARGE syndrome)[13] and an acrocentric chromosome. Choanal atresia is thought to be a multifactorial disorder and about 8% of cases are hereditary, although some studies have suggested single gene models that include both autosomal dominant and recessive patterns of transmission.[14] More commonly, CA is found to occur sporadically and to recur infrequently in siblings and in subsequent generations.[14-16]

abnormalities were noted, viz., anteposed anal opening and a systolic murmur. Subsequently, two-dimensional echocardiography detected arterial septal defect (ASD). The baby did well after opening up of left-sided atresia, though noisy breathing persisted.

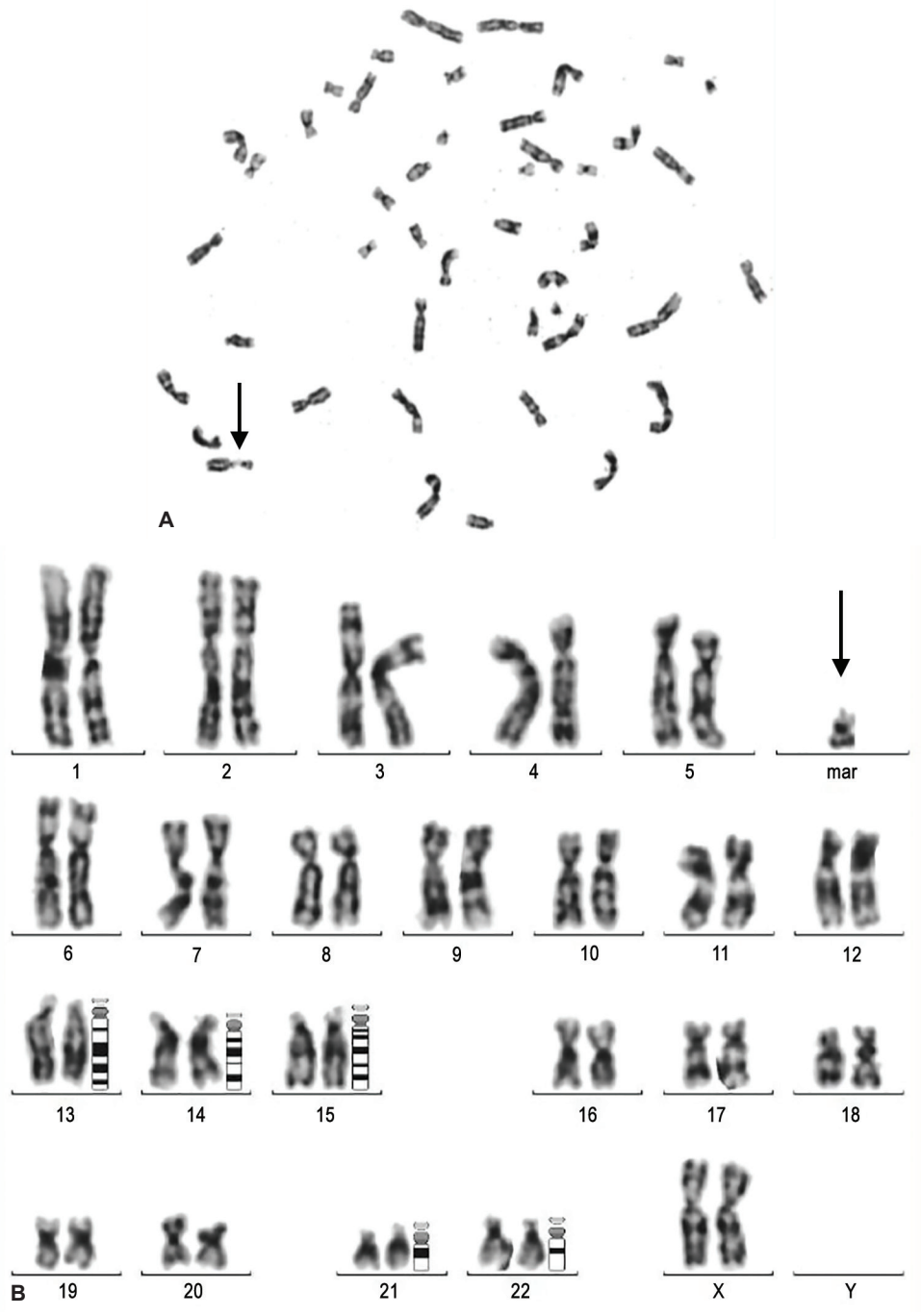
In view of the three physical deformities, karyotyping was considered as the first line of genetic diagnosis for exclusion of chromosomal association with the clinical condition. Routine conventional cytogenetic analysis was carried out on day 6 after birth, following standard phytoheamagglutinin-stimulated culture of the peripheral blood in serum-supplemented Roswell Park Memorial Institute 1640 medium (GIBCO, USA) for 72 hours at 37°C.[2] G-banding karyotyping using IKAROS imaging software (MetaSystems, Germany) detected an abnormal karyotype with 47,XX,+mar in all 25 metaphases examined (Figs 1A and B). The marker was confirmed as an acrocentric chromosome from its participation in acrocentric association with "D/G" group chromosomes (Fig. 1A); however, it was not a complete "D/G" group member but a recombinant one. It was a rearranged chimeric chromosome wherein an acrocentric chromosome was a partner, which can be called as an unbalanced translocation. This rearrangement indicates partial trisomy of two different chromosomes and appeared as the marker in the present case.

Father had nasal deformity since birth for which he had undergone surgical correction. The 7-year-old sibling also used to suffer from chronic cold and cough due to nasal blockade. Therefore, one common clinical symptom was identified in both children with a possibility of paternal transmission. The father was explained about the nature of the abnormality present in the newborn baby, in view of which necessity of carrying out his and his wife's stepwise karyotyping was explained to him. He was also told that if one of the parents was detected to have the chromosomal aberration, his elder child will also require karyotyping. He was not willing. His greater concern was about the mental development of their newborn child because the elder sibling is "very intelligent." The family declined for further counseling and testing of themselves and their second child stating that "we have already so much of tension and we do not want to increase it further."

It was apparent that meiotic nondisjunction in one of the parents must have occurred resulting in aneuploidy with an extra chromosome in the proband. Chance of parents carrying normal karyotype was least possible in the present case. In case it turned out to be normal, it would have been due to a de novo mutation during gametogenesis in one parent. So normal karyotype would have been found in both parents and also the elder sibling. Neither maternal nor complete family history of either side of both the parents could be collected due to lack of their cooperation. Their refusal was not due to financial constraints because financial grant was provided by the institution.

DISCUSSION

Genetic screening and testing are poised to play a great role in reducing incidence of genetic defects. Unfortunately, as the present case shows, there is severe lack of awareness in the general public. They do not cooperate fully for carrier screening even if offered free. Grinzaid et al[17] reported that despite efforts by medical and Jewish communities, many people of those communities in the reproductive age group remain unaware of the benefits of genetic screening, thus carrying the risk of bearing children with genetically transmitted diseases. Morgan et al[18] and Qureshi et al[19] also reported lack of awareness in the public about genetic screening during their surveys of screening programs for genetic diseases. In cases of known genetic diseases, prenatal or pre-implantation genetic diagnosis will cause definite reduction of the prevalence of these diseases, as demonstrated by studies of Cousens et al[20] and Dondrop et al,[21] who reported 90% reduction in the incidence of birth of children with Tay–Sachs disease in the Askenazi



Figs 1A and B: Karyotype (47, XX, +mar) of the proband with unbalanced chromosomal rearrangement: (A) Metaphase shows the marker chromosome in an acrocentric association; and (B) karyogram shows the marker chromosome

Jewish community as well as in the incidence of hemoglobinopathies.

In addition to financial implications and lack of awareness, which dissuade prospective parents in India to undergo carrier screening for genetic diseases, another important factor is fear of stigmatization and psychological trauma, if they test positive for genetic mutations. These perceived fears have to be alleviated by good prescreening and postscreening counseling. In India, 90% of medical colleges do not have medical genetics and genetic counseling in their curricula.[22]

American College of Obstetrics and Genecology[23] and American College of Medical Genetics[24] have described in detail as to how genetic counseling must be carried out. The individuals undergoing genetic testing must be explained about the purpose, importance, and appropriateness of the tests. They must be told about what information is expected from the tests, their sensitivities and specificities, possible consequences of mutations, and possible risk of psychosocial trauma and stigmatization. A proper "informed consent" should be taken after thoroughly educating the subjects about purposes and

limitations of the tests and the potential consequences of positive tests which will help them to make informed decisions.[25]

To conclude, the present case illustrates that to reduce the incidence of genetically transmissible diseases, we must spread awareness in common public about importance of carrier screening, so that their attitude toward screening becomes positive. Also medical genetics and genetic counseling must be made a part of curriculum in all medical colleges. Authorities at national level must frame policies to achieve these goals.

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CASE REPORT

Spontaneous Chylothorax

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ABSTRACT

Chylothorax is the occurrence of chyle (lymph) in the pleural cavity due to damage to the thoracic duct. Leakage of chyle and lymph leads to significant loss of essential proteins, immunoglobulins, fat, vitamins, electrolytes, and water. The presence of chylomicrons and a triglyceride level >110 mg/dL in the aspirated pleural fluid confirms the diagnosis of chylothorax. Identifying the etiology using different diagnostic tests is important in planning treatment. Definitive therapy consists of obliteration and prevention of recurrence of chylothorax. We report a case of chylothorax which resolved spontaneously with conservative management.

Keywords: Lymphoscintigraphy, Pleural fluid triglycerides, Thoracic duct.

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INTRODUCTION

"Chylothorax" is the occurrence of chyle in the pleural space and is due to damage or blockage of the thoracic duct. Triglyceride levels greater than 110 mg/dL are highly suggestive of a chylous effusion. Triglycerides below 50 mg/dL virtually exclude the diagnosis of chylothorax. "Pseudochylothorax" or "cholesterol pleurisy" or "chyliform effusion" is a fluid which has a very high content of cholesterol. Both conditions have a common characteristic that the pleural fluid is usually thick, opalescent, and whitish or the color of café-au-lait or chocolate milk, due to its very high fat content. Diagnosis is made by analysis of the pleural fluid. Cholesterol values should always be measured simultaneously, since high triglyceride levels can occur in pseudochylothorax but are associated with elevated cholesterol levels (>200 mg/dL).[1] The thoracic duct is the common channel draining lymphatic fluid from the body to the venous system with exception of the right face and neck, right arm, right thorax, right lung, and the convex surface of the liver. The thoracic duct originates in the cistern chyli anterior to the second lumbar vertebra (T10–L3) and passes to the aortic hiatus and ascends posterior to the esophagus between the aorta and azygous vein to the right of the midline. At the 6th thoracic vertebra, it crosses to the left side and ascending till the neck terminates into the posterior confluence of the left jugular and subclavian veins. The duct has various valves along its course. The primary function of thoracic duct is to transport chyle and lymph from the intestines, liver, abdominal wall, and lower extremities into the systemic venous system. Chylothorax is the occurrence of chyle (lymph) in the pleural cavity due to damage to the thoracic duct. Leakage of chyle and lymph leads to significant loss of essential proteins, immunoglobulins, fat, vitamins, electrolytes, and water. The presence of chylomicrons and a triglyceride level >110 mg/dL in the aspirated pleural fluid confirms the diagnosis of chylothorax. Chylothorax is a rare disease with varied etiologies and challenges in management based on each case. We discuss a rare spontaneously resolving traumatic chlyothorax.

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CASE REPORT

A 37-year-old man was apparently alright 2 months back when he developed right-sided pleuritic chest pain and breathlessness which was MMRC (Modified Medical Research Council) grade I and which progressed to grade II. There was no history of cough or fever; however, he complained of weight loss and fatigue. He was a plumber by occupation, chronic tobacco chewer, and occasional alcohol consumer. He was hospitalized in a private nursing home for 5 days where he was managed with intercostal tube drainage which drained approximately 1 to 1.5 L of fluid/day and subsequently referred to us for further evaluation and management. On clinical examination, his vitals were within normal limits. Respiratory system examination suggested a right pleural effusion. Other systemic examination showed no abnormality. On evaluation with chest roentgenogram and ultrasonography of thorax, there was marked right-sided pleural effusion. On diagnostic thoracocentesis, light pink-colored pleural fluid was aspirated which on cytobiochemical analysis revealed an exudate (protein—5.3 gm/dL, total cell count—1,020/mm^3) with lymphocyte predominance and normal adenosine deaminase. Further analysis

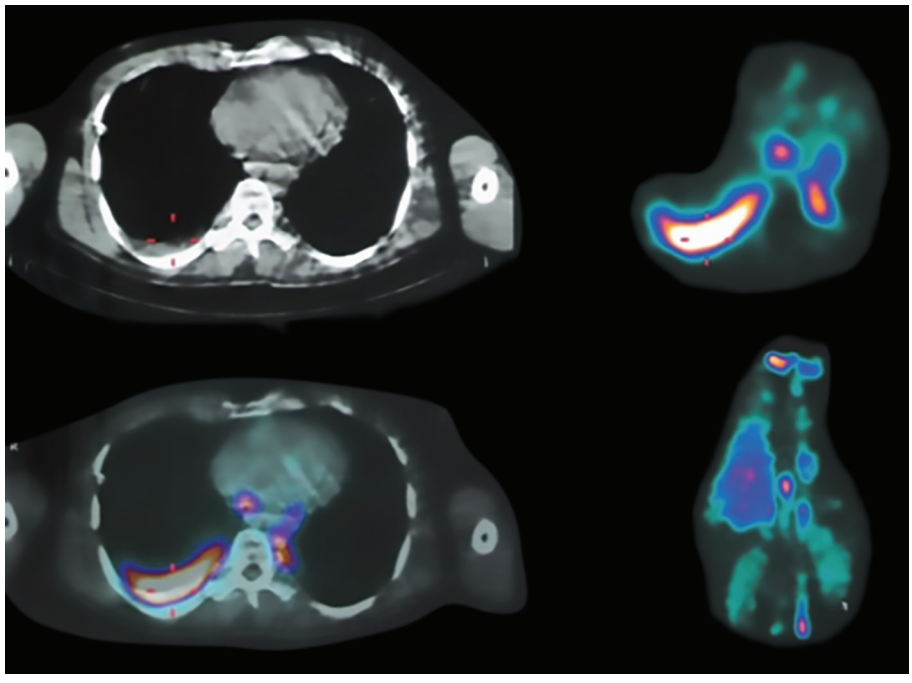


Fig. 1: The SPECT image showing significant tracer uptake in right pleural cavity and abnormal dilated lymphatic channels in the left prevertebral, paraaortic, left supraclavicular regions with mild tracer up

reported high triglycerides—2,294 mg/dL—and normal cholesterol—34 mg/dL. The pleural fluid showed no evidence of malignant cells on cytology and was negative for Gram-positive, -negative organisms, and acid-fast bacilli. In view of the clinicoradiological and pleural fluid analysis, the diagnosis of chylothorax was made. On detailed enquiry for the probable etiology, the patient gave past history of fall from bike 5 months ago which was managed conservatively. Contrast-enhanced computed tomography (CECT) of thorax revealed a right pleural effusion. To find the exact site of leakage and decide further management, a single-photon emission computerized tomography (SPECT) imaging with lymphoscintigraphy (Figs 1 and 2) was done. The procedure details were as follows: 0.5 mCi of ^{99m} Tc-sulfur colloid filtered through Millipore filter was injected in web spaces in both feet, and static images of feet, knee, anterior pelvis, and abdomen were acquired in succession with delayed views. Initial dynamic and 1 hour delayed whole body image showed good ascent of tracer. At 2 hours postcontrast injection, significant diffuse uptake of tracer in right thoracic region and abnormal increased uptake in left supraclavicular region and in a linear irregular pattern in the left side of chest were noticed. The SPECT images showed significant tracer uptake in right pleural cavity and abnormal dilated lymphatic channels in the left prevertebral, para-aortic, left supraclavicular regions with mild tracer uptake in the left pleural cavity. This suggested abnormal lymphatic collection in right pleural cavity and abnormal dilated lymphatic channels in the left prevertebral, para-aortic, left supraclavicular regions with mild tracer uptake in the left pleural cavity. Findings represented lymphatic leak secondary to obstruction in the thoracic lymphatic pathway though the exact site of obstruction could not be ascertained. The patient was kept under observation and was discharged with diet modification in the form of diet containing only medium-chain triglycerides and ambulatory intercostal tube drainage. On follow-up, the pleural fluid drainage kept on decreasing and finally stopped within 15 days following which the intercostal tube was removed.

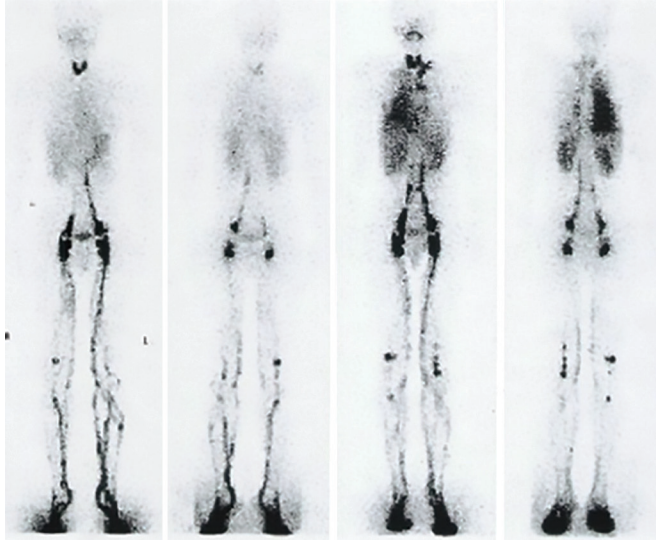


Fig. 2: Lymphoscintigraph image (2 hours post injection) showing significant diffuse uptake of tracer in right thoracic region and abnormal increased uptake in left supraclavicular region and in a linear irregular pattern in the left side of chest

DISCUSSION

The composition of normal chyle is summarized in Table 1.[2] The normal daily flow of chyle in an adult is around 2 L.[3,4] The flow of chyle increases substantially with intake of food and drink, and decreases to a small trickle with starvation. With repeated thoracocentesis or continuous drainage of a chylothorax, large amounts of fat, proteins, and lymphocytes are lost, quickly resulting in negative effects on the patient's nutritional and immunological status. The causes of chylothorax are enumerated in Table 2. Our patient had right-sided pleural effusion. On thoracocentesis, a pink-colored pleural fluid was aspirated. Usually gross appearance of pleural fluid is milky in case of chylothorax, but variable gross appearance of pleural fluid has been reported.[1] Chylothorax in our case was proved on analysis of pleural fluid which revealed high triglyceride content in the range of 2,000 mg/dL (>110 mg/dL) and normal cholesterol levels.

Table 1: Composition of normal chyle

Component	*Concentration per (100 mL)*
Total fat	0.4–6 gm
Total cholesterol	65–220 mg
Total protein	2.21–6 gm
Albumin	1.2–4.1 gm
Globulin	1.1–3.6 gm
Fibrinogen	16–24 gm
Sugar	48–200 gm
Electrolytes	Similar to plasma
Cellular elements	
Lymphocytes	400–6,800 per µL
Erythrocytes	50–600 per µL
Antithrombin globulin	25% of plasma level
Prothrombin	25% of plasma level
Fibrinogen	25% of plasma level

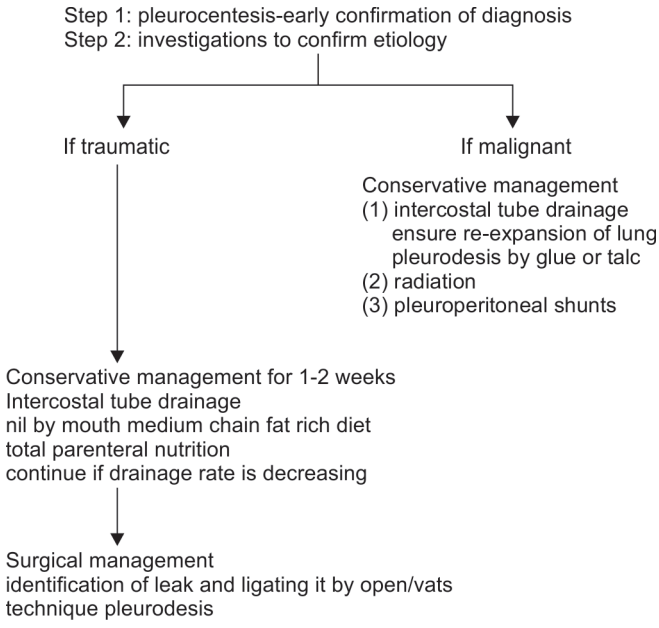
Table 2: Classification of chylothorax

Congenital	Atresia of thoracic duct
	Birth trauma
	Pleural thoracic duct fistula
Traumatic	Blunt
	Penetrating
Surgical	Cervical
	• Excision of lymph nodes
	• Radical neck dissection
	Thoracic
	• Ligation of patent ductus arteriosus
	• Postpneumonectomy
	• Postesophagectomy
	Abdominal
	• Postsympathectomy
	• Radical lymph node dissection
	Diagnostic procedures
	• Lumbar arteriography
	• Subclavian vein catheterization
Neoplasms	
Miscellaneous	
Disease affecting lymph vessels	Yellow nail syndrome
	Lyphangioleiomyomatosis
	Hemangiomatosis (Gorham's syndrome)

Chylothorax is usually seen on right side, as the largest part of the duct is within the right hemithorax where it is most easily damaged due to stretching. When the leakage from the duct occurs where it passes over the mid-line, a bilateral chylothorax can occur[5]; above the level of the aorta, the chylothorax tends to appear on the left side.[6] The thoracic duct has an approximate length of 36 to 45 cm and a diameter of 2 to 3 mm. When the duct starts to leak, a collection of chyle below the pleura, called "chyloma," is formed which is rarely seen clinically as a swelling of the supraclavicular fossa.[5] The formation of a "chyloma" can be a very dramatic clinical event mimicking myocardial infarction or pulmonary embolism. Soon, the pleura rupture and the chyle collects in the pleural space. Some rare variations can occur, for instance chylomediastinum[7] or chylopericardium.[8] Conventionally, the etiology of chylothorax is diagnosed by CECT of thorax, lymphangiography, or lymphoscintigraphy. Computed tomography has limited use in localizing a site of chyle leakage, although it is simpler than others. Lymphangiography enables direct visualization of lymphatic collection system, but this technique involves complex and invasive manipulation. Lymphoscintigraphy can visualize lymph ducts up to the thoracic duct shortly after subcutaneous radioisotope injection. It is a simple and noninvasive modality and is used to detect the site of chyle leakage by planar and SPECT imaging.[9] The site of chyle leakage can be partially diagnosed by these techniques, though accurate determination is sometimes difficult. These latest techniques enable us to obtain fusion images with little displacement of both images for accurate identification of lesions. Lymphoscintigraphy with SPECT enabled accurate determination of the chyle leakage site in the thoracic cavity of our patient, but the exact site of obstruction could not be identified.

The management of chylothorax depends on the etiology. The treatment protocol for management of chylothorax is given in Flow Chart 1.[10] Our patient was managed with intercostal tube drainage and dietary advice in the form of medium-chain triglycerides, as they are absorbed directly into the portal venous system. No surgical intervention was required as there was no associated thoracic injury and chylothorax resolved with conservative management. Operative intervention in chylothorax should be considered when chyle flow has not diminished over 14 days, and/or nutritional complications appear imminent.

Flow Chart 1: Protocol for management of chylothorax



CONCLUSION

A case of "spontaneous" chylothorax (R), possibly related to blunt trauma sustained 5 months earlier in a 37-year-old man is presented. Line of management is discussed. Although lymphoscintigraphy showed the site of leakage, it failed to demonstrate the exact site of lymphatic obstruction. This patient was treated successfully with conservative management.

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CASE REPORT

Unsafe Chronic Suppurative Otitis Media with Cerebellar Abscess

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ABSTRACT

A 30-year-old female patient presented with fever, altered sensorium, vomiting, and right-sided ear discharge. She was diagnosed as right-sided squamosal chronic suppurative otitis media (CSOM) with cerebellar abscess for which she underwent modified radical mastoidectomy with transmastoid cerebellar abscess drainage. After surgery, the patient made an uneventful recovery. Brain abscess due to suppurative otitis media is a potentially fatal complication and needs to be treated aggressively.

Keywords: Abscess, Cerebellum, Cholesteatoma, Otitis media, Mastoiditis.

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INTRODUCTION

Unsafe (squamosal) CSOM in untreated cases can present with either extracranial complications like sensorineural hearing loss (progressive or sudden), facial nerve palsies, labyrinthitis, labyrinthine fistulas, Bezold's abscess, apex petrositis, and postauricular abscess. Intracranial complications include meningitis, brain abscess, extradural abscess, subdural abscess, lateral venous sinus thrombosis, and otitic hydrocephalus. Traditionally, ears with squamous epithelial disease have been regarded as being more at risk of serious complications as opposed to those with mucosal disease. In fact, the evidence confirms that there is a significant risk with both types of diseases.

Intracranial complications most commonly occur due to direct erosion of osteitic bone by the inflammatory process or via the infected thrombophlebitis of the emissary veins traversing the bone and the dura. Infection may spread to the cranial vault via fractures in the temporal bones, preformed anatomical pathways, or normal anatomical structures, such as the round window, the oval window, and the cochlear aqueduct.

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CASE REPORT

A 30-year-old female patient was brought to the Department of Emergency Medicine, Mahatma Gandhi Mission Medical College & Hospital, Navi Mumbai, Maharashtra, India, on November 5, 2016, with history of fever with chills for 3 days, right-sided otorrhea since 4 days, vomiting for 6 hours prior to admission, and altered sensorium for 6 hours. She had prior history of discharge from the right ear for last 4 years which was intermittent and mucopurulent.

Patient had undergone a left ear modified radical mastoidectomy 18 years back. On admission, her pulse was 108/min, blood pressure was 110/70 mm Hg, and she had neck rigidity. On admission, her provisional diagnosis was meningitis probably secondary to CSOM. In the intensive care unit, she was given injections—ceftriaxone, artemesinin, acyclovir, dexamethasone, and mannitol. Her plain computed tomography (CT) of the brain at the time of admission showed destruction of right sinodural plate, tegmen tympani and lateral wall of right mastoid, right-sided CSOM with cholesteatoma, bony destruction, and brain abscess. Cerebrospinal fluid examination showed presence of neutrophils with increased protein and decreased sugar suggestive of bacterial meningitis. Samples sent for culture were sterile. Ear, nose, and throat (ENT) examination showed presence of foul smelling mucopurulent discharge in the right external auditory canal. High-resolution CT of the temporal bone indicated similar findings to CT brain (plain) along with right sinodural plate destruction (Fig. 1). On neurologist's advice, patient was started on parenteral vancomycin and oral chloramphenicol. Magnetic resonance imaging (MRI) of brain (plain + contrast) was done on November 8, 2016, showing presence of 1 cm × 1 cm abscess in the right cerebellar lobe. Computed tomography venogram done on November 14, 2016, showed a cerebellar abscess measuring 2.4 × 1.4 × 2.2 cm and a mastoid abscess measuring 2.9 × 1.4 × 2.6 cm without sigmoid sinus involvement. On November 13, 2016, the patient developed a swelling in the postaural region. Using a wide-gauge 18G needle, the mastoid abscess was drained on November 14, 2016,

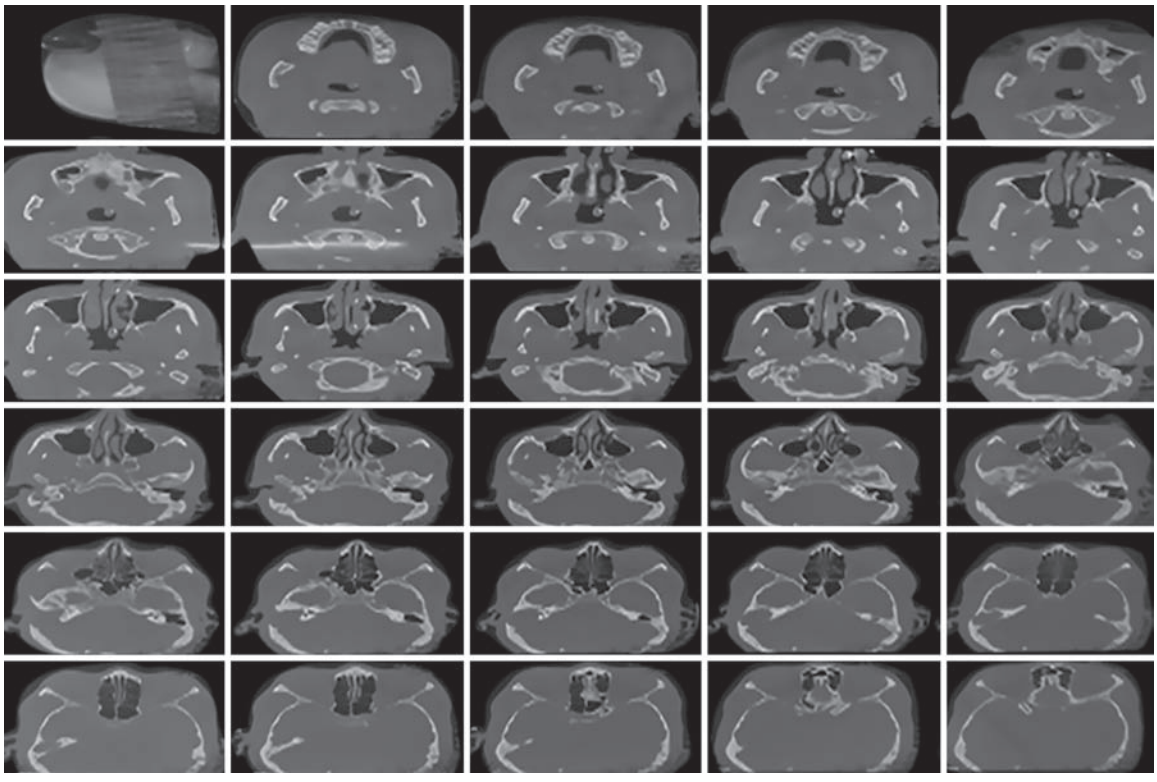

Fig. 1: High-resolution computed tomography of temporal bone depicting destruction of right sinodural plate and right tegmen tympani (November 6, 2016)

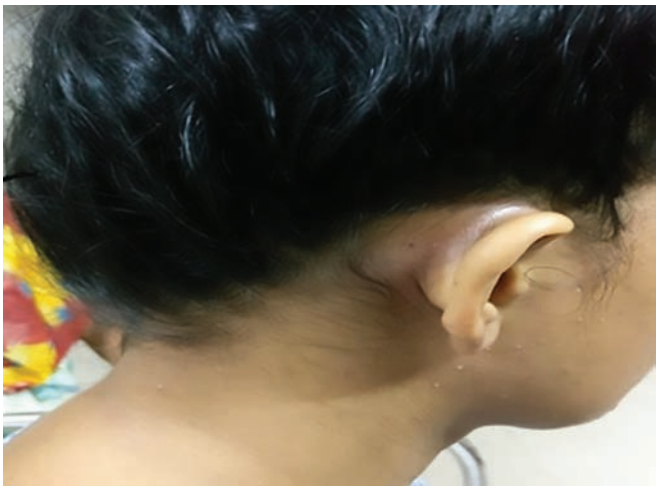

Fig. 2: Postauricular mastoid abscess (before drainage)

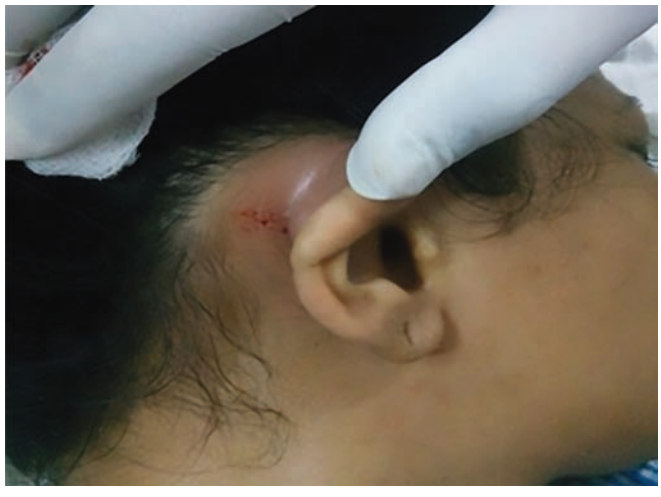

Fig. 3: Postauricular abscess (after drainage)

and approximately 6 mL pus was aspirated and sent for culture sensitivity (Figs 2 to 4).

Patient was taken up for surgery on November 16, 2016, by a joint ENT–neurosurgical team. Modified radical mastoidectomy was done. Intraoperatively, cholesteatoma was seen in the mastoid antrum, attic, and the middle ear cleft. The lateral wall of the mastoid was found to be destroyed with a large cavity occupying its place. There was patchy destruction of the tegmen tympani and the sinodural angle. However, the sinus plate was intact. Medial wall of the mastoid was destroyed. The dura of the cerebellum, which was covered with granulation tissue, was exposed with slight discoloration in one spot, suggesting presence of an abscess beneath. Using a transmastoid approach, the cerebellar abscess was drained using a wide-bore needle followed by gentle probing in the area of the granulation tissue over the dura. About 10 mL of pus was obtained. No ossicles were present in the middle ear cleft, and a temporalis fascia graft was placed by underlay technique (type IV tympanoplasty). Another temporalis fascia graft was used to cover the exposed dura followed by surgical closure (Figs 5 to 7). Postoperatively, patient was continued on parenteral ceftriaxone, metronidazole, vancomycin, and oral chloromycetin and

Fig. 4: Pus aspirated from mastoid abscess

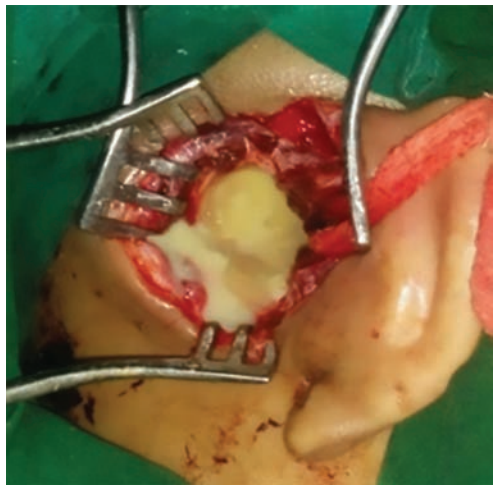

Fig. 5: Intraoperative pus seen in the mastoid antrum

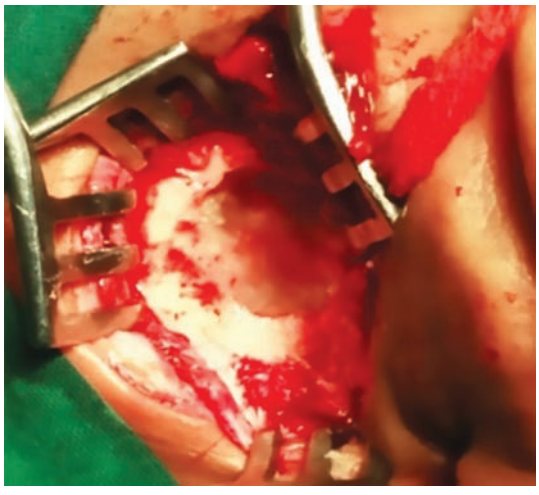

Fig. 6: Mastoid antrum seen after draining pus

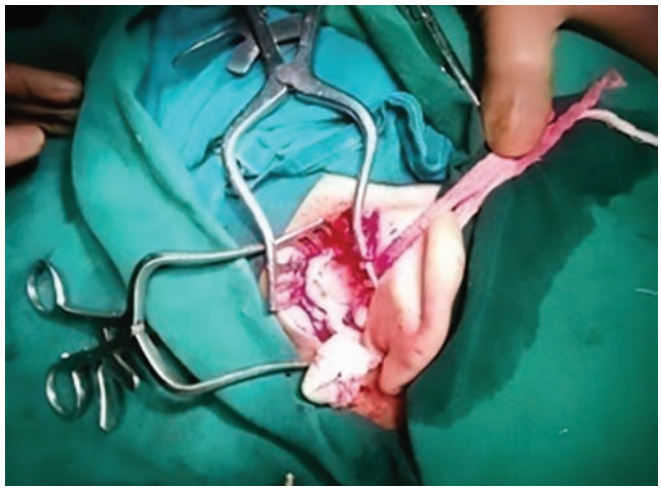

Fig. 7: Cholesteatoma seen in the middle ear

acetazolamide. Culture showed presence of pseudomonas in the cerebellar abscess and *Escherichia coli* in the mastoid abscess, following which antibiotics were changed to injection cefotaxime, injection metronidazole, injection amikacin, and oral amoxicillin+clavulanic acid as per culture sensitivity. Histopathology report of the tissue recovered showed cholesteotoma. Antibiotic therapy was continued for 21 days. With this line of management, the patient made an uneventful recovery. Computed tomography brain (plain + contrast) done on postoperative day 12 showed no residual disease or abscess formation.

DISCUSSION

The incidence of intracranial complications of chronic otitis media (COM) is estimated to be between 0.02 and 1.97%.[1] The extracranial and intracranial complications occur when chronic infection within the middle ear and mastoid spaces extends to the region beyond the bony confines. Osama et al[1] reviewed 2,890 cases of COM from 1990 to 1999 and found that 57 (1.92%) cases had intracranial and 39 (1.35%) extracranial complications. They observed that meningitis and brain abscess were common among the intracranial complications group, whereas subperiosteal abscesses (Mastoid and Bezold's abscess) were common complications in the extracranial complications group. Despite widespread use of antibiotics, brain abscess following CSOM remains a major problem for the pediatricians, neurologists, otologists, and neurosurgeons.[2] Otogenic brain abscesses constitute about 70% of brain abscesses.[3] Middle ear suppurative disease may extend to temporal lobe or cerebellum due to destruction by cholesteatoma, through fracture lines, preformed pathways, or the Haversian system of veins or the periarterial space of Virchow Robin.[4] Management of intracranial abscesses differs in various stages of evolution.[5,6] Antibiotics are quite effective in early and late cerebritis stage, but their efficacy is reduced in the stage of capsule formation due to acidic medium in the abscess cavity and the inability to have adequate therapeutic concentration of antibiotic within the abscess. Therefore, surgical intervention is essential once the capsule is formed.[7-10]

In their study, Asma et al[11] noted that cholesteatoma was seen in all cases of otogenic brain abscess. They presented with a history of chronic ear discharge, headache, otalgia, and fever. The underlying pathology for cerebellar abscess was cholesteatoma. Cholesteatoma produces enzymes that cause demineralization of bone. The infection can spread through this bony erosion into the posterior cranial fossa and cause cerebellar abscess.[12]

Less than 50% of patients with brain abscess present with the classical triad of fever, headache, and neurological deficit.[13] Youngs[14] and Harker and Shelton[15] described signs and symptoms of brain abscess according to the stages of its development. The first stage corresponds to the encephalitis stage that results from the invasion of brain tissue. The symptoms are general malaise, headache, fevers, chills, nausea, and vomiting. They are usually quite mild and often mimic an exacerbation of COM. During the second stage or "latent stage," the abscess localizes and the symptoms may disappear. The third stage is characterized by signs and symptoms associated with both increased intracranial pressure and compression of specific structures in the brain. Severe headache is present in 50 to 60% of patients. Nausea and vomiting (often projectile) occur in 25 to 50% of cases. About 20 to 30% of patients may present with seizures.[16] Untreated abscess may rupture into the ventricle or the subarachnoid space. This will result in rapid clinical decline and even death due to severe ventriculitis.

Computed tomography scan with and without intravenous (IV) contrast remains the most important investigation in the diagnosis of brain abscesses and for observing its progress during treatment. Magnetic resonance imaging is equally useful.[17] Conditions to be differentiated from brain abscess include meningitis, subdural abscess, lateral sinus thrombophlebitis, and otitic hydrocephalus. Brain abscess is the dreaded otogenic complication, both in severity and difficulty of management.[18] Management requires a combined neurosurgical and otologic approach, along with use of large doses of systemic antibiotics. Surgery of the abscess includes aspiration through a burr hole or formal craniotomy, open drainage, or rarely total excision. This may be carried out simultaneously with surgery for CSOM, or it may precede management of the ear if the intracranial problem is life-threatening. Surgical management for CSOM is based on the extent of the underlying disease.

In their case series of eight cases of cerebellar bacterial brain abscess, Hsu et al[19] noted that dizziness is a frequent symptom. Early diagnosis and a combination of antimicrobial and neurosurgical intervention is important for its treatment. Three out of eight patients with cerebellar brain abscesses had ear symptoms. One patient had cholesteatoma, one patient had acute suppurative otitis media, and one had mastoiditis with diabetes mellitus.

Computed tomography with IV contrast is the imaging modality of choice in screening for complications of CSOM. It can demonstrate the site of complications, the extent of the abscess, and any bone involvement.[15] Magnetic resonance imaging with contrast and magnetic resonance angiography are useful in the definitive diagnosis of certain intracranial complications, such as lateral sinus thrombosis. Both contrast-enhanced CT and MRI will demonstrate ring enhancement for brain abscesses.[20-21] The abscess is usually encircled by an area of low density representing edema in the surrounding brain tissue.[22] Intravenous antibiotic therapy should be started as early as possible. Polymicrobial infection is common in CSOM and its complications.[12] Therefore, broad-spectrum antibiotic coverage for aerobic and anaerobic organisms is recommended. Combination drug therapy may be necessary to accomplish this goal. Surgical treatment may involve aspiration or excision of the abscess.[23] The treatment of the condition is tailored to the clinical presentation of each patient and neurological considerations. The importance of early and appropriate treatment of the abscess cannot be overemphasized.

With prompt treatment and a proper regimen of antibiotics, otogenic brain abscesses are curable and patient recovers fully with no long-term sequalae, as shown in the present case.

CONCLUSION

Otogenic brain abscess is a life-threatening condition if left untreated. It can prove fatal if immediate intervention is not done. In addition to medical management, early surgical intervention in the form of removing the septic foci in the ear is of vital importance to ensure complete recovery.

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CASE REPORT

Selective Mutism with Social Anxiety Disorder and Sibling Rivalry Disorder

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ABSTRACT

A rare case of selective mutism, social anxiety disorder, sibling rivalry disorder, and temperamental difficulties in an 8-year-old girl has been reported. The relevant literature about clinical assessment and management of this disorder has been reviewed.

Keywords: Selective mutism, Sibling rivalry disorder, Social anxiety disorder, Temperamental difficulties.

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BACKGROUND

Selective mutism is a rare childhood disorder characterized by persistent failure to speak in specific contexts where speech is expected, like at school or with playmates despite hearing and speaking appropriately in other contexts, such as at home with parents and siblings. Social anxiety disorder is a marked or intense fear or anxiety of social situations in which the individual may be scrutinized by others. There is fear or anxiety that occurs in peer settings for children. Diagnostic and Statistical Manual 5 describes the aforementioned disorders under anxiety disorders.[1] Sibling rivalry can create a stressful and challenging situation for parents. The arrival of a new baby often causes older siblings to feel displaced, frustrated, angry, and even unloved.[2] Limitations and gaps in the knowledge about selective mutism and social anxiety disorder still persist with sparse literature on comorbidities and management. We describe a rare case of an 8-year-old girl with selective mutism and multiple comorbidities.

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CASE REPORT

An 8-year-old girl was brought to the child psychiatry clinic at the Department of Psychiatry in MGM Medical College & Hospital, Kamothe, Navi Mumbai, Maharashtra, India, by parents with complaints of not speaking at school and in social settings despite having the ability to do so at home. Parents also reported that the child was reluctant to have conversation with others and would not meet new people. She would speak at home with parents and her family members comfortably. The child had minimal involvement with children of her age and was often seen crying or clinging to her mother on social gatherings and cultural activities. Birth and developmental history was normal. There was history of sibling rivalry reported as well in the form of increased aggression toward younger sibling, feeling jealous, and showing anger and contempt toward the younger sibling and increased attention-seeking behavior and temper tantrums when her sibling was appreciated by parents. Her parents reported that right from her early childhood days she was very shy, withdrawn, and slow to warm up and had temperamental difficulties. There was no history of autism, language regression, seizures, and obsessive-compulsive symptoms. No significant family, personal, or medical history was reported. Child was not fully cooperative for mental status examination. The child continued to be mute throughout the assessment. After lot of efforts at building rapport with her, she uttered her name and spoke a little. She was found to be very anxious and appeared tensed. Her palms were sweating and she appeared restless. Based on history and clinical evaluation, she was diagnosed as selective mutism, social anxiety disorder, sibling rivalry disorder with slow to warm up temperament. Her routine investigations were normal. She had earlier been shown to a pediatrician and a pediatric neurologist and their clinical opinion had ruled out any medical or neurological morbidity in her. Her intelligence quotient as assessed by Binet Kamat Test, which was already carried out by a pediatrician, was normal. Anxiety Disorder Questionnaire Scale was administered at our setting, which revealed significant social anxiety. Children's apperception test analysis report suggested anxiety, feeling of neglect, and jealousy toward the younger sibling and fear of school and friends. Parents were psychoeducated about the role of medications in

selective mutism and social anxiety disorder and the need for psychotherapy sessions focusing on cognitive behavior therapy, relaxation training, and familial interventions, in liaison with clinical psychologist. Patient was started on syrup Fluoxetine 5 mg per day along with weekly sessions of cognitive behavior therapy. Parents reported 70% improvement after 8 weeks and 90% improvement after 6 months. The child is currently doing well with regular follow-up and syrup Fluoxetine 5 mg per day.

DISCUSSION

Selective mutism can present with a variety of comorbidities including enuresis, encopresis, obsessive-compulsive disorder, depression, premorbid speech and language abnormalities, developmental delay, and Asperger's disorders. The specific manifestations and severity of these comorbidities vary based on the individual. Many etiologies have been proposed for selective mutism including psychodynamic, behavioral, and familial. A developmental model that includes a transactional dynamic interplay of the above etiologies is gaining perspective. The treatment model includes nonpharmacological therapy (psychodynamic, behavioral, and familial) and psychopharmacological therapy—mainly selective serotonin reuptake inhibitors (SSRIs).[3] A variety of temperamental and behavioral characteristics, comorbid psychiatric conditions, neurodevelopment delay, and family factors have been associated with selective mutism. These children are described as excessively shy, withdrawn, "slow to warm up," and inhibited. They often avoid eye contact, fear social embarrassment, and experience significant anxiety on separation from their attachment figures.[4] Diagnosis of selective mutism is often missed in the formative years because the child does speak at home. Early diagnosis and treatment provide a vital key to addressing this rare disorder.[5] Wong[6] reviewed literature and found that 38% of children with selective mutism have premorbid speech and language problems and can exhibit broader developmental delays. Karakaya et al[7] found a teacher-rated prevalence and clinician prevalence of selective mutism of 0.83 and 0.033% respectively. Selective mutism and its comorbidities can be debilitating in a child. Unfortunately, there is little research examining effective treatments for this disorder, and so designing an evidence-based treatment plan can be difficult.[8] Kaakeh and Stumpf[9] report that although data are limited to case reports and trials with small patient populations and short follow-up periods, some patients with selective mutism do respond to therapy with SSRIs. Fluoxetine is the most studied SSRI as treatment for the condition, although further investigation is required to determine the optimal dosage and duration of therapy.

CONCLUSION

A relatively rare case of selective mutism with social anxiety disorder and sibling rivalry disorder in an 8-year-old girl has been reported. She made good recovery with cognitive behavioral therapy and medication with SSRI drugs. Relevant literature in the subject is reviewed.

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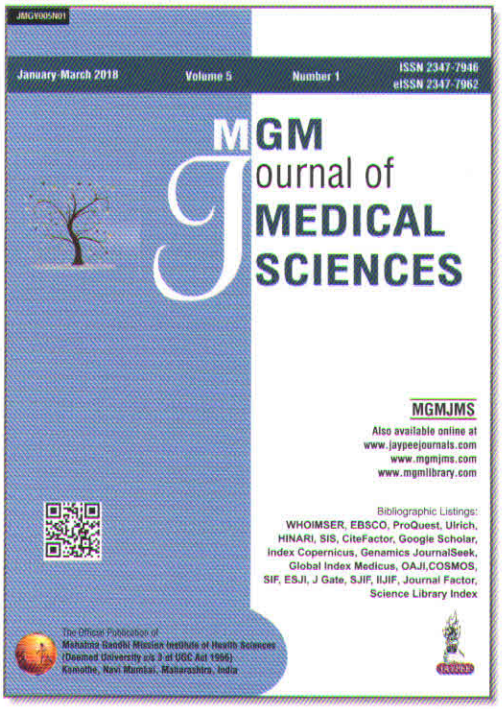

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