ORIGINAL ARTICLE

Is Plummer–Vinson Syndrome Endemic in Puducherry? A Single-center Retrospective Study of this Rare Syndrome

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Abstract

Objective: Although Plummer–Vinson syndrome (PVS) is rare, it is imperative to be aware that this group of patients is at an increased risk of squamous cell carcinoma (SCC) of the pharynx and the esophagus, which can be identified early. The aim of this study was to determine the prevalence of cricopharyngeal webs, iron deficiency anemia (IDA), and dysphagia among individuals diagnosed with PVS in Puducherry.

Materials and methods: Over a span of 2 years, a total of 30 patients who were diagnosed with PVS and had presented to the department of ENT at a tertiary care center were included in this single-center study with a review of past events. Dilatation of postcricoid webs was done, followed by a postoperative iron correction. A regular follow-up for 1 year was done to examine the occurrence of cancerous alterations and the reappearance of symptoms.

Results: We found the highest incidence (90%) to be in females presenting at the 4th and 5th decades of life, with the most significant presenting complaint in all patients being dysphagia. The majority of them had features of IDA like pallor, koilonychia, glossitis, angular stomatitis, and bald tongue. All patients (100%) showed iron deficiency status in biochemical analysis and postcricoid web in barium swallow. Three patients had associated malignancies, of which two were esophageal and one was hypopharyngeal.

Conclusion: Plummer–Vinson syndrome (PVS) is a symptom complex consisting of dysphagia, IDA, and esophageal webs. It is a condition that carries an increased risk for the development of malignancy and has a higher prevalence among people of South Indian descent, especially in the Puducherry region, and comprehensive evaluation should be conducted in these patients to exclude the presence of concomitant malignancy. The esophageal web in PVS can be safely dilated, and the response is sustained during follow-up despite rare recurrences.

Keywords: Anemia, Dysphagia, Plummer–Vinson syndrome, Postcricoid webs.

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Introduction

Plummer–Vinson syndrome (PVS) is a rare disease of the 21st century characterized by the triad of classical dysphagia, IDA, and esophageal webs.[1] This syndrome is named after two doctors who worked at the Mayo Clinic, Henry Stanley Plummer (1874–1936) and Porter Paisley Vinson (1890–1959).[2,3] Although the exact cause of this syndrome is uncertain, iron deficiency is thought to be the most likely etiological factor. Other possible causative factors may include undernourishment, an inherent susceptibility, or immunological mechanisms, although their precise involvement in the etiopathogenesis of this syndrome remains unclear. In 1938, Waldenstrom and Hallen demonstrated that this disease could arise with iron deficiency itself, unaccompanied by anemia, thereby coining the term "sideropenic dysphagia."[4]

Symptoms of PVS include dysphagia, glossitis, bald tongue, atrophic oral mucosa, angular cheilitis, koilonychia, weakness, pallor, fatigue, and tachycardia. Splenomegaly and goiter may be associated occasionally.[5] PVS can be successfully treated with iron supplementation, followed by mechanical dilation. PVS is a recognized risk factor for SCC of the pharynx and the esophagus, and hence, these patients should be followed up closely.[6–8]

As there are very few studies on this syndrome in the English literature, especially from India, we conducted a clinical retrospective study to understand the predisposing factors, the distribution of the disease, and its association with malignancy in patients from Puducherry, India.

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Conflict of interest: None

Materials and Methods

This study was a retrospective single-center study conducted in a tertiary care teaching hospital in Puducherry, India, involving 257

patients who presented to the outpatient clinics of the Department of Otorhinolaryngology and Head and Neck Surgery. After receiving approval from the Institutional Ethical Committee, data was collected over a period of 3 years, spanning from January 2017 to December 2019. The inclusion criteria included—all adult (>18 years) patients presenting with a history of dysphagia and documented anemia with other clinical features of PVS. The exclusion criteria included—patients with only anemia but no other symptoms of PVS, patients with inflammatory conditions, paralytic conditions, and anatomical conditions leading to dysphagia, and patients with a history of previous trauma, surgery, or radiotherapy of the pharynx or esophagus. Based on these exclusion criteria, 227 patients were excluded, of which 24 patients were found to have laryngeal malignancies on video laryngoscopy. After obtaining informed consent, the remaining patients underwent video laryngoscopy, barium swallow, and baseline hematological investigations. The diagnosis of IDA was made when a patient presented with reduced hemoglobin levels (below 13.0 g/dL in males and below 12.0 g/dL in nonpregnant females), a microcytic hypochromic appearance on the peripheral blood smear, serum ferritin levels of <30 µg/L, and mean corpuscular volume (MCV) <80 fL. PVS was diagnosed when a patient presented with IDA, a postcricoid web on barium swallow, and other clinical features consistent with PVS. PVS was diagnosed in 30 patients with historical analysis, clinical examination, video laryngoscopy, barium swallow, and baseline hematological investigations as per standard protocols. After obtaining anesthetic fitness, the patients were taken up for rigid esophagoscopy for dilatation of postcricoid web under general anesthesia. Postoperatively, the causes of patients' IDA were investigated and treated accordingly. Patients were regularly followed up for 2 years to monitor for any recurrence of symptoms and to evaluate their iron deficiency status.

Monitored parameters included estimation of hemoglobin, serum ferritin, total iron binding capacity, and contrast radiograph barium swallow examination. Barium swallow studies were performed with barium sulfate as the contrast medium using fluoroscopy at 1000 mA. Hemoglobin levels were measured using the calorimetric method with the Mindray BC-5200 automated hematology analyzer. Serum iron and total iron-binding capacity were analyzed on a Hitachi 902 automatic analyzer employing the ferrozine method. Serum ferritin levels were measured with the Hitachi Cobas E411 employing electrochemiluminescence immunoassay. Indentation or partial or eccentric constrictions in the postcricoid area from C4 to C6 vertebral level were marked as postcricoid webs.

We used the Statistical Package for the Social Sciences (SPSS) version 20.0 (SPSS Inc., Chicago, Illinois, United States of America) software with regression modules installed for statistical analysis. Chi-squared tests were employed to calculate the results, with *p*-values of 0.05 or less considered statistically significant. The categorical data were presented as ratios and proportions, while numerical data were presented as the median and interquartile range (IQR).

Results

In this single-center retrospective study, 30 patients were diagnosed with PVS. The median age of presentation was 45.5 years (IQR 27–69 years). PVS was seen most in patients in the 41–60 years range [*n*, 19 (63.33%)]. There was a clear female preponderance as 27 (90%) patients were female (male:female ratio, 1:9).

All our diagnosed patients had dysphagia as the presenting complaint, and the mean duration of dysphagia was for 38 months (range 5–96 months). Among the diagnosed 30 patients, three (10%) had odynophagia, 17 (56.67%) had easy fatigability, 15 (50%) had palpitations, and four (13.33%) had epigastric pain. In addition to the above symptoms, three had menorrhagia and two had bleeding per rectum. On general physical examination, angular cheilitis was noted in six patients (20%), koilonychia in 19 (63.33%) patients, and glossitis in 22 (73.33%) patients. Associated goiter was seen in one patient (Table 1).

Microcytic hypochromic anemia was diagnosed with mean hemoglobin of 6.4 g/dL (normal value 12–14 g/dL), MCV of 72.4 fL (normal value 80–95 fL), and mean corpuscular hemoglobin (MCH) of 24.2 pg (normal value 27–32 pg). The various iron parameters like serum iron, serum ferritin, and total iron binding capacity were assessed for all 30 patients. The mean value of serum iron was 28.9 µg/dL (range of 32–42 mcg/dL), serum ferritin was 22 ng/mL (range 18–24 ng/mL), and total iron binding capacity was 495 mcg/dL (range 480–505 mcg/dL) (Table 2).

Among the diagnosed 30 patients, three of them showed concomitant malignancy in upper gastrointestinal (GI) endoscopy. Out of these three, one (3.33%) patient had malignancy of the hypopharynx, and the other two patients had (6.67) lower esophageal malignancy.

Table 1: Demographic and clinical characteristics of the study population

Total number of patients	*30*
Mean age (range), years	45.52 (27–69)
Male:female ratio	1:9
Clinical manifestations, *n* (%)	Dysphagia, 30 (100) Odynophagia, 3 (10) Easy fatigability, 17 (56.67) Palpitations, 15 (50) Epigastric pain, 4 (13.33) Menorrhagia, 3 (10) Bleeding per rectum, 2 (6.67) Spleenomegaly, 2 (6.67) Goiter, 1 (3.33) Cheilitis, 6 (20%) Koilonychia, 19 (63.33) Glossitis, 22 (73.33)
Duration of dysphagia in months [mean(range)]	38 (5–96)
Concomitant malignancy, *n* (%)	3 (10) Hypopharyngeal malignancy, 1(3.33) Lower esophageal malignancy, 2 (6.67)

Table 2: Hematological parameters in the study population (*n* = 30)

Parameter (normal range)	*Value, mean (range)*
Hemoglobin (12–14 g/dL)	6.4 (4.4–7.3)
MCV (80–95 fL)	72.4 (68–76)
MCH (27–32 pg)	24.2 (21–26)
Serum iron (40–165 mcg/dL)	28.9 (32–42)
Serum ferritin (30–300 ng/mL)	22 (18–24)
Total iron-binding capacity (245–450 mcg/dL)	495 (480–505)

Discussion

An esophageal web is a thin membranous structure located in the cervical esophagus, typically measuring 2–3 mm in thickness and featuring a pink mucosal covering made up of mucosal, and submucosal tissue but lacking a muscle layer. This can cause mechanical dysphagia. The esophageal webs could be annular, semilunar, or eccentric. When the diameter of the lumen is <12 mm in size, it can cause a worsening of dysphagia. This condition is more frequently observed in the proximal 4–5 cm of the esophagus and it is considered one of the uncommon reasons for dysphagia. The exact prevalence and incidence are not known but are reported to be higher in middle-aged females than in males.[7]

Among the various factors included in the pathogenesis, the strongest association is with IDA. The improvement in symptoms, luminal stenosis, and even esophageal motility after iron supplementation provides evidence of this causal association. The alimentary tract is particularly susceptible to iron deficiency because of its high cell turnover rate. Iron deficiency can reduce the activity of iron-dependent oxidative enzymes, leading to degeneration and atrophy of the mucosal tissue, and myasthenic changes in the pharyngeal muscles. The cervical portion of the esophagus is encircled by skeletal muscles and cartilage, and when the atrophic mucosal tissue rubs against the cartilage during swallowing, it can result in injury and the formation of a thin, shelf-like web. Additionally, a lack of iron can disrupt regular sensation in the throat, causing hypo pharyngitis. As a consequence, the cricopharyngeal muscle may not relax, which can result in postcricoid spasms.[9]

Plummer–Vinson syndrome (PVS) has been documented worldwide, with notable occurrences in Northern European countries, particularly in Scandinavia during the early 1900s. In African countries, despite the high prevalence of iron deficiency, PVS seems to be a rare disease.[6] While PVS syndrome is now rare in Western populations, the incidence in the Indian subcontinent is still high, especially in Southern India.

We carried out a comprehensive literature review, adhering to the preferred reporting items. We conducted searches using web-based search engines such as PubMed/MEDLINE, EMBASE, ProQuest, Scopus, and Web of Science. Both Medical Subject Headings terms and keywords were used for the searches. We did not place any restrictions on language and utilized controlled vocabulary and text word searches for all databases. In addition, we manually searched through references and consulted Google Scholar to identify any additional relevant articles. Our systematic review included case reports and case series, as well as retrospective and prospective case studies conducted in India between 2014 and 2022. According to this systematic review, only six studies of PVS have been reported in India to date, including our study. Among these, two are from Andhra Pradesh, two from Karnataka, and two from Puducherry including the present study, which clearly denotes a predilection for this disease in Southern India.

In comparison with other Indian studies, our retrospective study also showed dysphagia as the main presenting complaint for all the diagnosed patients of PVS (Table 3). There was a clear preponderance of PVS among middle-aged females (90%) in our study, which is consistent with the findings of the other studies. The mean age of presentation in our study was 45 years, which is comparable with the other studies. In a study by Ifthekar et al.,[10] the mean duration of symptoms was 56 months, which is comparable to our study with a mean duration of 38 months, as most of the other studies showed a lesser duration.[11–14] In spite of postcricoid web dilatation, our study showed a recurrence rate of 6.67% (two patients) as compared to another prospective study, which showed a recurrence rate of 10%.[12] PVS being regarded as a precancerous lesion, it has been shown to have a high-risk of malignant transformation (3–30%).[7] During our follow-up period of 2 years, concomitant malignancy was noted for three of our patients, with one having hypopharyngeal malignancy, and the other two patients having esophageal malignancy. Similar findings

Table 3: Comparison of Indian studies and case series of PVS

Author, year	*State*	*Type of study*	*No. of patients*	*M:F ratio*	*Average age (years)*	*Average duration of symptoms (months)*	*Period of follow-up*	*Recurrence*	*Concomitant malignancy or malignancy on follow-up*
Rasool et al.	Andhra Pradesh	Case series	3	0:3	32.3	56	3 years	None	None
Bakshi et al., (2015)	Puducherry	Case series	5	5:0	44.2	3	–	None	None
Goel et al., (2016)	Puducherry	Prospective study	37	1:7.4	40	24	1–24 months (median, 10)	3 (10%)	None
Rajesh et al., (2019)	Andhra Pradesh	Retrospective study	52	1:16.3	27	6	9 months	5 (9.5%)	Concomitant lower esophageal tumors (2, 3.84%) and gastric antrum tumor (1, 1.92%)
Kavya et al., (2020)	Karnataka	Case series	3	1:2	51	8.66	–	None	None
Patil et al., (2021)	Karnataka	Ambidirectional study	132	1:5.9	43.5	54	3–120 months (mean, 38)	10 (7.57%)	Concomitant esophageal tumors (4, 3.03%) Postcricoid/esophageal SCC on follow-up (6, 4.5%)
Present study (2022)	Puducherry	Retrospective study	30	1:9	45.52	38	2 years	2 (6.67%)	Concomitant hypopharyngeal malignancy (1, 3.33%) and lower esophageal malignancy (2, 6.67%)

were noted in another two studies showing esophageal malignancy as more common in follow-up.[13,15]

Our study had some limitations as we have included only symptomatic patients, irrespective of the fact that asymptomatic webs have been reported. However, our study and other series pursue to highlight the increased risk of upper GI malignancy in this subset of patients. Hence, annual surveillance with upper GI endoscopy and regular follow-up is required.

Conclusion

Plummer-Vinson syndrome (PVS) is a symptom complex consisting of IDA, dysphagia, and esophageal webs. It is a premalignant condition that is more commonly observed in individuals from South India, particularly in the Puducherry region. A thorough evaluation should be performed on these patients to exclude the possibility of concurrent malignancy. Dilating the esophageal web in PVS is considered a safe procedure and patients typically exhibit a sustained response during follow-up, with only rare recurrences.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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