

CLINICAL PERSPECTIVE ON PLUMMER-VINSON-SYNDROME IN SOUTH INDIA

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Abstract:

Plummer-Vinson-Syndrome (PVS) is a clinical triad of dysphagia, Iron deficiency anemia and post cricoid web. Prevalence of PVS is reported to be higher in females than in males with a striking ratio of about 8:1. A long time lag is noted for patients seeking medical attention following initial dysphagia symptoms as it starts insidiously and patients adapt to it by changing their dietary habits. Dysphagia gets worse when the luminal diameter in the web region narrows further. Endoscopic examination of the esophagus is often employed for both diagnosis and treatment of dysphagia. PVS being a rare disorder but can put patient into a great degree of distress and it is important to seek adequate data on the disease and effective treatment strategies. In this retrospective study we attempted to furnish clinical data on the patients who were treated for the disorder within 2 years of the clinical practice in a hospital in south India.

Keywords: Plummer-Vinson Syndrome, Dysphagia, Iron deficiency anemia and post cricoid web.

Introduction:

Plummer-Vinson-Syndrome (PVS) is a clinical triad of dysphagia, Iron deficiency anemia and post cricoid web (1). Exact cause of PVS is not clear but attributed to malnutrition, genetic predisposition, autoimmune disorder and other dietary deficiencies (2). PVS now is considered to be a rare medical condition in western world as malnutrition isn't a common problem, however in third world countries including India this entity isn't uncommon (3-5). Prevalence of PVS is reported to be higher in females than in males with a striking ratio of about 8:1 (6). Among the clinical triad, dysphagia is most commonly

reported complaint followed by symptoms of iron deficiency anemia and some patients do not even exhibit esophageal web (7, 8). A long time lag is noted for patients seeking medical attention following initial dysphagia symptoms as it starts insidiously and patients adapt to it by changing their dietary habits. Dysphagia gets worse when the luminal diameter in the web region is less than 12 mm (9, 10). Laboratory methods to diagnose the disease in suspected patients include hematological, radiological and the endoscopic investigations (11). Hematological investigations are aimed to identify anemia, its causes and severity, whereas radiological examination (barium swallow) followed by endoscopic

investigation are done to confirm the diagnosis of web, its location and also to grade the severity of web (12). In certain cases, more investigations may be required such as tests for thyroid disorders (13), celiac disease (14) and tests to rule out other causes for anemia (15). Endoscopic examination of complete upper gastrointestinal tract after dilatation is required to identify any lesions such as hypopharyngeal or esophageal malignancies which may occur in PVS (16)

Endoscopic examination of the esophagus can be both diagnostic and therapeutic to avoid repeated esophageal endoscopic intervention (9, 17). Various endoscopic dilatation methods for treatment of post cricoid webs are Savary-Gilliard dilatation, Endoscopic balloon dilatation, Endoscopic laser division and electro incision (18, 19). All of them lead to dilatation of the narrowed web region there by dysphagia is relieved which is the most commonly reported symptom (20). However, a proper differential diagnosis is needed to rule out the other causes of dysphagia (11). In few cases of mild dysphagia sometimes just iron supplementation corrects the disease without any further endoscopic dilatation (21).

In this retrospective study clinical data of the patients who were treated for PVS in past two years is reported.

Materials and methods:

A retrospective study was performed in which patients who attended outpatient clinics of gastroenterology and other departments at NRI medical college and hospital were selected during two year period between September 2016 and September 2018. Patients who met the following inclusion and exclusion criteria for the study were selected.

Inclusion criteria:

- Patients with history of dysphagia
- Patients with anemia
- Patients diagnosed with post cricoid web by endoscopy and or barium swallow

Exclusion criteria:

- Patients only with anemia but with no other symptoms of PVS
- Diagnosed patients with PVS and who are on dual

anti platelets medications

- Diagnosed patients with PVS and who have severe cardio respiratory compromise

Standard procedures were followed for the management of patients with post cricoid web based on endoscopy. Post cricoid web dilatation was done by Savary Gilliard dilators. Fluoroscopy guidance wasn't used during dilatation. Endoscopic treatment was performed under sedation using intravenous propofol. Dilators with a diameter ranging from 7 to 15 mm were selected based on degree of narrowing.

Majority of the cases were done by Dr RB¹ (88%) and rest of the cases were done by Dr PA⁴. In brief, the following steps were undertaken, a metallic guidewire was inserted under endoscopic control through the web and pushed into the stomach. Endoscope was withdrawn gradually, and later dilators were passed over the wire with gradual increase in size without exceeding 3 successive calibers per session. Finally, an endoscopic control was performed to visualize the rupture of the web and to check for the integrity of the esophageal mucosa. Sometimes direct endoscopic dilatation was possible but was not done routinely due to high risk of esophageal tears. No prophylactic antibiotics were given, and procedure was postponed if patients were on anti-platelets and anti-coagulants in view of risk of bleeding. If there were no major peri procedural adverse events, patients were asked to take soft diet for 1 day and normal diet from following day.

Statistical methods: All the statistical calculations were performed in SPSS Version 25. Demographical data is presented as mean and the clinical data is presented as the percentages of the patients in their respective groups.

Results:

After reviewing the medical records of the patients who visited gastroenterology outpatient clinic and outpatient clinics of other departments at NRI medical college and hospital during the period between September 2016 and September 2018, 52 patients are identified to meet the inclusion and exclusion criteria for this study. These patients were diagnosed with PVS based on gastroscopy. Majority of patients were females (94%, n= 49) and rest were males (6%, n=3). Demographic data of the patients presented in table 1.

Table 1.
Demographic data of the patients included in this study

Variable	Value
Age (mean years)	27
Gender (%)	
Males	6
Females	94
BMI (mean)	19.5

Mean age of the patients was 27yrs (range: 17 to 60 years). Mean duration of symptoms was 6 months (range: 2 days to 3 years). Even though dysphagia is the most common presenting symptom, severity of dysphagia varied in many patients. Grade I dysphagia (able to swallow some solid diet) seen in 9 pts, Grade II (able to swallow only semi solid diet) seen in 22 pts, Grade III (able to swallow only liquids) severity seen in 17 pts and most severe grade IV (unable to swallow anything) dysphagia seen in 4 pts. Figure 1 shows the severity of dysphagia pictorially. Associated symptoms and signs of malnutrition seen especially anemia (92 %) with mean Hb level was 8.1 gm/dl. Many patients (92.3 %) had low normal BMI with a mean BMI of 19.5.

Savary Gilliard dilators were used in 50 patients (96%) and direct endoscopic dilatation used in rest of the patients (4%). 94% patients had immediate relief of dysphagia and rest of the patients had intra procedure adverse events (6%), therefore immediate relief of dysphagia wasn't documented as they had to be on nil by mouth for few days. But later they even had relief of dysphagia. However significant relief of dysphagia noted in 50 patients. Adverse events documented in 3 patients (6%) and all had complete mucosal tear exposing submucosal space. All of them were managed conservatively with nil by mouth, RT feeds and IV antibiotics. Check endoscopy done after one week and documented healing of mucosa. 3 patients had tumors elsewhere (2 had lower esophageal tumors and one had tumor in the antrum of the stomach). All found to have adenocarcinomas.

Table 2
Clinical modalities implemented

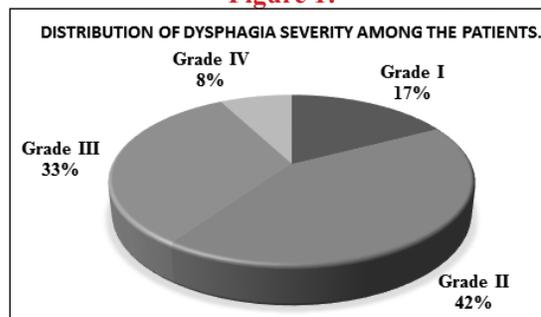
Treatment	Percentage of patients (%)
Savary gilliard	96
Direct endoscopic dilatation	4

Table 3.
Treatments outcomes

Treatment outcome	Percentage of patients (%)
Immediate relief from dysphagia	94
Adverse events due to procedures	6
Overall significant relief from dysphagia	96
Recurrence of dysphagia (9 months follow-up)	9.5

Mean follow up was for 9 months. Recurrence of dysphagia noted in (9.5%) patients and recurrence was observed at mean of 7 months. All patients who had recurrence, had repeat endoscopy, documented post cricoid web followed by repeat dilatation and had complete relief of dysphagia with one additional dilatation. During follow up no patient had developed post cricoid malignancy after diagnosis of post cricoid web was made.

Figure 1:



Discussion:

The combination of dysphagia, post cricoid webs, and iron deficiency anemia is known as Plummer-Vinson syndrome (PVS) (aka Paterson Brown Kelly syndrome, sideropenic dysphagia).

Exact causes of the post cricoid web formation are still under investigation. Probable etiopathogenic mechanisms include iron and other nutritional deficiencies, autoimmune diseases such as rheumatoid arthritis, pernicious anemia, celiac disease, thyroiditis and probably genetic predisposition.

Possible mechanism of iron deficiency causing post cricoid web is the depletion of iron-dependent oxidative enzymes, which may produce myasthenic changes in muscles involved in the swallowing mechanism with

esophageal mucosal atrophy and formation of webs as epithelial complications (21, 22). The improvement in dysphagia after iron therapy provides evidence of causal association between iron deficiency and post cricoid web (21). Moreover, the decline in incidence of PVS seems to parallel an improvement in nutritional status, including iron supplementation. However, some demographic studies haven't shown relationship between postcricoid dysphagia and malnutrition (23).

In this study overwhelming majority of patients were females (94.2%) and is consistent with findings of the other studies (6). Reasons for female preponderance are probably higher prevalence of iron deficiency and unknown hormonal influences (6).

Mean age of patients in this study is 27 years and it is less than the average age described in western studies (24). Probable reason for this difference is that our patients have more severe grades of dysphagia and hence early presentation (24). However, studies done in Africa and Asia shows similar age distribution (25). Dysphagia in PVS is typically intermittent initially and is limited to solids and is usually felt in the throat. Choking spells and aspiration may occur because of the proximal location of the web.

Dysphagia is the most common symptom in this study and it is initially intermittent but later it is progressive and persistent. Even though dysphagia is the most common symptom, it is well tolerated, and patients adapt to it by changing their dietary habits. Hence there is a long symptom duration before diagnosis. Mean duration of symptoms in this study was 9 months and is comparable to other studies (26). However, some patients present with acute dysphagia due to sudden esophageal obstruction by hard foods like chicken bone. Other associated symptoms include weight loss, generalized weakness and occasionally throat pain. Some of the clinical features are related to iron deficiency. Anemia is very common in these patients and 92% of patients in this study have iron deficiency anemia and other studies show similar figures (21). Mean Hb level was 8.1 gm/dl and many patients (92.3%) had low or low normal BMI (< 20).

Upper gastrointestinal endoscopy is the gold standard test for the diagnosis of post cricoid webs. In this study, endoscopy is 100% successful in identifying post cricoid webs. Dia et al (27) and Okamura et al reported that the web was identified at endoscopy in all the patients included

in their studies (28, 29). However, in some cases webs may be thin, incomplete and hence they get accidentally ruptured before visualization by endoscope. Moreover, at times they get broken if endoscope is not introduced under vision. Therefore endoscopic identification of post cricoid webs can only be 84.2% as described by Ben Gamra et al (30). Treatment of post cricoid webs is basically endoscopic guided. Iron supplementation and blood transfusion depending on severity of anemia may be given. Most common endoscopic treatment used is Savary Gilliard dilatation as described in material and methods. Same has been used in 96% of patients in this study. In our study, all patients underwent successful bougienage and 3 (6%) patients had dilatation induced post cricoid perforation. Endoscopic dilatation is recognized by several authors as a safe procedure with a low adverse event rate ranging between 1% and 3%. In our patients after dilatation had significant relief of dysphagia (96%). Patients who had post dilatation perforation recovered well with conservative treatment. Other therapeutic options described are argon plasma coagulation therapy or laser YAG lysis of the web, especially in cases of multiple recurrences. Surgery has no role in the management. Recurrence rates ranged between 14% and 30% in some series (21). It was 9.5% in our study in the follow up period. PVS is associated with a high risk of malignant transformation (3%-30%) and is considered as a precancerous lesion. In this study, malignancy in the postcricoid region hasn't been encountered during follow up. However, many patients who were diagnosed to have post cricoid malignancies might have had an undiagnosed post cricoid web previously. An association with cancers of the oral cavity, hypopharynx, distal esophagus, and stomach were also described. Therefore, long-term follow up of these patients is required. Prognosis is generally good, unless PVS is complicated by hypopharyngeal or esophageal carcinoma. Limitations of this study are that it is a single centre study and therefore number of patients included are relatively low in count. Another limitation is that there is no long term follow up of the patients, there by the risk post cricoid malignancy couldn't be evaluated.

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