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# Association of Iron Deficiency with Dysphagia: Review Article

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## ABSTRACT:

**Objective:** Patients will Iron Deficiency Anemia has been found to have Dysphagia associated with Oral, Pharyngeal and at esophageal level however, limited data and studies are available to discover the relation of this nutrient with swallowing difficulty. Therefore the following review of the available studies has been conducted to proof the direct relation of Iron deficiency in the cause of dysphagia and the same supplements can help to improve swallowing difficulty.

Purpose: The study made here under, hypothesizes to identify the following aspects:

1. Does Iron deficiency Anemia affects all levels of Dysphagia?

2. Can Iron supplements be used to improve swallowing difficulty with adult patients?

3. Is it the Iron deficiency that causes impairment in the pharyngeal and esophageal track or, does is it the dysphagia that causes Anemia?

**Method:** A systematic review analysis was conducted through the published studies from Skyhub or Pub Med to form a critical investigation and view point. The included readings taken into account were from 2001 to present date.

**Conclusion:** The association of Iron with Dysphagia was found to be positive, how the exact nature of interdependence remained ambiguous.

**Keywords:** Plummer Vinson Syndrome, Kelly Peterson Syndrome, Sideropenic Dysphagia, Anemia, Carcinoma, Papillae, Epidermis

## I. INTRODUCTION

Iron is one of the most important nutrients a human blood requires which is normally found as hemoglobin and myoglobin within the red blood cells and muscle cells respectively. Deficiency of this important nutrient within a biological being specifically at the blood echelon can result in a decreased range of hemoglobin level which creates the absence or abridged number of adequate healthy red blood cells. This condition is typically termed as Iron-Deficiency Anemia and the blood fails to transfer sufficient amount of oxygen from the lungs to the cellular tissues. Unrelated to our current topic of concern, there are other types of Anemia that may have an indirect relation with Dysphagia, which will be unveiled in the later part of the paper.

People who are under the condition of Iron Deficiency Anemia have been found to encompass Dysphagia associated with Oral, Pharyngeal and at esophageal level. The following paper presents a hypothesis that states a direct relation of Iron deficiency in the etiology of dysphagia hence; the same supplements are ought to be beneficial in treating swallowing difficulty.

The most widespread cause of dysphagia that has an inextricable link with Iron deficiency is pharyngeal and upper esophageal difficulty with swallowing. Pain while ingesting the food into the esophagus, sensation of food getting stuck in the throat or behind the chest bone, heartburn, regurgitation of food, stomach acid back into the larynx, frequent cough or gag during swallow and significant weight loss are regular indicators of dysphagia.

Alongside, neurologic disorders such as, cancers, GERD, scars at any level of digestive track, radiation

therapies, and muscle weaknesses are the common etiology for this disorder. Most popular and one of the many causes of pharyngeal and esophageal dysphagia are the laryngeal and esophageal webs, post cricoids carcinomas that are said to be the linked symptoms of Plummer Vinson Syndrome. Plummer Vinson syndrome, which is also known as hysterical dysphagia Kelly Petterson syndrome, or technically (in the field of speech and Swallowing pathology) called sideropenic dysphagia is a premalignant clause, in which the subject reports to have iron deficiency anemia, experiences dysphagia and a notable post-cricoid web that can predispose to malignant change and create carcinoma. It is of note worthy that Laryngeal webs are typically congenital; however can also be developed due to prolonged intubation. On the other hand, laryngeal carcinomas are a type of cancer that has developed at the region of larynx. The incidence of Plummer Vinson Syndrome is rare, nonetheless according to World Health Organization around 15% of the patients admitted at hospitals for the management of swallowing has a developed web and are strongly exposed to establish Laryngeal/esophageal carcinoma.

During the past years, iron deficiency anemia has been a vital concern of study to discover its role in the development of Laryngeal webs and sideropenic Dysphagia. This paper would shed light over the association of Iron deficiency Anemia with Dysphagia specific to laryngeal and upper esophageal region.

#### II. IRON DEFICIENCY AND ORAL PHASE OF SWALLOWING

The Oral phase that plays a significant role in typical swallowing function has said to be affected by iron deficiency type anemia. Tongue plays a vital role in formation of the bolus and preparing it to pass through the pharynx into the digestive tract. The tongue as a muscle is covered with two components; one is the Mucosa the moist pink tissue that covers the whole, while the other is called the Papillae. The tiny bumps known to be the papillae are of three types, vallate, fungiform and fuliform. It has to be taken into account that filliform papillae are responsible to augment the exterior area and rasping the food particles that adhere to the glossal surface. On the other hand fungiform papillae play a significant role in food sensation, as they comprised of taste buds. Their responses prompt the brain cells with the taste type (sweet, sour or bitter). Collectively the absence of any of the papillae can result in difficulty withi the oral prep and oral phase of the swallowing.

The association of Iron deficiency Anemia with Dysphagia and tongue mucosa atrophy has been a subject of light in the past years. Walden – storm (2000) performed an experimental research providing iron supplements as a treatment for seven patients. Six out of them reported positive results concluding that iron therapy has helped to heal the epithelial defects at the corners of the mouth, tongue and throat.

Cheli et al. (2003) reported no relation of tongue depapillation with glossal atrophical changes. This suggest to the fact that hemoglobin does not impacts directly towards the tongue papillae. Beutler (2005) stated that iron deficiency may be due to the disturbance in the metabolism of tissue rather than just hemoglobin level. Hence we cannot progress to say that anemia may be the only cause of iron deficiency leading to Oral phase of swallowing difficulties.

#### III. IRON DEFICIENCY AND PHARYNGEAL PHASE OF SWALLOWING

Over the history researchers are hunting to find the answer for the delimma of chicken and egg that has built up to clear the phenomena of iron deficiency causing difficulty with swallowing. Previous studies made in late 1990's presented us with the facts that patients with a prolonged period of iron deficiency with accompanied complains of swallowing, have less contraction amplitude through the passage of bolus, in comparison to controls. On the basis of a study made by Dantas et al. (2000), it was evident that the reduced capacity for energy metabolism un-deviatedly affects the ability of skeletal muscle exercise. Through their experiment based on rabbits, they found that thyropharyngeal, crico-pharyngeal, and cervical esophageal muscles with iron-deficiency anemia illustrated morphological changes parallel to those noticed in muscular dystrophy. It is to be noted that these muscle intricacy is only related to the skeletal muscles and not the smooth muscles. It is known that fibers of skeletal muscles are always involved in brisk movements who do not require continuous power hence they are principally dependent on glycolysis as an energy source because their poor nature of oxidation. Due to reduced Iron in their blood, these contractions are difficult to regulate frequently. As per Miranda et al.(2003) iron deficiency can cause impairment in muscle contraction. A prospective study made by Am. College of Gastroenterology (2003) published a study which indicated that the astringent influence of the pharyngeal muscle for the propulsion of bolus into the esophagus is less than those whose iron levels were within normal limits. They also suggested that it was normalized by iron administration. Miranda et al's study of transit explains cases with slower incursion of the water into the proximal esophagus, in conformity with the risk of a condensed function of pharyngeal contraction. Within the esophagus the passage was deemed in patients than in the other group which was the control one. The lump at the posterior esophageal wall via a solid bolus or liquid increases the tension of passive elasticity within the circular muscles.

## IV. IRON DEFICIENCY AND ESOPHAGEAL PHASE OF SWALLOWING

In account of upper Gastro intestinal tract, the major dysphagia causing disorder is Plummer Vinson Syndrome, commonly known as Kellly Brown Peterson Syndrome or Sideropenic dysphagia. Studies that have reviewed Plummer Vinson Syndrome, have provided significant proofs of the laryngeal webs caused by Iron deficiency. Dantas et al. (2008) conducted a survey on the patients at a hospital, which summarized that manometric inspection data results of subjects demonstrated low-amplitude contractions and high intrabolus pressure in a plummer Vinson patient. It is of note worthy that after the presentation of iron supplements, the amplitude of contraction in these patients were greater than before and the intrabolus pressure reduced. Conversely, it is will be still of a surprise to know, why iron supplementation improves esophageal peristalsis and dysphagia in patients with this syndrome. Case reports provided by Hoffman et al. (2015) concludes that Iron supplements given as medicines to patients with Plummer Vinson syndrome improved their swallowing difficulty. According to him, numerous reports have provided us with the evidence that iron deficiency in the patients with this disorder may be due to the functional disorder of the esophagus rather than the morphological obstructions faced due to web, carcinoma or a lumph. Hence it is difficult to indicate the outcome, is due to the cause or may be the cause is due to that outcome. Simplifying it will be absurd to state Plummer Vinson Syndrome has caused iron deficiency, or is the anemia that has been the primary reason of developing the disease. Stated by Tahara et al. (2015) in her case reports she mentioned the unknown pathogenesis of Plummer Vinson Syndrome. Nonetheless, the most apparent mechanism of this syndrome is deficiency of iron in the blood stream.

The other contributing factors involve immunological, environmental and genetic features; however which have not been verified to participate as an accurate role in the pathogenesis of this syndrome. Regardless of its basis, the premise is based on deficiency of iron in blood, which leads to swift loss of enzymes that are iron- dependent. Decline in the number of these enzymes forms web and eventually may escort towards the development of laryngeal of upper esophageal carcinomas which is known as cancer of upper gastrointestinal tract.

# V. IRON DEFICIENCY AND CANCER

According to a recent study by Hung et al. in (2005) that states, people with Iron deficiency anemia have a significantly elevated overall risk of cancer than of those whose iron levels are within the normal limits, and the possibility of acquiring malignant cells is significantly higher after the diagnosis of iron deficiency. On the flick, the entire cancer family is allied with an increased peril of emergent iron deficiency anemia, though this possibility is limited to be with certain type of cancers that are particularly formed at the level of pharynx and esophagus. And the consequences of iron deficiency anemia can be particularly stern in people surviving with cancer, potentially interfering with treatment and minor survival chances.

Rare. (2006) performed an experiment to observe the epidermal changes at the post pharyngeal wall in the patients with Plummer Vinson Syndrome. Due to reduced Iron level in the blood and tissues; the hemoglobin and myoglobin the fresh cell growth of epidermis had developed a pause creating the stagnant web at the epidermis of the pharyngeal and upper esophageal wall. The width of the epidermal cell tissue was also found to be shorter than a typical one. With given Iron supplements orally, a notable increase in size of the epidermis was observed with improvement in swallowing and reduced web size.

#### VI. DISCUSSION

Iron resides in a human body as a considerable nutrient that acts to be the salt in a food. With its presence, nothing seems to be evident; however the absence of the same creates a hole in the overall body functions. There are millions of structures dependent on this nutrient just as the growth of cells particularly epidermis of liver, esophagus and bladder. In addition to that its significance for our blood plays a major role contributing to the overall blood function. Moving from a body nutrient based discussion towards a biological phenomenon will be swallowing. A typical passage of food from mouth towards the pharynx and finally into the esophagus is an appropriate function that constitutes to the positive working of our oral, phrayngeal muscles. Any discrepancy within this flow of bolus can be termed as dysphagia.

As stated above regarding the job that Iron plays, previous researches have attempted to prove it's relation with one of the cause of dysphagia that is intertwined with the pharyngeal and esophageal phase. Plummer Vinson syndrome presents with the characteristics of web at the post criciod region or within the food pipe and his condition is always related with iron deficiency. Since the web creates the block at the region of its growth, the subject complains of dysphagia. However it is of note worthy that a minority of the patients accessed to be an experimental subject has a history of dyphagia, few had iron deficiency anemia before that may have resulted in the revision of the web into a carcinoma. Another position to stand on is the uncertainity of the precedence of dysphagia and Iron deficiency anemia. Merely it is unsure if dysphagia has developed first or the iron deficiency held the laryngeal web. Also if both of them could be due to the presence of plummer Vinson syndrome, it still cannot make a certain decision about the efficacy of anemia's role in determining the etiology.

Mentioned above in few studies who tried Iron supplements to improve the condition associated with Plummer Vinson syndrome, have found to be surprisingly successful. Improvements with the reduction of web size and fading complains of dysphagia were reported. Also to mention due to the presence of iron as myoglobin in the cell tissue level, it improves the physical condition of the epidermal tissues present at the pharyngeal and esophageal level, which helped in reduction of the web size. Moving towards the modification of this web into the carcinoma, exposing it for a threatening malignant condition has also been reported to be associated with Iron deficiency anemia. Studies suggest that due to the absence of this nutrient in the blood stream or at cell tissue level, the vulnerability of post cricoids carcinoma rises up. Having said that, this can clearly state a direct and proportional dependence of the sideropenic type dysphagia with Iron. However it is still aunclear over the notion of pharyngeal phase dysphagia and esophageal dysphagia as a whole. For the reason that Plummer Vinson syndrome can be one of the cause for it, and cannot be generalize with other etiologies as neurologic or GERD without performing a cross sectional study. Keeping in view of the sustainable change that Iron supplements whether provided orally or injected into the blood stream, it is fair to say that if this has helped with one of the obstructions present on way. However, further researches are required to test the efficacy.

Adding to the improvements mentioned for Plummer Vinson Syndrome, researchers have also noticed the duration of the bolus transit from oral cavity into the pharyngeal cavity and, from pharyngeal cavity into the esophageal cavity. Unpredictably the data summarized demonstrated a delay in the total time duration of the subjects who presented with Iron deficiency Anemia from the bolus passed from the oral cavity into the pharyngeal cavity at the point of pharyngeal trigger. Additionally pharyngeal to esophageal transit was insignificant only if there is not any obstruction seen via modified barium Swallow. However the studies do mentioned few subjects having a swollen esophageal wall, giving them the benefit of doubt in presenting the pharyngeal to esophageal delay. To be noted that epidermal swelling of the post pharyngeal or esophageal wall progressed after the iron level falls into the normal range. Hence, neglecting the point of view that Iron supplements may only improve webs or carcinomas, it may be beneficial in increasing the transit duration giving a doubt on the thought of neurological etiology. It may be reasonable to state that iron does affect the worth of neurons responsible to bring the pharyngeal trigger.

Another realm of the iron deficiency has been hypothesized to be linked with oral cavity of a human body. As mentioned regarding the structure of human tongue, its purpose correlated with food is strongly adhered with the

papillae present on the mucosa. Since each papilla is responsible to perform a respective task, the frequency of its presence on the glossal surface speaks about the ability of the sensation it holds. The fungiform papillae that are at the sides of the lingua have the taste buds in them. Absence of the same may ground the loss of oral sensation within the oral cavity, hence affecting the oral prep phase which prepares the bolus to fall into the pharynx. Increasing the quantity of iron into the blood via providing iron therapy, amplifies the growth of papillae thus improving the oral sensation and decreasing the complain of swallowing difficulty that are often heard by family caregivers.

Comparing to all the three phases of dysphagia and the impact of Iron, the dilemma of Chicken and egg still remained unanswered. The literature does not provide us with enough evidence to rule out the perplexity of iron affecting the functions of body organs related to swallowing, or the discrepancy of the organ functioning have created the deficiency of iron.

#### VII. CONCLUSION

The provided review of the studies aided us to conclude that Iron deficiency Anemia does affect all the levels of dysphagia, but not in the same manner and frequency. It also co- relates with the etiology that has caused swallowing difficulty. According to the literature, Iron supplements have proven to improve the complains of dysphagia, however it remains specific to certain symptoms, making it a symptomatic improvement suggestion. However the dilemma of the Iron deficiency being the cause of impairment in the pharyngeal and esophageal track or; does is it the dysphagia that causes Iron deficiency Anemia remained unknown as to what have caused what. Conversely larger number of supports articles favors to the fact the due to Iron deficiency anemia a person develops Plummer Vinson Syndrome. This restricts it to pharyngeal and esophageal phase only.

#### VIII. References

- 1. Goel, A., Bakshi, S. S., Soni, N., & Chhavi, N. (2017). Iron deficiency anemia and Plummer– Vinson syndrome: current insights. *Journal of blood medicine*, *8*, 175.
- Tahara, T., Shibata, T., Okubo, M., Yoshioka, D., Ishizuka, T., Sumi, K., & Arisawa, T. (2015). A case of plummervinson syndrome showing rapid improvement of Dysphagia and esophageal web after two weeks of iron therapy. *Case reports in gastroenterology*, 8(2), 211-215.
- 3. Sugiura, Y., Nakagawa, M., Hashizume, T., Nemoto, E., & Kaseda, S. (2015). Iron Supplementation Improved Dysphagia Related toPlummer–Vinson Syndrome. *The Keio journal of medicine*, *64*(3), 48-50.
- 4. Miranda, A. L. M., & Dantas, R. O. (2003). Esophageal contractions and oropharyngeal and esophageal transits in patients with iron deficiency anemia. *The American journal of gastroenterology*, *98*(5), 1000-1004.
- 5. Rodríguez, M. J. L., Andrés, P. R., Jiménez, A. A., Maíllo, M. R., Lafuente, A. L., & Carrera,
- (2002). Sideropenic dysphagia in an adolescent. *Journal of pediatric gastroenterology and nutrition*, 34(1), 87-90.
- 7. Hartfield, D. S. (2010). Reversible sideropenic dysphagia in a toddler with iron deficiency. *Clinical pediatrics*, *49*(2), 180-182.
- 8. Costa, D. B., & Drews, R. E. (2009). Peripheral effects of iron deficiency. In *Iron Deficiency and Overload* (pp. 159-180). Humana Press, Totowa, NJ.
- 9. Ganapathy, K. S., Gurudath, S., Balikai, B., Ballal, S., & Sujatha, D. (2011). Role of iron deficiency in oral submucous fibrosis: An initiating or accelerating factor. *Journal of Indian Academy of Oral Medicine and Radiology*, 23(1), 25.
- 10. Novacek, G. (2006). Plummer-vinson syndrome. Orphanet Journal of rare diseases, 1(1), 36.
- 11. BÜYÜKBERBER, M., & GÜLfiEN, M. T. (2005). Plummer-Vinson syndrome and dilation therapy: a report of two cases. *Turk J Gastroenterol*, 16(4), 224-227.
- Rupak, S., Baby, G. G., Padiyath, S., & Kumar, K. R. (2012). ORAL SUBMUCOUS FIBROSIS AND IRON DEFICIENCY ANEMIA RELATIONSHIP REVISITED-RESULTS FROM AN INDIAN STUDY. *E-Journal of Dentistry*, 2(2). Liu, K., & Kaffes, A. J. (2012). Iron deficiency anaemia: a review of diagnosis, investigation and management. *European journal of gastroenterology & hepatology*, 24(2), 109-116.
- 13. Chisholm, M. (1974). The association between webs, iron and post-cricoid carcinoma. *Postgraduate medical journal*, *50*(582), 215-219.
- 14. Bredenkamp, J. K., Castro, D. J., & Mickel, R. A. (1990). Importance of iron repletion in the management of Plummer-Vinson syndrome. *Annals of Otology, Rhinology & Laryngology, 99*(1), 51-54.

- 15. Puntis, J. W., Chapman, S., Proops, D. W., & Sartori, P. (1989). Dysphagia due to oesophageal web. Archives of disease in childhood, 64(1), 141-143.
- 16. Dysphagia, S. Cancer Association of South Africa (CANSA).