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An Entity called Sports Anaemia, does it really exist or is a misnomer: A systematic review of existing literature.

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Background: Iron is critical for optimal athletic performance because of its role in energy metabolism, oxygen transport and acid base balance. Traditionally empirical iron supplementation is done in all elite athletes because athletes involved in endurance sports have a decreased haemoglobin and haematocrit which is termed as "sports anemia".Some investigators say that the slight decrease in haematocrit after heavy physical training is brought about by increased plasma volume due to renal sodium reabsorption and water retention. They say that sports anaemia is a dilutional pseudo anaemia and is a beneficial adaptation to aerobic exercise and the ritual of routine iron supplementation in athletes is not recommended. They advocate that the decision to supplement iron should be based on serum Ferritin levels which should be monitored in conditioned athletes. Recently many other causes of anemia have been identified in sportspersons like increased iron loss, reduced iron absorption and exercise induced inflammation which needs to be treated because it is the goal of sports physicians to help every athlete achieve their maximum level of performance. The aim of our study is to review existing literature and find out whether "sports anemia" really exists or is a misnomer.

Research methodology: A PubMed, Research gate, Embase , The Cochrane Central, Scopus and Google scholar search through March 2022 was performed using the following terms: sports anaemia, iron supplements in athletes , nutrition in sports, Ferritin levels in sports, hematological changes in sports. A bibliographical review of the various articles searched was done. Citations including observational studies, review articles, guidelines and consensus statements, relevant documents like thesis and conference proceedings by eminent sports physicians were narratively summarized.

Inclusion criteria : Studies conducted on sports persons both male and female in the form of controlled trials, observational studies , consensus statements by eminent sports physicians , review articles and thesis in English language on the topic of sports anaemia , iron supplements in athletes, sports physiology, nutrition in athletes, ferritin levels in athletes, haematological changes in sports were included.

Exclusion criteria : Studies on anemia and haematological studies not including sports persons or athletes.

Key findings: The term "Sports anemia" is not a specific clinical entity and is a misnomer and should be replaced by "Anemia/Iron deficiency in sportspersons".

Abbreviations: Hb-Hemoglobin, Hct-Hematocrit, Hp-Haptoglobin, TIBC-Total iron binding capacity, PCV- Packed cell volume, RBC-Red blood cells.

The term "Sports Anemia" is defined as a low hemoglobin and hematocrit value seen in endurance athletes involved in intense physical training. Anemia and iron deficiency has been linked to adverse health outcomes in athletes in the form of overuse injuries and a decline in physical and cognitive performance (Katheryn E Myhre 2016 et al(1)).

An initial response to intense physical exercise is sodium and water retention which causes dilutional pseudoanemia in the athletes. The increased plasma volume is a beneficial adaptation as it increases the stroke volume and also it decreases the viscosity of blood thus increasing the blood supply and oxygen delivery to the exercising muscles. At the same time it also contributes to heat regulation by increased perspiration. Endurance athletes especially runners are prone to hemolysis due to mechanical injury which further contributes to anemia. Stimulation of erythropoiesis occurs secondary to an increased oxygen demand by the exercising muscles but it is initially outpaced by the hemodilution and hemolysis due to footstrike , thus leading to anemia. Therefore at this stage, simply measuring the blood levels of hemoglobin and hematocrit does not take into account the hemodilution that occurs in these athletes. Due to increased erythropoiesis, there is a toll on the existing iron stores to meet the increased requirement of iron which leads to decreased serum Ferritin levels even in the absence of anemia. Iron deficiency is common in female athletes and exertional fatigue is known to occur in athletes with iron deficiency alone even in the absence of anemia.

Review of literature:

First mention of the term "Sports Anemia" was done by Hisato Yoshimura(2) , M.D. in a review article named "Anemia during physical training" in the year 1970 in the Journal Nutrition Reviews.

Hemolysis and Sports Anemia:

Hemolysis has been implicated as one of the factors contributing to anemia in endurance athletes. Hemolysis induced by exercise occurs due to rupture and destruction of RBCs . Footstrike hemolysis is the term given to intravascular hemolysis in feet of runners due to impact forces. Various causes of hemolysis in athletes include mechanical injury, repeated muscle contractions, vasoconstriction and metabolic factors like lactic acidosis, hyperthermia , dehydration, hypoxia etc (3)

In a study by Jacqueline L. Puhl and William S. Runyan in 1980(4), the haematological variations during Aerobic Training of 19 college women were noted and it was suggested that although aerobic training of increasing intensity in young women may be accompanied initially by decreases in Hb , Hct , and RBC count and an increase in MCV , these changes result from RBC destruction rather than hemodilution, the return to hematopoetic balance could impose a draw on body iron stores.

In a comparative study "Hematologic features of Olympic volleyball athletes" by JJ Faintuch et al (5) in 1992, questionnaires , physical examination and lab investigations were used to study 16 volley ball highly trained athletes and 23 outpatients with the same ages and gender that have not had any significant disease. All athletes and patients had Hb levels of >13 g/dl, but the athletes had Hb and Hct lower than the control subjects , 25% of athletes had both total and indirect bilirubin increased indicating hemolysis. Seven patient controls and only one athlete had intestinal parasitic infestation. They concluded that volleyball athletes were in a borderline anemic state.

An article in the year 2003 by Telford, RD et al(6) named "Footstrike is a major cause of hemolysis during running" published in the Journal of applied Physiology, the authors said that intravascular hemolysis during running occurs because of footstrike due to the impact forces. They studied 10 male triathletes who each completed 2 separate sessions of 1 hour each of running and cycling at 75% peak oxygen uptake one week apart. Plasma free haemoglobin and haptoglobin concentrations were measured as indicators of hemolysis. The plasma free Hb concentration increased after both running and cycling but the increase was four fold greater after running. It was concluded that footstrike was a major contributor to hemolysis during running though general circulatory trauma to red blood cells may result in exercise induced hemolysis in both groups.

K Shiraki in 1977(7) did an experimental study which consisted of two series of observations to find the association of protein nutrition and sports anemia . In the first series, 4 healthy male students were selected from a tennis club of a university and

they were subjected to training and it was found that tennis training (1000 kcal of energy expenditure per day) induced sports anemia in previously untrained subjects typically on 3rd to 7th day of training period. In the second series of experiments it was confirmed that the reduction of blood cells induced by the exercise was closely related to the nutritional status of the individuals especially to intake of protein because in the low protein group the reduction of red cells was most pronounced and the recovery from anemia was most delayed. It was noted that the osmotic fragility of red cells increased from the third to tenth days of the exercise period in the standard and low protein groups but not in the high protein group.

In an another comparative study in 19 top level male soccer players and 20 male controls, A Resina et al in 1991(8), did a haematological comparison and found that serum iron , TIBC, transferrin saturation and serum Ferritin were not significantly different in athletes and controls but serum Haptoglobin was significantly lower in soccer players indicating an increase in intravascular hemolysis. Since formed Hb – Hp complex is taken up and metabolized by hepatocytes so soccer players had a redistribution of iron stores among tissue compartments. They suggested a multiparametric haematological monitoring of iron metabolism is therefore necessary in these players in order to detect subjects at real risk of iron deficiency. The pharmacological iron supplementation should be limited to these subjects only when clinical evidence of reduced tissue iron supply is present.

Hemodilution and sports anemia:

A decreased haematocrit and haemoglobin after training has been explained by an increased plasma volume in endurance athletes due to stimulation of the renin angiotensin system leading to increased sodium and water retention.

Williams E.S., Ward M.P. , Milledge J.S., Withey W.R. et al(9) of London in 1979, studied 5 male subjects and measured the sodium balance , fluid homeostasis and plasma renin activity and plasma aldosterone concentration during prolonged exercise of hill walking for 5 consecutive days which was preceded by a 4 day control period and followed by a 4 day recovery period .It was found that by the end of the exercise period there was a positive water balance of about 0.9 litres. There was net movement of 0.94 litre of fluid from the intracellular to the extracellular space. Packed cell volume decreased from a mean 43.5% to 37.9% after 5 days of exercise, indicating that about 0.9 litre of extracellular fluid entered the vascular compartment. Also during the exercise period plasma renin activity rose and there was a significant correlation between these values and sodium retention and leg oedema. It was concluded that the post training increase in plasma volume in highly trained athletes is likely caused by aldosterone dependent renal sodium reabsorption and water retention.

James Douglas Busch in 1982(10), in his thesis named "The demonstration and evaluation of hemoglobin and hematocrit Testing as support services in preparing elite swimmers for serious competition" monitored Hb and Hct in 9 male swimmers during 2 months of hard training , tapering and post competition rest. He also monitored Hb and Hct levels of 18 male and 19 female members of the1978 Commonwealth Games swimming teams during maintenance training before competition. Weekly variations were observed during hard training in first study. Reduced work load and /or coach determined iron supplementations seemed to increase Hb and Hct levels in most athletes. It was concluded that Hb and Hct screening is a feasible and beneficial support service in the preparation of elite swimmers for competition. A significant decrease in Hb and Hct occurred temporarily during training but normal values returned when training was completed.

Another study named "Athletes pseudoanemia" in the year 1991 by Lindsay M.Weight etal(11) was published in the European Journal of Applied Physiology and Occupational Physiology . To characterise the so called pseudoanemia of endurance trained athletes, the plasma volume, red cell volume and total blood volume of 12 male and 12

female athletes and 5 male and 5 female non-exercising controls were measured using I-125 labelled human serum albumin and Cr-51 labelled erythrocytes. The mean plasma volume in male athletes was found to be 37.5% higher than the controls and that of female athletes was 18.1% higher than plasma volume of female controls. It was concluded that the decreased blood haemoglobin levels in athletes was due to mainly a dilutional effect.

E R Eichner in 1992(12) published an article in Med Sci Sports Exerc.in which it was concluded that sports anemia is a misnomer and a false anemia which is in fact is an adaptation to benefit the endurance athletes and is caused by an increase in plasma volume leading to hemodilution. It was suggested that iron supplementation was of benefit only in women athletes who developed iron deficiency despite a diet rich in iron or in those athletes that had true anemia that decreased athletic performance.

Ferritin Levels and Iron supplementation in sports anemia:

Many factors contribute to low Ferritin levels in athletes like increased iron loss in sweat which may lead to a loss of upto 2.5 micrograms of iron /litre of sweat(13). Hematuria is common in runners due to bladder contusions owing to repeated contact of posterior bladder wall with fixed bladder neck or due to renal ischemia and increased glomerular permeability.(14) Gastrointestinal bleeding , inflammation and hemolysis also contribute to iron loss in athletes.(15) Heavy menstrual bleeding in female athletes can lead to hypeferritemia and anemia.(16)

There is an increased iron demand to meet the increased rate of erythropoiesis and muscle hypertrophy. Reduced iron absorption due to exercise induced inflammation and redistribution of gastrointestinal blood flow can also decrease serum iron levels.(17)

Nutritional iron deficiency is common in athletes on restrictive diets like dancers and gymnasts in order to be in the ideal body weight category for their sport.(18)

A significant comparative study was done by Magnussan et al(19) in 1984 in which a haematological comparison was performed between 43 middle and long distance male runners and 119 male controls. The haematocrit, serum iron, transferrin saturation , and serum Ferritin values were significantly lower in athletes. There was shift in red cell catabolism in athletes from reticuloendothelial system to the hepatocytes and this may explain the paradoxical findings of low serum Ferritin concentrations and reduced content of bone marrow hemosiderin in athletes.It was concluded that runners anemia is no true anemia and thus no indication for routine iron supplementation.

In a study conducted by L M Weight et al(20) in 1992 , the authors compared the red cell indices and iron status of 60 male and female distance runners and ballet dancers to 30 each of male and female non-exercising controls of both sexes. They found that the mean Hb levels of all groups were within the normal ranges and there was no difference between the athletic and control groups of each sex. The mean Ferritin concentration of the male distance runners was significantly lower than that of controls. Iron deficiency anemia occurred in only 1.7 % and 3.3 % of male and female distance runners and 3.3% of dancers. However 11.7 % of male and female distance runners and 20.0% of dancers recorded Hb values in the lower range of the normal (14 gm/dl in males and 12 gm / dl in females.) It was concluded that the term sports anemia was misleading and it did not define a specific clinical entity and observed that athletes were at no greater risk for developing a frank anemia than the normal non-exercising population.

Richard E Rodenberg et al(21) wrote a review in Curr Sports Med Rep 2007 July issue , on the controversial issue of iron supplementation for iron depleted non-anemic athletes. It was observed that athletes who are anemic secondary to iron deficiency do benefit and showed improved performance with appropriate iron supplementation. There is

contradictory evidence for iron supplementation and improving performance in the iron depleted non-anemic athlete. Though serum Ferritin is monitored to know the iron status , there is no consensus as to the appropriate maintenance levels of Ferritin in athletes.

Cosimo Ottomano and Massino Franchini (22) in the year 2012 published a review article named "Sports anemia: facts or fiction ?". It was concluded that there is no evidence that iron supplementation increases athletic performance, except in individuals in whom iron deficiency is established. In athletes with low Ferritin concentrations without anemia iron supplementation might be useful . Determination of serum transferrin receptor saturation and red blood cell free protoporphyrin concentrations may identify those in whom iron administration is likely to be beneficial. It was suggested that serum Ferritin concentrations should be monitored in conditioned athletes and physiological decreases in ferritin during the early stages of training should be taken into account when individuals are examined and before any decision to give iron is made and uncontrolled use of iron should be avoided.

Takahiro Nabeyama et al (23) in 2020 performed a health assessment on anemia and serum ferritin levels, along with nutrient intake evaluation for Kendo practitioners in a university in Japan. A total of 56 Kendo practitioners (39 male and 17 female) aged between 18 and 23 years participated in the study and none of them exhibited the WHO defined criteria for anemia (<13 or 12g/dl of hemoglobin in males and females respectively) while hypoferritinemia (less than 30ng/dl) was found in 7 (41%) females but not in males. They proposed a future study with larger cohorts in multiple sites to assess the prevalence of iron deficiency for validation and to devise a strategy for improving the iron status in Kendo athletes.

In 2022 another retrospective study conducted on 435 male and female adolescent students involved in a sports club by Kana Yamamoto et al(24) , the authors analysed the profiles of anemia and found that the prevalence of anemia was 16.5% and it was significantly more in female athletes. They found a significant association between low ferritin and an elevated creatinine kinase level with anemia in these athletes. They concluded that both hypoferritinemia along with excessive physical training which is indicated by an elevated creatinine kinase level, contribute to the risk of developing anemia in athletes . Therefore the sports physicians should assess the amount of physical activity along with the iron stores in clinical practice.

Multifactorial etiology of anemia in sports persons:

Etiology of Anemia in sportspersons is multifactorial ranging from plasma volume expansion , hemolysis, reduced iron intake, reduced iron absoprption, increased iron demand , increased iron loss to genetic factors and inflammation.

RR Pate in 1983(25) did a review of literature available till then and concluded that a many athletes had Hb concentrations below optimum levels for endurance sports. He delineated that the cause for this sports anemia was plasma volume expansion, increased erythrocyte destruction combined with reduced erythropoiesis , dietary deficiencies and increased iron losses. The treatment depends on the causes of anemia and it may include training modifications and iron supplementation.

A review article named "Iron deficiency and anemia in female athletes causes and risks" by Shawn Portal et al(26) in 2003 October was published in which the author reviewed the causes and risks of iron deficiency and anemia in female athletes. It was concluded that athletes are a special group of subjects with additional reasons for iron deficiency such as plasma volume expansion, increased perspiration , footstrike hemolysis and occasionally malnutrition and menstruation in female athletes. However the most common cause for a low Hb in an athlete is dilutional psuedoanemia which is caused by exercise induced fluid retention.

In 2021, a narrative review namely "Anemia in sports" by Marc-Tudor Damain et al(27) , the authors have listed many more reasons for anemia in athletes

including hemodilution and redistribution , iron deficiency caused by increased demands, dietary restrictions to be in the ideal body weight category for a particular sports event ,decreased absorption of iron , increased iron losses via sweating , hematuria , gastrointestinal bleeding , inflammation , and intravascular and extravascular hemolysis., Celiac disease etc. Females and adolescent athletes on dietary restrictions are especially at risk for iron deficiency. The authors concluded that Serum Ferritin and Hemoglobin cut off values should be further assessed with respect to age, sex, and type of sport .

Discussion:

After going through the existing literature beginning from the year 1970 till 2022, we have found that though every author acknowledged the existence of iron deficiency in most endurance athletes , WHO defined criteria for anemia (Hemoglobin <13 g/dl in males and <12 g/dl in females) that is attributed to sports was not documented in most of the studies . Therefore the answer to our question that Sports Anemia truly exists in every endurance athlete is "No".

In a review article published by Heimo Mairbaural (28) of the department of sports medicine university of Heidelberg Germany in the year 2013, the author said that trained athletes, particularly in endurance sports, have a decreased hematocrit which is sometimes called sports anemia. In a review article published in1992, in journal of Clin Sports Med , EP Balaban (29)of the department of internal medicine university of Texas concluded that athletes may be at a higher risk to develop decreased iron stores but iron deficiency anemia is uncommon and the ritual of routine iron supplementation is not recommended.

Cosimo Ottomano and Massino Franchini(22) in the year 2012 published a review article named "Sports anemia: facts or fiction ?". They concluded that sports anaemia does not exist and some athletes are anemic and consequently must be diagnosed and treated.

Many factors contribute to iron deficiency and iron deficiency anemia in the sportspersons . In addition to the estimation of hemoglobin and hematocrit serum Ferritin levels should also be monitored at regular intervals in endurance athletes. Though there is a wide range for what is considered to be a "normal Ferritin" ranging from 15 to 200 ng /ml in males and 15-150ng/ml in females(WHO guidelines to assess iron deficiency and overload) , there is no consensus on what is the baseline level of Ferritin to start iron supplementation in various types of sports and in males and female athletes of different age groups. Therefore the various studies conducted on the benefits of iron supplementation in athletes have shown mixed results. Yuki Kobayashi et al (30) in 2020 tried to determine the cut off value of ferritin in male runners for iron deficiency and found that serum Ferritin levels below 40ng/ml to be the cut off value to determine iron deficiency in male runners. Trent Stellinwerff , PhD, senior advisor for Canadian Sport Institute Pacific aims for a Ferritin level greater than 35ng/ml with a normal hemoglobin in athletes. In another study by Takahiro Nabeyama(23) hypoferritemia in Kendo athletes of Japan was defined as a serum Ferritin value below 30 ng/ml. The 2009 joint consensus statement from the American Dietary association and American College of Sports Medicine states that athletes may begin to have symptoms like a decreased performance and fatigue if Ferritin falls below 30 ng/ml. They aim to keep a Ferritin level in athletes above 40 ng/ml so there is a reserve of stored iron.

Another consensus statement of the Swiss Society of Sports Medicine, the authors suggested that in healthy male and female athletes(>15 years of age) Ferritin values<15 ng/ml are equivalent to empty iron stores, values between 15-30 ng/ml indicate low iron stores, and 30ng/ml is the cut off value of serum ferritin in adult athletes.

On the other end of the spectrum, Metler et al in 2010(31) said that incidence of iron excess was common in male athletes and iron supplementation should be done only if iron levels were found to be low. Therefore nowadays many sports physicians are against empirical iron supplementation in all elite

athletes especially males.

Another study published by Zotter et al(32) reported abnormally high serum ferritin levels among professional road cyclists. 1000 serum samples for ferritin assessment were collected . 45 % of the cyclists displayed ferritin values over 300 ng/ml. They concluded that professional road cyclists used excessive iron supplementation leading to high serum ferritin levels, which is related to health complications later in life.

Empirical iron supplementation especially in male athletes can cause liver failure and early onset of complications in cases of hemochromatosis (common in 1 in 200 adult white men). Therefore nowadays many sports physicians are against empirical iron supplementation in all elite athletes especially males. Women may need more iron in view of menstrual blood loss.

Most of the studies on sports anemia are observational studies and reviews by eminent sports physicians and a very few studies are controlled trials. Moreover even the controlled trials have been conducted in a very small number of elite sports persons involved in different type of sports having different levels of physical efforts involving different groups of muscles and the controls chosen in most of these studies were people not so physically active . There can be other causes of anemia like parasitic infestations, occult blood loss in stools, hematuria, drug induced haemolytic anemias, malabsorption syndromes, coeliac disease, Thalassemic trait etc that need to be ruled out before recruiting individuals in these trials .

Since there is a lot of pressure on the sportspersons to perform at the best of their ability as well as a pressure on the coaches and sports physicians to extract maximum performance from their sports teams, conducting randomized controlled trials in this group of people is next to impossible and subject to bias. Also the few controlled studies documented in the literature are on elite sports persons involved in different types of sporting activities with different levels of physical exercises and they cannot be merged together to reach a conclusion on the existence of anemia in all types of sports.

The physiological changes in sports and exercise is a vast topic that needs to be thoroughly studied and an understanding of the sports physiology is must for every sports physician so that they can appropriately treat and extract optimal performance from the athletes.

Conclusions:

To conclude, whether "Sports anaemia" truly exists or is a misnomer seems to be an enigma. This term may be replaced by "Anemia/ iron deficiency in sportsperson".

Serum Ferritin levels should be monitored closely in athletes . Low Ferritin levels are associated with a poor athletic performance.

The level of physical training depending on the type of sport should also be taken into consideration in clinical practice.

Levels of iron stores and haematological parameters should be tested at regular intervals before and during an intense training period and also during periods of rest, in view of acute variations that may occur due to intense physical exercise and strain.

Menstrual abnormalities especially polymennorhoea in the female athletes should be treated. Exertional fatigue especially in a female athlete should be investigated and iron supplementation may be started early.

Empirical iron supplementation in all athletes especially males is not indicated.

Iron deficiency anemia limits athletes capacity for work and iron supplements are required in such cases. It is important to realise that anemia in sports is relative and the signs of anemia are subtle.

More studies need to be conducted to find out the optimum levels of serum Ferritin in various types of sports with variable levels of physical training.

Finding and fixing anemia in athletes renews their stamina and enables them to perform their best.

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