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Original Article

Internal Medicine Section

Food Faddism Complicating Jaundice in Gilbert's Syndrome Patients- A Prospective Cohort Study

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ABSTRACT

Introduction: Food faddism is a term that refers to a particular food or food group that is overemphasised in the regular diet or omitted to cure a specific condition. It affects an individual's health by complicating the health status of already infected individuals, which harms their nutritional status in particular, causing macro and micronutrient deficiencies. In the present study, authors have analysed the effect of food faddism in Gilbert's syndrome patients. The state of vitamin B12 deficiency (Megaloblastic anaemia) is observed because of dietary restrictions due to food myths causing ineffective erythropoiesis prolonging hyperbilirubinemia in Gilbert's syndrome patients.

Aim: To study the effect of food faddism on haematological parameters in recently diagnosed Gilbert's syndrome patients.

Materials and Methods: A prospective cohort study was conducted in a tertiary care centre of north coastal Andhra Pradesh, India, from June 2019 to June 2021. A total of 125 consecutive patients, newly-diagnosed with Gilbert's syndrome, were enrolled. A constant rise in the indirect bilirubin levels between 2-5 mg/dL with normal serum liver transaminases was considered for diagnosing Gilbert's syndrome. On monthly follow-up for six months, 21 patients presented with extreme fatigue and limb paraesthesia. Every month during the follow-up, thorough history about any recent changes in food habits was noted. Blood investigations like complete blood pictures and Vitamin B12 levels were done at the time of diagnosis, after six-month follow-up, and after treatment with co-methyl (Cyanocobalamin) B12 injections. Comparison of study variables at the time of diagnosis of Gilbert's syndrome, before and after the treatment with co-methyl (Cyanocobalamin) B12 injections was done using paired t-test based on nature of distribution, and p-value was calculated.

Results: Out of 125 Gilbert's syndrome patients with a mean age distribution of 36.15±11.82 in (109) males and 36.06±11.93 in (16) females, 21 patients presented with symptoms after six months of follow-up, a habit of practicing a fad diet was noted, along with depression of cell lines showing pancytopenia. There was a significant decrease in the mean values of Haemoglobin (Hb)% (12.68 to 7.95), Total Count (TC) (8219.05 to 3819 cells/cumm), Mean Corpuscular Haemoglobin Concentration (MCHC) (33.30 to 32.17) and Vitamin B12 (391.63 to 125.68) and increase in mean value of Mean Corpuscular Volume (MCV) (91.33 to 101.18), at the time of diagnosis and after six months of follow-up. On treatment of the patients with co-methyl (Cyanocobalamin) B12 injections a significant improvement in the mean values of Hb% (7.95 to 13.28), TC (3819 to 8652 cells/cumm), MCHC (32.17 to 33.43) and Vitamin B12 (125.68 to 311.81) along with decrease in the mean value of MCV (101.18 to 90.0) was noted.

Conclusion: The most common fad diet followed by Gilbert's syndrome patients is the restriction of high protein diet (mainly non vegetarian) and bland diet consumption leading to vitamin B12 deficiency and worsening jaundice. By taking thorough dietary history, considering cultural practices, one can tailor the therapy accordingly. A simple measure like dietary education and busting the myths can improve quality of life by accelerating recovery.

Keywords: Fad diet, Hyperbilirubinaemia, Megaloblastic anaemia

INTRODUCTION

Food faddism is a term that refers to the specific food type or food group that is overemphasised or omitted in the regular diet to cure a particular condition [1]. The practice of food faddism harms people's health in general, and it affects their nutritional status, causing macro and micronutrient deficiencies especially in the patients who have any co-morbidities [2]. There are limited studies in this aspect even though there are many food myths prevailing in India. In the lower socio-economic groups, consuming fad diets is a part of the cultural practice in jaundice patients, notably the diet less in protein. Diversity of cultures and religious belief plays an important role which is responsible for customising the food habits. In the normal individuals among all the macronutrients, cyanocobalamin (vitamin B12) deficiency is most common, especially in vegetarians, which is known to cause megaloblastic anaemia [1].

Gilbert's syndrome is a common autosomal dominant genetic illness characterised by persistent mild unconjugated hyperbilirubinemia without hepatic dysfunction or haemolysis [3]. Because of the lack of ability to communicate with patients about healthy and sustainable choices, these food myths have been increasingly prevalent for ages. Even though many food myths have been popular in the country, there is limited literature in this aspect. The most commonly practiced food myth, observed in Gilbert's syndrome, is complete restriction of intake of non vegetarian food (high protein diet). Immediately after the diagnosis evaluated by thorough history taking which was otherwise three time per week leading to a state of fatiguability, paraesthesias, anaemia and worsening of jaundice [4]. Anaemia commonly manifests as fatiguability, pallor, and paraesthesias, with investigations revealing moderate to severe anaemia or pancytopenia, macrocytic red blood cells, and hyper-sigmented neutrophils on a peripheral smear. The state of vitamin deficiencies causes maturation arrest of different cell lines leading to ineffective erythropoiesis and the sequelae, causing haemolysis complicating jaundice with anaemia especially in Glibert's syndrome patients [5]. The increase in indirect bilirubin was even more profound in known cases of Gilbert's syndrome because of fad diets [6]. The primary aim of the study was to evaluate the effect and type of fad diet consumed in the newly diagnosed Gilbert's syndrome patients to find the solution for the symptoms, they landed after a certain period of follow-up.

MATERIALS AND METHODS

This was a prospective cohort study, conducted in a tertiary care centre in north coastal Andhra Pradesh, India from June 2019 to June 2021. Participants were involved in the study after obtaining informed written consent. Approval to carry out the study was sought and granted by the Institutional Ethics Committee (IEC) (009/IEC/GIMSR/2019).

Total 125 (109 males, 16 females) consecutive patients newly-diagnosed with Gilbert's syndrome, from June 2019 to December 2020, attending the Gastroenterology OPD were enrolled for study and followed-up monthly for six months. Before enrolling, thorough history about occupation, dietary habits, and personal habits was taken.

Inclusion criteria:

- Patients with constant raise in the indirect bilirubin levels between 2-5 mg/dL.
- Patients with normal serum transaminases, ceruloplasmin levels, and haemoglobin electrophoresis.
- Patients without any liver ailments and chronic diseases.

Exclusion criteria:

- Patients with chronic liver diseases.
- Patients with abnormal transaminases, ceruloplasmin levels, and haemoglobin electrophoresis.
- Patients who are alcoholics.
- Patients with other co-morbidities like chronic kidney disease, diabetes mellitus, hypertension, coronary arterial disease.

On monthly follow-up of the consecutively enrolled 125 GS patients for six months, 21 presented with symptoms like extreme fatigability, myalgias, and paraesthesias of the limbs within 4 to 6 months of the diagnosis. A thorough history of the symptoms, which were gradual, and any recent changes in food habits and diet restrictions were noted. Remaining 104 Gilbert's syndrome patients, taking normal diet without any restrictions, were normal without any complaints. Venous blood samples (5 mL) were collected from the study group after taking informed consent on initial diagnosis, after six months of follow-up and after treatment with co-methyl (Cyanocobalamin) B12 injections. Haemoglobin (Hb%), TC, Differential Count (DC), haematological indices (MCV, MCH, MCHC) were analysed on a fully automated analyser (Cell-Dyn Ruby Abbott Analyser) using standard reagents/kits. Vitamin B12 was analysed on a fully automated chemiluminescence analyser (Roche Diagnostics) using standard reagents/kits.

STATISTICAL ANALYSIS

Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) version 25.0. For comparison of variables at the time of diagnosis of Gilbert's syndrome, after six months of follow-up, and after the treatment with co-methyl (Cyanocobalamin) B12 injections. Paired t-test was applied based on the nature of distribution, and p-value was calculated. Percentages, mean, and standard deviation were also calculated. The p-value <0.05 was considered significant.

RESULTS

Among the 125 total enrolled patients with Gilbert's syndrome, 87.2% were males, and 12.8% were females, with a mean age distribution of 36.15±11.82 years in males, and 36.06±11.93 years in females [Table/Fig-1]. Out of these 125, 21 patients presented with symptoms after a follow-up of six months-95.2% were males, and 4.8% were females, with the mean age distribution of 36.45±10.79 in males, and 22.0 in females.

Parameters	n (Sample size)	Mean age±SD (years)
Total sample		
Age (years)	125	36.15±11.35
Males	109 (87.92%)	36.15±11.82
Females	16 (12.8%)	36.06±11.93
Diagnosed GS patients		
Age (years)	21	36.15±11.82
Males	20 (95.2%)	39.45±10.791
Females	1 (4.8%)	22

[Table/Fig-1]: Demographics of total enrolled and symptomatic GS patients.

For the 21 symptomatic Gilbert's syndrome patients, the haematological parameters were within the normal range at the time of diagnosis, with a mean Hb% of 12.68±0.75%, TC (8219.05±1488.16 cells/cumm), MCV (91.33±2.63 fL), MCHC (33.30±1.03%) and Vitamin B12 (391.63±45.35 pg/mL) [Table/Fig-2]. After six months of follow-up, a reduction in the haematological parameters of the symptomatic Gilbert's syndrome patients with a mean Hb% of (7.95±1.79), TC (3819.05±1244.44 cells/cumm), MCHC (32.17±2.12) and vitamin B12 (125.68±34.51 pg/mL) along with increase in the mean value of MCV (101.18±16.51 fL) was observed. After initiation of treatment with co-methyl cyanocobalamin vitamin B12 injections for five weeks daily for a week and weekly for a month in 21 symptomatic Gilbert's syndrome patients, significant improvement in the haematological parameters with a mean Hb% of (13.28±0.68%), TC (8652.38±1247.65 cells/cumm), MCHC (33.43±1.21%), and Vitamin B12 (311.81±41.57 pg/mL), along with a decrease in the mean value of MCV (90.00±5.64 fL) was observed [Table/Fig-2].

On paired sample statistics, there was a significant association (p<0.001 highly significant) between the values of Hb%, TC, MCV, and vitamin B12 at the time of diagnosis and after six months of follow-up in 21 symptomatic Gilbert's syndrome patients [Table/Fig-3]. On paired sample statistics (p<0.001 highly significant), there was a significant association between the direct and indirect bilirubin levels at the time of diagnosis and after six months of follow-up [Table/Fig-4]. showing the exacerbation of jaundice.

Parameters	At the time of diagnosis of GS (n=21)			After six months of follow-up (n=21)			After treatment (n=21)		
	Minimum	Maximum	Mean±SD	Minimum	Maximum	Mean±SD	Minimum	Maximum	Mean±SD
Hb%	12	14	12.68±0.75	3.7	10.2	7.95±1.79	12	14	13.28±0.68
TC (cells/cumm)	6200	11500	8219.05±1488.16	1900	11800	3819.05±1244.44	7000	11800	8652.38±1247.65
Platelets (cells/cumm)	176000	207000	192666.67±7793.16	78000	760000	131476.19±145049.52	210000	360000	273809.52±40308.34
MCV (fL)	87	96	91.33±2.63	66.0	154.0	101.18±16.51	81	100	90.00±5.64
MCH (pg)	25	34	30.60±2.71	22.0	41.7	30.97±4.46	27	33	29.95±2.25
MCHC (%)	32	35	33.30±1.03	26.0	36.0	32.17±2.12	32	35	33.43±1.21
Vitamin B12 (pg/mL)	309	482	391.63±45.35	80.0	189.0	125.68±34.51	248	389	311.81±41.57

[Table/Fig-2]: Statistics for haematological parameters at the time of diagnosis in 21 symptomatic GS patients.

Parameters	Time of diagnosis Mean±SD	After six months follow-up Mean±SD	After treatment Mean±SD	p-value
Hb%	12.68±0.75	7.95±1.79	13.28±0.68	<0.001
TC (cells/cumm)	8219.05±1488.16	3819.05±1244.44	8652.38±1247.65	<0.001
Platelets (cells/cumm)	192666.67±7793.16	131476.19±145049.52	273809.52±40308.34	0.07
MCV (fL)	91.33±2.63	101.18±16.51	90.00±5.64	0.012*
MCH (pg)	30.60±2.71	30.97±4.46	29.95±2.25	0.66
MCHC (%)	33.30±1.03	32.17±2.12	33.43±1.21	0.051*
Vitamin B12 (pg/mL)	391.63±45.35	125.68±34.51	311.81±41.57	<0.001

[Table/Fig-3]: Paired sample statistics for haematological parameters at the time of diagnosis of GS and after 6 months follow-up and after 5 weeks of initiation of treatment with co-methyl (Cyanocobalamin) B12 injections in 21 GS patients.
*p-value <0.001-highly significant; *p-value <0.05-significant

Parameter	At the time of diagnosis Minimum	Maximum	Mean±SD	After six months of follow-up Minimum	Maximum	Mean±SD	p-value
Direct bilirubin (mg/dL)	0.3	0.8	0.595±0.132	0.8	1.4	1.119±0.216	<0.001
Indirect bilirubin (mg/dL)	1.4	1.9	1.576±0.134	1.9	2.6	2.290±0.212	<0.001

[Table/Fig-4]: Paired sample statistics for direct and indirect bilirubin levels in 21 GS patients.

DISCUSSION

The most common lifestyle that affects health of an individual is his/her dietary habits. Diversity of cultures and the use of natural remedies lead to rise in the practice of food myths. The major myths that were observed regarding food intake are exaggeration of certain foods with special properties for cure of specific disease, elimination of certain foods from diet due to the belief of presence of harmful constituents and belief that intake of certain combination of foods would lead to either superior health enhancement or health dimunition [7]. The current study focused on studying the effect of practicing food faddism on jaundice in Gilbert's syndrome patients. The study found that, out of enrolled newly diagnosed 125 GS patients, 21 patients who had been following dietary restrictions presented with symptoms like fatigability and limb paraesthesias within 4-6 months, and had depressed cell lines with a picture of pancytopenia in Complete Blood Count (CBC) increased indirect bilirubin levels and reduced vitamin B12 levels. Out of the 21 patients presented with weakness 95.2% were males and 4.8% were females. This finding was in accordance with the study by Thoguluva Chandrasekar V et al., which revealed that Gilbert's syndrome is seen majorly in men during puberty because of increased indirect bilirubin production due to the effect of change in sex steroid hormones [7]. The most common food faddism practiced by patients with jaundice known after taking thorough dietary history is the restriction of high protein diet (especially non vegetarian diet) leading to vitamin B12 deficiency [6]. The main sources of vitamin B12 include fish, chicken, mutton, eggs, and the avoidance of which will lead to its deficiency. It was observed that there was pancytopenia with depressed cell lines and increase in indirect bilirubin levels with aggravation of jaundice in all the 21 patients of Gilberts syndrome practicing food faddism because of vitamin B12 deficiency which was in accordance with Oh R and Brown DL, Vitamin B12 exists as many forms like methyl-, cyano-, hydroxy-cobalamin, and deoxy-adenosyl cobalamin [8]. Methylcobalamine acts as co-factor for methionine synthase which is essential for the synthesis of pyrimidines and purines. This reaction also depends on the folate in which methyl group of methyl tetrahydrofolate is transferred to homocysteine to form methionine and tetrahydrofolate [9]. Interruption of this reaction occurs in B12 deficiency which leads to megaloblastic anaemia. This ineffective erythropoiesis leads to haemolysis aggravating pre-existing indirect hyperbilirubinemia in Gilbert's syndrome patients. Methyl malonyl CoA mutase converts Methyl malonyl CoA to succinyl CoA, with 5-deoxyadenosylcobalamin required as a cofactor. The defect in this reaction, results in accumulation of methyl malonyl CoA that is thought to be responsible for the neurological effects in vitamin B12 deficiency.

O'Leary F and Samman S stated that low levels of vitamin B12 is associated with raised circulating levels of homocysteine and methylmalonic acid which results in vascular complications [10]. On treatment of these 21 patients with co-methyl (cyanocobalamin) injections daily for a week and weekly for a month, improvement in the cell lines and indirect bilirubin levels and decrease in the symptoms like fatiguability and limb paraesthesia was observed which was in accordance with the study by Naha K et al., [6]. The studies highlighting the role of food faddism in jaundice are limited till date even though the practice of food faddism is very common. The main motive of the present study was to emphasise the role of food faddism, and food myths that ultimately leading to complication of already pre-existing jaundice in patients with Gilbert's syndrome.

Limitation(s)

The limitation of present study was that bigger sample size could not be taken.

CONCLUSION(S)

Gilbert's syndrome is a common and benign cause of mild hyperbilirubinemia, which when complicated with B12 deficiency leads to worsening of jaundice. Practicing food myths like restriction of high protein diet (mainly non vegetarian), and consumption of bland diets lead to complicating existing hyperbilirubinemia. Role of food faddism needs to be considered while evaluating patients with jaundice. By taking thorough dietary history, considering cultural practices one can tailor the therapy accordingly. Simple measures like dietary education and busting the myths, can improve quality of life by accelerating the recovery.

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