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Integrated Effects of Vitamins B6 and C with Selected Minerals in Enhancing Immunomodulatory and Reducing Obesity Risk in Rats

Shwan Shorsh Abdalrahman*[1a] and Ahmed Farhan Shallal[1b]

[1]*Department of Biology, College of Science, University of Raparin, Rania-Sulaymaniyah, Kurdistan region – Iraq.*
[2]*College of Medicine, University of Sulaimani, Sulaymaniyah, Kurdistan Region - Iraq.*

[b]E-mail: ahmed.farhan@uor.edu.krd
[a*]Corresponding author: shwan94shorsh@gmail.com

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***Abstract*— The study aimed to assess the impacts of vitamins (C, B6) and minerals (magnesium, calcium, and zinc) on pathways of immunoglobulins (IgA, IgM, IgE, IgD, and IgG), cytokines (IL-10, IL-12, LEP, ADP and TNF- α), lipid profile (S.CH, S.TG, LDL, HDL and V.LDL), and the body weight in standard diet and high-fat diet rat models. Sixty male albino rats were designated into two groups (S.D = 30 rats) and (H.F = 30 rats) during the period from October 2024 to May 2025. ELISA was used to detect immunoglobulins and cytokines; lipid profile was estimated by (Cobas C111) and body weight was measured by lab balance. IgA was non-significant in both groups. IgM in both groups was not significant. IgD was significant ($p<0.05$) in standard diet group but was non-significant in high-fat diet group. The variations in both groups for IgE and IgG were not remarkable. IL-10 was significant ($p<0.05$) in S.D group but not in H.F.D group while IL-12 and TNF-α were not significant in neither groups. Adiponectin was significant ($p<0.05$) in both groups. Leptin was non-significant in S.D group but was significant ($p<0.05$) in the H.F.D group. Cholesterol was reported to be significant ($p<0.05$) in both groups while TG was only significant ($p<0.05$) in S.D group. LDL and HDL were significant ($p<0.05$) in both groups. V.LDL was significant ($p<0.05$) in S.D but not in H.F.D. The body weight was increased significantly ($p<0.05$) from the first week to last week.**

***Keywords*—Immune Modulation, Vitamins, Minerals, Lipid Profile, Rats.**

I. INTRODUCTION

Immunomodulation is activated by various sources, which either intrinsic or extrinsic [1-2].The important influence of immune and biochemical factors in interpreting health issues, particularly regarding inflammation, immune dynamics, and metabolic activities [3]. The immune system is a cohesive team which composed of various components, all those components work together to fight off the invaders such as bacteria, viruses, parasite and toxins (chemicals secreted by microbes) in order to prevent infection and disease [4-5].The principle of action of adaptive immune response involves the activation of lymphocytes and production of antibodies as well as memory cells will be formed to offering sustainable long-term protection as there is no memory formation in innate immune system [6]. Additionally, antibodies are specified to target the pathogens and neutralize them, so antibodies are proteins produced by B cells [7] while the complement system is the group of proteins work in a cascade which one activates another to eliminate pathogens [8]. Tumor necrosis factor (TNF) is a signaling molecules to assist coordinating the immune responses [9]. A diet is a weight loss program to maintain the healthiness which is considered as the quality of foods consumed to support metabolic processes as nutrient overconsumption has also a detrimental and reversible consequence on an individual's health and society [10]. The capacity of certain minerals like (Zinc and Magnesium) and vitamins to influence the immune system has drawn more attention in the recent years, particularly when it comes to experimental animals like rats [11-12]. The different vitamins and minerals including vitamin C and vitamin B6, and calcium (Ca^{2+}), zinc (Zn^{2+}) and magnesium (Mg^{2+}) play significant role in enhancing and maintaining immunity [11-13-14].The body relies on vitamin B6 (pyridoxine) for various functions, including the production of neurotransmitters and the metabolism of amino acids. Although, T and B cells contribute to the development and appropriate working of adaptive immune response in which vitamin B6 plays crucial role whereas its absence reduces the production of antibodies and lymphocytes [15]. The immune system utilizes Vitamin C (Ascorbic acid) to help combat free radicals, which can lead to oxidative damage [16]. The vitamins whose are soluble in water such as vitamin C has been proven to enhance the activity of phagocytes to eliminate and destroy bacteria and viruses [17-18].In addition, it is essential for the development of lymphocytes and the maintenance of the skin's protective layer, both of which aid in defending the body against infections and viruses [17]. Calcium (Ca^{2+}) is essential for the structure of bones and the maintenance of the skeletal system. However, it has also been demonstrated that calcium has a role in various biological functions, such as improving the immune system. In addition to its structural functions, calcium is an important secondary messenger in several signaling cascades that are essential for the immune cell activation, proliferation, and function [13]. Thus, the current study aims to assess the

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effects of some vitamins (C and B6) and selected minerals (Ca^{2+}, Mg^{2+}, and Zn^{2+}) on the immunological aspects including immunoglobulins (IgA, IgM, IgD, IgE, and IgG), cytokines (IL-10, IL-12, TNF-α, LEP, and ADP) and on the physiological aspects involving lipid profile (S.CH, S.TG, LDL, HDL, and V.LDL) and body weight.

II. MATERIALS AND METHODS

A. Animal housing

Sixty male albino rats (Rattus norvegicus) weighing approximately (180–220 grams) and aged 8 weeks were used in the present study. The female rats were excluded. The animals were obtained from the animal house/College of Science, University of Raparin. The breeding was conducted in the same facility and began nearly 12 weeks prior to the experiment to ensure a sufficient number of rats of the same age group. After weaning, females were separated, and males were maintained under standard laboratory conditions (12 hours light and 12 hours dark) at the temperature 22 ± 5 C° to reach the appropriate age and weight for the experiment. The rats were housed in clean polypropylene cages under favorable environmental conditions, with five rats per cage. They also had free access (ad libitum) to food and water throughout the study. The diet was specially formulated to precisely meet their daily nutritional requirements, wheat (%66), soya (%25.6), oil (%4.35), omega 3 (%0.13), salt (%0.063), limestone (%0.15), methionine (%0.16). lysine (%0.244), choline (%0.05), ca2po4 (%0.064), vitamins (%0.058), and trace elements (%0.062). The high fat diet was prepared according to the food of the standard diet with the additional of sugar (%0.3) and oil (%13.05) [19].

B. Experimental Design

Sixty rats were randomly assigned to standard diet (S.D) and high-fat diet (H.F.D) groups (n=30 each group). Diet group was subdivided into six groups (n=5): Control, Vitamin C, Vitamin B6, Calcium, Magnesium, and Zinc. Supplements were administered daily by oral gavage (Vitamin C 100 mg/kg [20].Vitamin B6 100 mg/kg [21]. Calcium 16 mg/kg [22]. Magnesium 50 mg/kg [12]. and Zinc 30 mg/kg [12]. The study duration was 8 weeks. The groups of standard diet were given standard diet along with each specified supplements except for the control which was only given standard diet without additional supplements. However, the same procedure was repeated for high-fat diet groups as the high fat diet had higher amount of oil compared to standard and additional sugar.

C. Materials

TABLE 1. The kits and Materials were used in the present study.

No.	Kits	Company	Country
1.	Rat Immunoglobulin A (IgA) ELISA Kit	SUNLONG	CHINA
2.	Rat Immunoglobulin M (IgM) ELISA Kit	SUNLONG	CHINA
3.	Rat Immunoglobulin D (IgD) ELISA Kit	SUNLONG	CHINA
4.	Rat Immunoglobulin E (IgE) ELISA Kit	SUNLONG	CHINA
5.	Rat Immunoglobulin G (IgG) ELISA Kit	SUNLONG	CHINA
6.	Rat adiponectin (ADP) ELISA Kit	SUNLONG	CHINA
7.	Rat Leptin (LEP) ELISA kit	SUNLONG	CHINA
8.	Rat Tumor Necrosis Factor α (TNF-α) ELISA Kit	SUNLONG	CHINA
9.	Rat Interleukin 12 (IL-12) ELISA Kit	SUNLONG	CHINA
10.	Rat Interleukin 10 (IL-10) ELISA Kit	SUNLONG	CHINA
11.	Serum Cholesterol (S. CH)	ROCHE	GERMANY
12.	Serum Triglyceride (S. TG)	ROCHE	GERMANY
13.	Serum Low Density Lipoprotein (S. LDL)	ROCHE	GERMANY
14.	Serum High Density Lipoprotein (S. HDL)	ROCHE	GERMANY
15.	Ketamin %10	ALFASAN	HOLLAND
16.	Xilazina	OVER	ARGENTINA

D. Methods

Following the housing process which lasted for 8 weeks, the rats were kept for 24 hours fasting as before drawing their blood via cardiac puncture. Ketamin %10 and Xilazina were used to for anesthesia and blood collection. The specimens were collected under standard conditions. The blood was conducted through centrifugation at power 1000 rpm for 30 minutes. The samples were divided into three tubes, the first tube was allocated for estimation of immunoglobulins (IgA, IgM, IgD, IgE, and IgG), the second tube was used to detect cytokine levels (IL-10, IL-12, ADP, LEP, and TNF-a) and third tube was reserved for lipid profile concentration (S.CH, S.TG, S.LDL, S.HDL, and S. VLDL). Enzyme Linked Immunosorbent Assay (ELISA) was used to detect the concentration of immunoglobulins and cytokines. The Cobas C111 was utilized to measure the concentration of lipid profile. The administration of supplements has recorded different results as in immunoglobulins (IgA, IgM, IgD, IgE, and IgG) and cytokines (IL-10, IL-12, TNF-α, adiponectin, and leptin). Furthermore, the lab balance was used to measure the body weight of rats in each week.

E. Statistical Analysis

Data were analyzed using SPSS v27 and GraphPad Prism 10. Group comparisons used one-way ANOVA within each diet, followed by appropriate post hoc tests where applicable; p-Value<0.05 was considered statistically significant. Data were presented as mean ± SE (n=5 per group).

III. RESULTS

A. Immunoglobulins

Immunoglobulins were influenced by treatments in different ways as in standard and high fat diet conditions. The effects were evaluated through the analysis of (Mean ± Standard error) and (p-Value) for each immunoglobulin. The variation of IgA and IgM were not significant among the groups in both standard and high-fat diet status as displayed in Table 2. The detection of IgD and IgE provided different

results as it can be illustrated in Table 3, and IgG is shown in Table 4.

TABLE 2. IgA and IgM in both Standard and High Fat diet styles

Treatments	Means ± SE (IgA)		p-Value (IgA)		Means ± SE (IgM)		p-Value (IgM)	
	S.D	H.F.D	S.D	H.F.D	S.D	H.F.D	S.D	H.F.D
Control	55457.142 28878.971	56994.764 4185.940	0.242	0.313	0.164 0.023	0.174 0.050	0.660	0.243
Magnesium	40285.868 4462.360	54637.066 7343.865			0.168 0.040	0.133 0.017		
Calcium	52586.896 19616.402	51151.774 10820.605			0.160 0.038	0.162 0.041		
Vitamin B6	43258.616 3045.211	50229.196 8224.675			0.150 0.026	0.162 0.020		
Vitamin C	53714.490 12114.892	44181.194 3040.895			0.173 0.022	0.144 0.014		
Zinc	46436.384 6448.679	52894.422 10437.518			0.182 0.026	0.175 0.026		

TABLE 3. IgD and IgE in both Standard and High Fat diet styles

Treatments	Means ± SE (IgD)		p-Value (IgD)		Means ± SE (IgE)		p-Value (IgE)	
	S.D	H.F.D	S.D	H.F.D	S.D	H.F.D	S.D	H.F.D
Control	2625.015 220.323	2761.303 356.395	0.001	0.693	7.160 0.811	11.060 3.153	0.022	0.552
Magnesium	2382.068 302.580	2814.633 206.333			6.700 1.257	7.700 0.803		
Calcium	2571.685 356.395	2737.600 169.681			6.760 1.717	7.980 0.814		
Vitamin B6	3371.634 245.570	2921.293 305.467			10.900 3.559	8.600 0.822		
Vitamin C	2808.707 430.061	2998.324 236.466			8.280 1.331	8.220 0.646		
Zinc	2838.335 155.933	2862.037 366.235			7.260 0.727	8.460 2.094		

TABLE 4. IgG in both Standard and High Fat diet styles

Treatments	Means ± SE (IgG)		p-Value (IgG)	
	S.D	H.F.D	S.D	H.F.D
Control	1.557 0.315	1.283 0.223	0.655	0.013
Magnesium	1.265 0.193	1.031 0.207		
Calcium	1.320 0.218	1.555 0.316		
Vitamin B6	1.349 0.547	1.318 0.382		
Vitamin C	1.289 0.168	1.708 0.195		
Zinc	1.498 0.365	1.542 0.322		

B. Cytokines

The effects of supplementation on cytokines have been analyzed in both standard and high fat diet status. The impacts were evaluated via the analysis of (Mean ± Standard error) and (p-Value) for each cytokine. In the frame of detection of cytokines, Interleukin 10 and Interleukin 12 had shown various results among the groups in both standard and high fat diet status as displayed in Table 5. Therefore, the statistical analysis of adiponectin and leptin have been illustrated in Table 6, while Tumor Necrosis Factor (TNF-a) is shown in Table 7.

TABLE 5. IL-10andIL-12inbothstandardandhighfatdietstyles

Treatments	Means ± SE (IL-10)		p-Value (IL-10)		Means ± SE (IL-12)		p-Value (IL-12)	
	S.D	H.F.D	S.D	H.F.D	S.D	H.F.D	S.D	H.F.D
Control	1.137 0.125	1.198 0.102	0.272	0.001	1.578 0.181	1.431 0.196	0.321	0.921
Magnesium	1.054 0.063	0.691 0.204			1.477 0.108	1.458 0.113		
Calcium	1.031 0.098	0.736 0.028			1.614 0.272	1.492 0.316		
Vitamin B6	0.996 0.094	0.911 0.151			1.630 0.294	1.447 0.140		
Vitamin C	0.970 0.057	1.131 0.065			1.488 0.157	1.560 0.150		
Zinc	1.050 0.087	0.798 0.225			1.359 0.165	1.477 0.182		

TABLE 6. Adiponectin and Leptin in both Standard and High Fat diet styles

Treatments	Means ± SE (ADP)		p-Value (ADP)		Means ± SE (LEP)		p-Value (LEP)	
	S.D	H.F.D	S.D	H.F.D	S.D	H.F.D	S.D	H.F.D
Control	0.304 0.037	0.329 0.023	0.013	0.003	8.982 1.517	21.652 4.486	0.246	0.029
Magnesium	0.249 0.068	0.292 0.040			8.049 1.088	15.363 1.317		
Calcium	0.186 0.044	0.316 0.024			7.070 1.386	23.489 2.765		
Vitamin B6	0.309 0.040	0.270 0.023			8.569 1.221	22.739 6.120		
Vitamin C	0.240 0.051	0.260 0.017			9.151 1.777	22.708 4.725		
Zinc	0.297 0.083	0.294 0.026			8.768 1.497	18.959 2.437		

TABLE 7. TNF-a in both standard and high fat diet styles

Treatments	Means ± SE (TNF-a)		p-Value (TNF-a)	
	S.D	H.F.D	S.D	H.F.D
Control	121483.148 14945.601	95770.900 6670.595	0.175	0.169
Magnesium	105160.204 14477.548	95337.548 18121.240		
Calcium	109493.729 19558.290	95626.450 10610.009		
Vitamin B6	112671.648 22500.274	108049.221 19717.671		
Vitamin C	88981.711 13679.044	113827.254 15696.362		
Zinc	106315.811 11053.085	91148.474 15851.792		

C. Lipid Profile

The statistical analysis of lipid profile has demonstrated clear results for each parameter that they were either significant or non-significant. The results of analysis for Serum Cholesterol Fig.1 and Fig.2 and Serum Triglyceride Fig.3 and Fig.4 have been concluded in which serum cholesterol was significant among groups on both standard and high fat diet while serum triglyceride was only significant on standard diet and nor for high fat diet. However, serum low density lipoprotein showed significant in both conditions standard and high fat diet among the groups as illustrated in Figu.5 and Fig.6. Serum high density lipoprotein showed significant differences among groups in both standard and high-fat diet style as shown in Fig.7 and Fig.8. In the meantime, serum very low-density lipoprotein has recorded significant among groups in standard diet but not in high fat diet as displayed in Fig.9 and Fig.10.

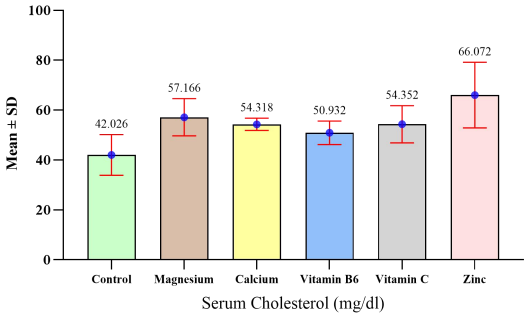

Fig.1: Comparison of Serum Cholesterol (S.CH mg/dl) Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**S.D**)

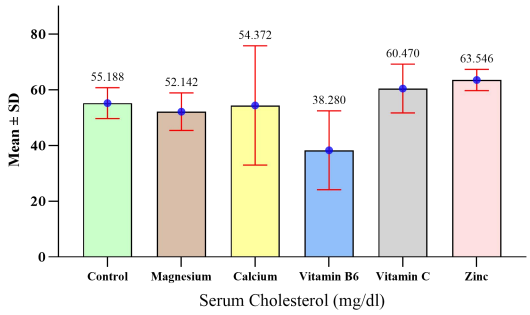

Fig.2: Comparison of Serum Cholesterol (S.CH mg/dl) Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**H.F.D.**)

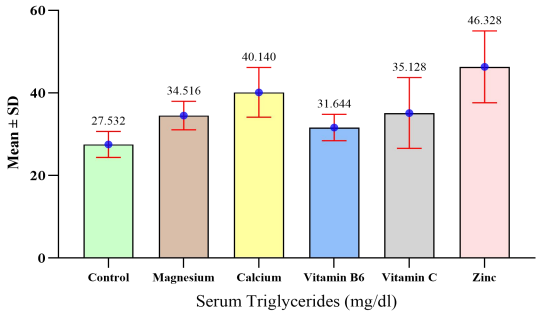

Fig 3: Comparison of Serum Triglyceride (S.TG mg/dl) Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**S.D**)

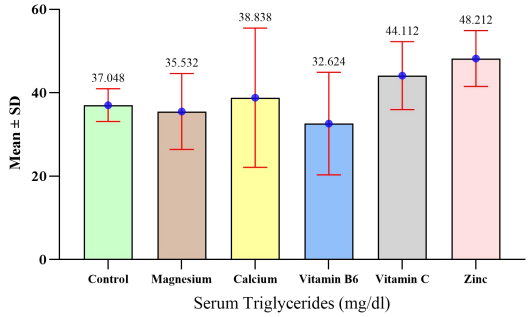

Fig.4: Comparison of Serum Triglyceride (S.TG mg/dl) Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**H.F.D**)

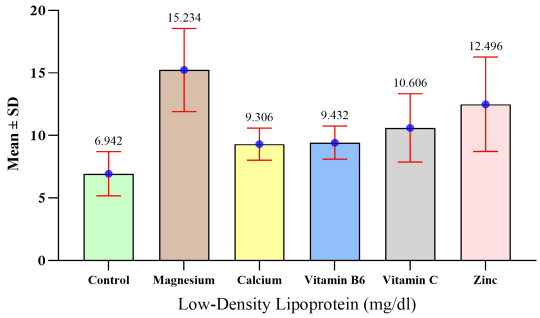

Fig.5: Comparison of Serum Low Density Lipoproteins (S.LDL mg/dl) Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**S.D**)

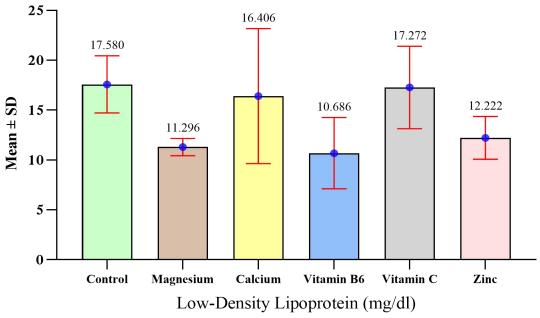

Fig.6: Comparison of Serum Low Density Lipoproteins (S.LDL mg/dl) Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**H.F.D**)

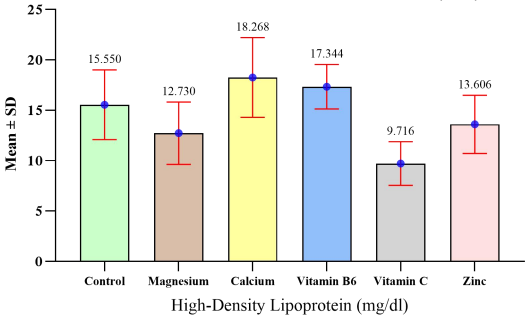

Fig.7: Comparison of Serum High Density Lipoproteins (S.HDL mg/dl) Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**S.D**)

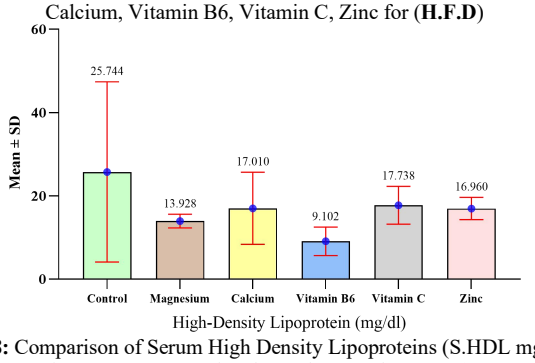

Fig.8: Comparison of Serum High Density Lipoproteins (S.HDL mg/dl) Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**H.F.D**)

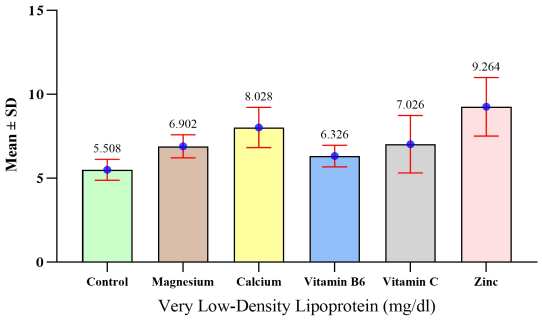

Fig.9: Comparison of Serum Very Low-Density Lipoproteins (S.HDL mg/dl) Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**S.D**)

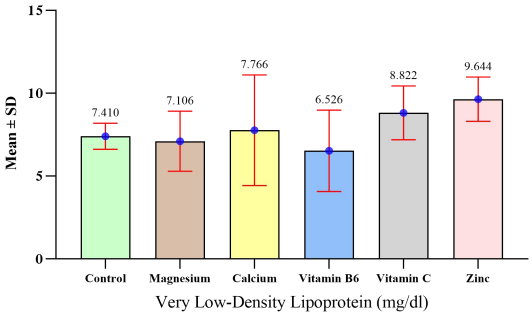

Fig.10: Comparison of Serum Very Low-Density Lipoproteins (S.HDL mg/dl) Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**H.F.D**)

D. Body Weight

The statistical analysis demonstrated the effects of supplements on body weight of rats in each single week of the treatment out of total eight weeks. The data proved that supplementation was significant during the weeks of treatment in both standard and high fat diet as displayed in the following Fig. 11 – 14. The statistical analysis clearly indicated the effects of supplements among the 8 weeks of treatment which was concluded as the histograms to determine the weights in first week and weights in last week.

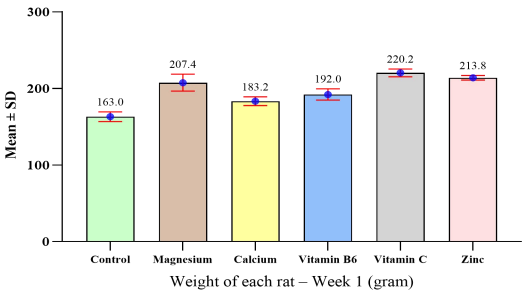

Fig.11: Comparison of Weight of each rat – Week 1 Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**S.D**)

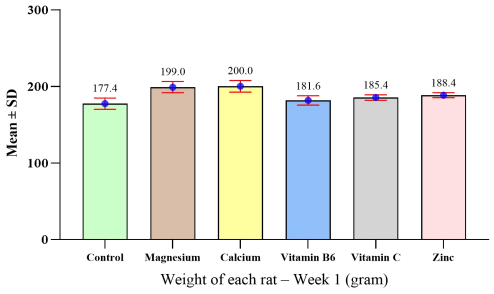

Fig.12: Comparison of Weight of each rat – Week 1 Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**H.F.D**)

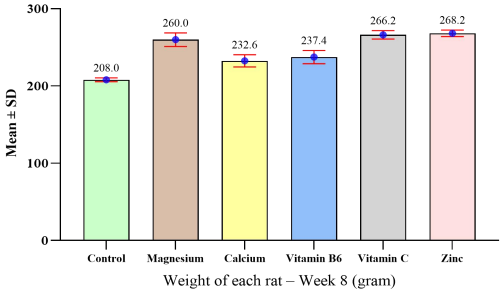

Fig.13: Comparison of Weight of each rat – Week 8 Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**S.D**)

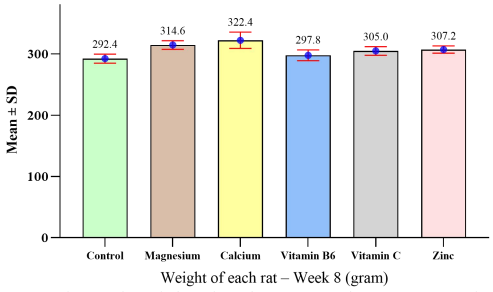

Fig.14: Comparison of Weight of each rat – Week 8 Concentrations Across Control and Supplemented Groups (Magnesium, Calcium, Vitamin B6, Vitamin C, Zinc for (**H.F.D**)

Legends: S.D = Standard Diet, H.F.D = High Fat Diet, SE = Standard Error, IL = Interleukin, TNF = Tumor Necrosis Factor, ADP = Adiponectin and LEP = Leptin, ELISA = Enzyme Linked Immunosorbent Assay

E. Correlation

The correlation matrix for the standard diet group demonstrates clear clustering within biological systems rather than widespread cross-system interactions. Among immunological and inflammatory markers, IgD showed a strong positive correlation with IgE ($r = 0.721$, $p < 0.01$), indicating coordinated humoral immune activity. IgG was strongly associated with TNF ($r = 0.614$, $p < 0.01$) and moderately correlated with IL-10 and IL-12, suggesting linkage between adaptive immunity and inflammatory regulation. In addition, IL-12 correlated strongly with TNF ($r = 0.650$, $p < 0.01$), reinforcing their shared pro-inflammatory role, while IgM correlated positively with IL-10 ($r = 0.393$, $p < 0.05$), reflecting interaction between early immune response and anti-inflammatory control. In contrast, the strongest correlations were observed within the lipid profile, reflecting physiological consistency rather than treatment effects. Total cholesterol showed strong positive correlations with LDL, triglycerides, and VLDL ($r = 0.767$, 0.646, and 0.646

respectively; $p < 0.01$). Triglycerides and VLDL were perfectly correlated ($r = 1.000$, $p < 0.01$), and LDL also correlated strongly with both TG and VLDL. Adiponectin displayed a significant negative correlation with total cholesterol, suggesting a protective metabolic association, while HDL and leptin showed no significant relationships with immune or inflammatory markers. Overall, under standard diet, immune–inflammatory interactions are evident but moderate, whereas lipid metabolism variables remain tightly interrelated and largely independent of immune parameters Table 8.

The correlation matrix for the high-fat diet group reveals a clearer integration between immune markers, inflammatory cytokines, and metabolic variables compared with the standard group. Within the immune system, IgD showed significant positive correlations with both IgE ($r = 0.414$, $p < 0.05$) and IgG ($r = 0.469$, $p < 0.01$), indicating enhanced coordination of humoral immunity under high-fat conditions. IgE was positively associated with IL-10 ($r = 0.382$, $p < 0.05$), while IL-12 correlated positively with TNF ($r = 0.432$, $p < 0.05$), reflecting an activated inflammatory environment. Notably, adiponectin showed a significant negative correlation with TNF ($r = -0.406$, $p < 0.05$), suggesting a counter-regulatory, anti-inflammatory role despite high-fat exposure. Metabolic variables again demonstrated the strongest internal relationships. Total cholesterol correlated strongly with triglycerides, LDL, HDL, and VLDL ($r = 0.607–0.744$, $p < 0.01$), while triglycerides and VLDL exhibited a perfect positive correlation ($r = 1.000$, $p < 0.01$). Leptin showed a significant negative correlation with triglycerides and VLDL ($r = -0.417$, $p < 0.05$), indicating altered adipokine–lipid interactions in the high-fat group. Overall, the high-fat treatment appears to strengthen the linkage between immune activation, inflammatory signaling, and lipid metabolism, suggesting a more metabolically driven inflammatory state compared with the standard diet Table 9.

TABLE 8. Correlation Matrix for (Standard Diet) between treatment groups

Standard		IgA	IgM	IgD	IgE	IgG	IL10	IL12	ADP	LEP	TNF	TC	TG	LDL	HDL	VLDL
IgA	Non-Normal	1	-0.011ş	0.217ş	0.173ş	0.008ş	-0.215ş	0.082ş	-0.015ş	0.313ş	-0.216ş	0.014ş	0.143ş	-0.087ş	-0.067ş	0.139ş
IgM	Normal	-0.011ş	1	0.048ṗ	0.133ş	0.174ṗ	.393*ṗ	-0.109ṗ	-0.041ṗ	0.211ṗ	-0.032ṗ	0.164ṗ	0.334ṗ	-0.1ş	-0.16ṗ	0.334ṗ
IgD	Normal	0.217ş	0.048ṗ	1	.721**ş	-0.141ṗ	-0.156ṗ	0.048ṗ	.474**ṗ	0.178ṗ	-0.005ṗ	-0.136ṗ	-0.078ṗ	-0.257ş	-0.015ṗ	-0.078ṗ
IgE	Non-Normal	0.173ş	0.133ş	.721**ş	1	-0.239ş	-0.081ş	-0.034ş	0.296ş	0.186ş	-0.244ş	-0.025ş	0.063ş	-0.05ş	-0.069ş	0.061ş
IgG	Normal	0.008ş	0.174ṗ	-0.141ṗ	-0.239ş	1	0.323ṗ	0.323ṗ	0.09ṗ	0.291ṗ	.614**ṗ	-0.186ṗ	-0.061ṗ	-0.323ş	-0.045ṗ	-0.061ṗ
IL10	Normal	-0.215ş	.393*ṗ	-0.156ṗ	-0.081ş	0.323ṗ	1	-0.071ṗ	0.181ṗ	0.136ṗ	0.241ṗ	-0.25ṗ	0.056ṗ	-0.217ş	-0.054ṗ	0.056ṗ
IL12	Normal	0.082ş	-0.109ṗ	0.048ṗ	-0.034ş	0.323ṗ	-0.071ṗ	1	-0.125ṗ	0.003ṗ	.650**ṗ	-0.255ṗ	-.393*ṗ	-0.208ş	0.096ṗ	-.393*ṗ
ADP	Normal	-0.015ş	-0.041ṗ	.474**ṗ	0.296ş	0.09ṗ	0.181ṗ	-0.125ṗ	1	0.223ṗ	0.123ṗ	-.392*ṗ	-0.224ṗ	-0.32ş	-0.202ṗ	-0.224ṗ
LEP	Normal	0.313ş	0.211ṗ	0.178ṗ	0.186ş	0.291ṗ	0.136ṗ	0.003ṗ	0.223ṗ	1	-0.004ṗ	-0.216ṗ	-0.046ṗ	-0.151ş	-0.222ṗ	-0.046ṗ
TNF	Normal	-0.216ş	-0.032ṗ	-0.005ṗ	-0.244ş	.614**ṗ	0.241ṗ	.650**ṗ	0.123ṗ	-0.004ṗ	1	-0.302ṗ	-.369*ṗ	-0.33ş	0.114ṗ	-.369*ṗ
TC	Normal	0.014ş	0.164ṗ	-0.136ṗ	-0.025ş	-0.186ṗ	-0.25ṗ	-0.255ṗ	-.392*ṗ	-0.216ṗ	-0.302ṗ	1	.646**ṗ	.767**ş	0.153ṗ	.646**ṗ
TG	Normal	0.143ş	0.334ṗ	-0.078ṗ	0.063ş	-0.061ṗ	0.056ṗ	-.393*ṗ	-0.224ṗ	-0.046ṗ	-.369*ṗ	.646**ṗ	1	.474**ş	0.009ṗ	1.000**ṗ
LDL	Non-Normal	-0.087ş	-0.1ş	-0.257ş	-0.05ş	-0.323ş	-0.217ş	-0.208ş	-0.32ş	-0.151ş	-0.33ş	.767**ş	.474**ş	1	-0.055ş	.472**ş
HDL	Normal	-0.067ş	-0.16ṗ	-0.015ṗ	-0.069ş	-0.045ṗ	-0.054ṗ	0.096ṗ	-0.202ṗ	-0.222ṗ	0.114ṗ	0.153ṗ	0.009ṗ	-0.055ş	1	0.009ṗ
VLDL	Normal	0.139ş	0.334ṗ	-0.078ṗ	0.061ş	-0.061ṗ	0.056ṗ	-.393*ṗ	-0.224ṗ	-0.046ṗ	-.369*ṗ	.646**ṗ	1.000**ṗ	.472**ş	0.009ṗ	1

ṗ: Pearson Correlation, ş: Spearman Rank Correlation, correlation tabulated value at 0.05, n=30 equal to (0.361) (-0.361), and at 0.01 equal to (0.463) (-0.463)

TABLE 9. Correlation Matrix for (High-Fat Diet) between treatment groups

High Fat		IgA	IgM	IgD	IgE	IgG	IL10	IL12	ADP	LEP	TNF	TC	TG	LDL	HDL	VLDL
IgA	Normal	1	0.232ş	-0.196ṗ	0.011ş	-0.325ṗ	-0.059ṗ	0.182ṗ	0.18ṗ	-0.273ṗ	-0.057ṗ	0.164ṗ	0.212ṗ	0.069ṗ	0.143ş	0.212ṗ
IgM	Non-Normal	0.232ş	1	-0.256ş	-0.005ş	0.108ş	0.183ş	-0.109ş	0.097ş	-0.056ş	0.048ş	-0.04ş	0.168ş	-0.132ş	0.123ş	0.168ş
IgD	Normal	-0.196ṗ	-0.256ş	1	.414*ş	.469**ṗ	0.014ṗ	0.014ṗ	-0.029ṗ	0.223ṗ	0.01ṗ	0.099ṗ	0.043ṗ	0.047ṗ	-0.174ş	0.043ṗ
IgE	Non-Normal	0.011ş	-0.005ş	.414*ş	1	0.244ş	.382*ş	-0.209ş	0.189ş	0.209ş	0.121ş	-0.142ş	0.079ş	0.059ş	-0.07ş	0.079ş
IgG	Normal	-0.325ṗ	0.108ş	.469**ṗ	0.244ş	1	0.135ṗ	-0.139ṗ	-0.064ṗ	0.289ṗ	-0.222ṗ	0.243ṗ	0.227ṗ	0.232ṗ	0.323ş	0.227ṗ
IL10	Normal	-0.059ṗ	0.183ş	0.014ṗ	.382*ş	0.135ṗ	1	0.173ṗ	0.092ṗ	0.174ṗ	0.359ṗ	-0.022ṗ	0.082ṗ	0.259ṗ	0.304ş	0.082ṗ
IL12	Normal	0.182ṗ	-0.109ş	0.014ṗ	-0.209ş	-0.139ṗ	0.173ṗ	1	-0.27ṗ	0.055ṗ	.432*ṗ	0.162ṗ	0.251ṗ	0.172ṗ	0.121ş	0.251ṗ
ADP	Normal	0.18ṗ	0.097ş	-0.029ṗ	0.189ş	-0.064ṗ	0.092ṗ	-0.27ṗ	1	-0.114ṗ	-.406*ṗ	0.146ṗ	-0.024ṗ	0.211ṗ	0.085ş	-0.024ṗ
LEP	Normal	-0.273ṗ	-0.056ş	0.223ṗ	0.209ş	0.289ṗ	0.174ṗ	0.055ṗ	-0.114ṗ	1	0.068ṗ	-0.2ṗ	-.417*ṗ	0.178ṗ	-0.007ş	-.417*ṗ
TNF	Normal	-0.057ṗ	0.048ş	0.01ṗ	0.121ş	-0.222ṗ	0.359ṗ	.432*ṗ	-.406*ṗ	0.068ṗ	1	-0.058ṗ	0.055ṗ	0.028ṗ	-0.069ş	0.055ṗ
TC	Normal	0.164ṗ	-0.04ş	0.099ṗ	-0.142ş	0.243ṗ	-0.022ṗ	0.162ṗ	0.146ṗ	-0.2ṗ	-0.058ṗ	1	.607**ṗ	.675**ṗ	.744**ş	.606**ṗ
TG	Normal	0.212ṗ	0.168ş	0.043ṗ	0.079ş	0.227ṗ	0.082ṗ	0.251ṗ	-0.024ṗ	-.417*ṗ	0.055ṗ	.607**ṗ	1	0.223ṗ	.376*ş	1.000**ṗ
LDL	Normal	0.069ṗ	-0.132ş	0.047ṗ	0.059ş	0.232ṗ	0.259ṗ	0.172ṗ	0.211ṗ	0.178ṗ	0.028ṗ	.675**ṗ	0.223ṗ	1	.666**ş	0.223ṗ
HDL	Non-Normal	0.143ş	0.123ş	-0.174ş	-0.07ş	0.323ş	0.304ş	0.121ş	0.085ş	-0.007ş	-0.069ş	.744**ş	.376*ş	.666**ş	1	.376*ş
VLDL	Normal	0.212ṗ	0.168ş	0.043ṗ	0.079ş	0.227ṗ	0.082ṗ	0.251ṗ	-0.024ṗ	-.417*ṗ	0.055ṗ	.606**ṗ	1.000**ṗ	0.223ṗ	.376*ş	1

ṗ: Pearson Correlation, ş: Spearman Rank Correlation, correlation tabulated value at 0.05, n=30 equal to (0.361) (-0.361), and at 0.01 equal to (0.463) (-0.463)

IV. DISCUSSION

The present study evaluated the effects of vitamins (C and B6) and minerals (magnesium, calcium, and zinc) on immune and metabolic biomarkers in rats fed either a standard and high-fat diet rat groups. Each micronutrient exhibited distinctive impacts on immunoglobulin levels, cytokine profiles, lipid metabolism, and body weight regulation, indicating that dietary conditions significantly modulate micronutrient responses [11-14]. Among minerals, magnesium demonstrated regulatory effects on inflammatory and lipid parameters. Under high-fat diet conditions, magnesium supplementation attenuated LDL elevation and partially improved lipid balance, which supports its contribution to insulin sensitivity, inflammation regulation, and enzymatic activation in lipid metabolism [12-20]. It also stabilized immunoglobulin concentrations and maintained cytokine activity within normal physiological limits, suggesting no inflammatory overload. Body-weight analysis revealed significant increases in the magnesium groups under both diets, especially in high-fat diet rats, consistent with improved nutrient utilization [23]. The supplementation of calcium maintained immunoglobulin stability and influenced cytokine activity, aligning with its known cellular signaling role in immune activation. It enhanced HDL under standard diet and moderated body-weight increases under high-fat diet, reflecting its involvement in adipocyte metabolism and energy utilization [13-24]. Leptin increased significantly in the high-fat diet, especially with calcium, while adiponectin was higher in standard diet controls, confirming their reciprocal relationship in lipid and glucose regulation [11- 14]. Vitamin B6 supplementation increased immune parameters, primarily by promoting lymphocyte proliferation and immunoglobulin synthesis through its essential function in the adaptive immune system, from which it derives that pyridoxine deficiency negatively affects lymphocyte differentiation and immunoglobulin production. It modulated IL-10 and IL-12 levels as well, suggesting the modulation of both anti and pro-inflammatory signals [15].and reduced LDL and lipid homeostasis in high-fat diet regime as well as low positive control of total cholesterol after fasted conditions [20-25]. Vitamin C increased serum immunoglobulins and cytokine activity in the normal diet group that could be the result of its antioxidative and lymphocyte supporting effects but this data is consistent with previous data which shows ascorbic acid acts on immune defence by triggering phagocytic functions and protects both these cells from oxidative injuries. It modified IL-10 and IL-12 suggesting its immunomodulatory potential and increased total cholesterol and triglycerides in supplemented standard-diet animals. Increases in body weight were larger on standard diet, reflecting greater metabolic efficiency [16].Enhanced immune and lipid measures by zinc supplementation are in agreement with the importance of zinc in immune cell activation and antioxidative defense. However, it raised serum triglycerides and VLDL in the standard diet status, indicative of a dietary dependent metabolic interplay. The cytokine role of TNF-α in zinc treated rats were balanced and there was not excessive production of it with no reduction on adiponectin despite of its higher level that maintained constant [26].Collectively, TNF-α responses in all supplemented groups remained within the physiologic range, suggesting that supplementation did not stimulate excessive inflammatory reaction. The unique indices of response imply a context specific nutrient effect, determined by the composition of the diet and metabolic steady state. Altogether, the results point toward the ability of these micronutrients to affect different immune and metabolic functions through a variety of mechanisms including cytokine production, lipid metabolism as well as antioxidant pathways [11-14]. The differential effects under standard and high-fat diets underscore the importance of dietary context in determining nutritional outcomes. Each vitamin and mineral contributed uniquely to immune enhancement and lipid balance, but the magnitude and direction of changes varied across nutrients and diets. These results confirm that micronutrient supplementation can modulate immunometabolic health in rats and may hold relevance for managing obesity related immune dysfunction in humans. Immunological, inflammatory, and metabolic indicators primarily cluster within their respective biological systems, according to the correlation analysis in the standard diet group. This suggests physiological balance rather than pervasive immunometabolic dysregulation. In line with findings that IgD contributes to B-cell activation and the regulation of IgE-mediated immune responses in non-pathological settings, the substantial positive connection between IgD and IgE indicates coordinated humoral immunological activity [27-28]. Furthermore, since IgG mediated immune activation is known to promote macrophage derived TNF-α production during immune surveillance and host defense, the strong correlation between IgG and TNF-α emphasizes the relationship between adaptive humoral immunity and inflammatory signaling [29-30]. A balanced immune regulation system is further supported by the weak associations between IgG, IL-10 and IL-12. While the positive correlation between IgM and IL-10 may indicate early immune activation accompanied by compensatory anti-inflammatory control mechanisms, a feature of immunological homeostasis, the significant positive correlation between IL-12 and TNF-α confirms their shared role in Th1-mediated inflammatory pathways [31]. Lipid metabolism showed the strongest and most reliable relationships, highlighting inherent physiological coupling as opposed to disease brought on by diet. Under normal metabolic settings, coordinated lipoprotein transport and hepatic lipid management are reflected in the well-established strong positive relationships between total cholesterol, LDL, triglycerides, and V.LDL [32-33]. Further evidence that circulating triglycerides are mostly carried within V.LDL particles comes from the perfect association between triglycerides and V.LDL. Adiponectin's proven beneficial metabolic role in improving lipid clearance and preserving insulin sensitivity is consistent with the negative connection between adiponectin and total cholesterol [34]. The absence of noteworthy associations between HDL or leptin and immunological or inflammatory markers implies that adipokine-mediated immune regulation persists under standard dietary settings. The immunometabolic effects of high-fat diet are reflected in the correlation pattern shown in the high-fat diet group, which shows a closer integration between immune activation, inflammatory signaling, and metabolic regulation as compared to the standard diet condition. In line with observations that high-fat diet stimulates B-cell activation and antibody class interactions linked to low-grade inflammation, the strong positive correlations between IgD and both IgE and IgG indicate improved coordination of humoral immune components under obesogenic stress [35]. Increased immune surveillance and the production of inflammatory mediators have been

connected to IgD associated immunological signaling, especially in metabolically demanding situations that aligns with the present study [36]. A mixed inflammatory profile with concurrent activation of pro-inflammatory and regulatory pathways is seen in the positive correlations between IgE and IL-10 and between IL-12 and TNF-α. The presence of a persistent inflammatory signals in animals given a high-fat diet is supported by the coordinated production of TNF-α and IL-12, which are important mediators of obesity-associated inflammation and macrophage activation. Simultaneously, the correlation between IgE and IL-10 might indicate a compensatory anti-inflammatory reaction intended to curb excessive immune activation [30-31]. Adiponectin showed a strong inverse relationship with TNF-α, confirming its established anti-inflammatory and immunomodulatory function even in the presence of a high-fat diet. The level of TNF-α and inflammatory signals are reduced by adiponectin balance which is a characteristic of immunological dysregulation associated with obesity. Adiponectin is known to regulate TNF-α production and prevent pro-inflammatory macrophage polarization. Adiponectin may function as a counter-regulatory factor reducing inflammation brought on by metabolic stress, as suggested by the preservation of this inverse association in the HFD group [34-37]. The strong internal correlations were seen in lipid profile variables, as predicted, suggesting that metabolic coupling within lipid transport routes was maintained. The important significance of hepatic lipid metabolism and lipoprotein remodeling during high-fat diets is confirmed by the substantial correlations between total cholesterol, triglycerides, LDL, HDL, and V.LDL. Triglycerides and VLDL share a biosynthetic origin, as evidenced by their perfect connection [38]. Significantly, leptin exhibited a negative connection with V.LDL and triglycerides, indicating changed adipokine–lipid interactions in obesity. This may be due to leptin resistance and dysregulated energy homeostasis, which are frequently seen in models of high-fat diets. The idea that obesity is an immunometabolic disorder marked by metabolically driven immune activation and persistent low-grade inflammation is supported by these findings, which show that high-fat feeding increases the interdependence between immune responses, inflammatory mediators, and lipid metabolism [39-40]. Overall, these results show that while lipid metabolism functions as a tightly linked system that is largely independent of immune parameters, reflecting a stable physiological state, immune-inflammatory interactions are present but restrained in the absence of dietary stress.

V. Conclusion

In rats consuming standard and high-fat diet, we determined the effect of vitamins (C and B6) and minerals (magnesium Mg^{2+}, calcium Ca^{2+} and zinc Zn^{2+}) on immune system and metabolism. The effect of each individual + micronutrient was aimed at various immunoglobulin levels, cytokine activities, lipid metabolism and control of body weight. The supplementation of magnesium resulted in the effective control of inflammatory and lipidic pattern. Calcium improved HDL level and regulated body weight. Vitamin B6 applied a beneficial role as to lymphocyte activity and antibody production. Vitamin C had an enhancing effect on immunoglobulin levels and cytokine balance, reflecting antioxidant and immune - supportive functions. Zinc enhanced immune system and lipid metabolism. In summary, these results support the fact that vitamins and minerals are key immunoregulatory mediators that could provide therapeutic agents to promote metabolic health and to reduce obesity-induced immune dysregulation. However, their effects are nutrient and diet specific so that regular supplementation is required to achieve the optimal immune and metabolic responses.

VI. DECLARATIONS

Ethics approval

Animal procedures were conducted in accordance with institutional guidelines [2866/28-5-2023].

Author Contributions

(Shwan Shorsh Abdalrahman and Ahmed Farhan Shallal) designed the study, followed the instructions, executed the experiment, analyzed the data, and wrote the paper

Data availability

All data generated or analyzed during this study are available.

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Competing interests

The authors declare no competing interests.

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