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The Implications of Incorporating Nutritional Supplements into the Treatment Regimen for Children Aged 5-12 Years with Visceral Leishmaniasis in Baringo and West Pokot Counties in Kenya

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Abstract

Purpose: The purpose of this article is to inform the Ministry of Health Management and all stakeholders in Kenya, the importance of the intervention, fills gaps, and provides guidance on future research direction to accelerate control and eventually eliminate Leishmaniasis. This will also shed new light on the importance of micronutrients and trace elements and their role in immunology, patient outcomes, and the physiology of Visceral Leishmaniasis (VL). The results of this study will also pave way to explore possibilities to fill the research gaps and address challenges like the resistance and relapse of the infection, in patients with VL. Furthermore, this study may help in developing evidence-based strategies related to malnutrition and trace elements, which may be implemented in the eradication program of VL.

Materials and Methods: A quasi-experimental study design was conducted in Kenya from January 2022 to March 2022 in 204 VL-infected children aged 5-12 years. Demographic and clinical data were abstracted from questionnaires and lab forms. Descriptive and inferential analyses were conducted to determine the effect of the intervention on VL outcomes among the study children. Variables with a P-value < 0.05 were considered statistically significant. A total of 204 VL study participants, 102 in each intervention and comparison group were included in this study. Baseline characteristics of the study participants were taken and recorded. The treatment and intervention were started and the trend of BMI, body temperature, vitamins A, B12, C, and D together with minerals Zinc, iron, and iodine levels were monitored weekly for four weeks to determine their effect on the treatment outcomes.

Findings: The results showed that the outcome of administering the micronutrients is significant at 5% level, indicating that the intervention has a favorable effect. The micronutrients increased their levels in the body by increasing BMI, reducing spleen size, and controlling the body temperature of the study participants. In conclusion, the intervention accelerated the recovery from VL.

Implications to Theory, Practice and Policy: This study was informed by the previous researchers' outputs (Mashayekhi Goyonlo V, 2020) indicating that administering the anti-leishmaniasis treatment alone will not yield a favorable treatment outcome in Visceral Leishmaniasis patients and also a study by Nweze JA, Nweze EI (2019) which indicated that malnourished patients with VL had an unfavorable outcome, which was recurrence in 21.4% and also that serum micronutrients levels favor good treatment outcome in Visceral Leishmaniasis. It is therefore important to note that Baringo and West-Pokot Counties, where the present study was conducted, are the Counties in Kenya with the highest percentage of VL patients. The study's outcomes highlight the potential benefits of micronutrients to improve treatment outcomes in this regard, we recommend that the MOH should encourage the integration of micronutrients with the VL treatment in Baringo and West Pokot Counties. This research provides this new insight indicating that micronutrients affect the nutritional status and the treatment outcomes of VL by controlling body temperature, improving BMI, decreasing spleen size, negative VL tests, and therefore there is need to incorporate micronutrients to the treatment of children with VL. This study also raises several questions that warrant further investigation, such as the research on all the other micronutrients that were not analyzed in this study.

Keyword: *Leishmaniasis, Micronutrients, Minerals, Vitamins, Implications*

JEL CODES: *B55.9, 112, 115*

1.0 INTRODUCTION

Leishmaniasis is caused by a parasite from the *Leishmania* species. It is a vector-borne illness that exists in three forms: cutaneous leishmaniasis, mucocutaneous leishmaniasis, and visceral leishmaniasis (VL). VL is the most lethal type of the illness, affecting around 90,000 individuals globally each year. Bangladesh, Brazil, Ethiopia, India, South Sudan, and Sudan were the first regions to report the illness. In the Amhara region, 500000 visceral leishmaniasis patients were reported annually[1]. Thus the current study aimed to determine the impact of nutritional supplements with the treatment outcomes of visceral leishmaniasis among children aged 5-12 years in Baringo and West Pokot Counties in Kenya. Malnutrition is a major determinant of VL outcomes and is associated with a high case-fatality rate. The death rate of infection in low-income regions is 50% [29]. In Sub-Saharan Africa, Kenya is among five East African countries with the largest share of the global VL burden. In those countries, more than 50% of children and young adults die of malnutrition, in any of its forms[23].

The endemicity of VL in Kenya is found in Rift Valley, Eastern region, and Northeastern regions which are arid and semi-arid regions (ASAL)[23] The most critical transmission foci in Kenya are currently Baringo, Isiolo, Marsabit, West Pokot, Turkana, Kitui, Garissa, and Wajir counties[23]. It is estimated that Post Kala azar Dermal Leishmaniasis (PKDL) occurs in less than 5% of VL cases in Kenya, although research on PKDL is very rare [4]

Micronutrients like zinc, iron, and vitamins A, B, C, and D are important in the body as they work as predictive markers for leishmaniasis, and when they are deficient in the body there will be a disruption of the regulation of innate and adaptive immunity, cell proliferation and human physiology. (WHO 2020). Inflammation reduces the levels of micronutrients and VL is among the disease condition that affects the patient's micronutrient level. This in turn disrupts normal physiological activities like functions of metabolic enzymes and the regulation of the immune system and the regulation of gene transcription. The deficiency of micronutrients can aggravate and delay the recovery of diseases.

In a study on human leishmaniasis, a significant decrease in some micronutrients, such as zinc concentration in plasma were found to be associated with the host's inability to kill the parasites or an indication of the inflammatory process[5]. Other research on leishmaniasis therapy has found that systemic use of antimony compounds combined with nutritional supplements results in a cure rate of **77**-90% (WHO 2021). There was a reduction in fever episodes and spleen size[6].

Problem Statement

Patients with VL in Kenya continue to have significant rates of micronutrient deficiencies despite the existence of programs to address these deficiencies. (2019, Njau J). Diets lacking in zinc, iron, Iodine, vitamins A, B, C, and D increase the risk that VL will progress to a full-blown disease. (WHO, 2023). Inadequate micronutrients not only increase the host's vulnerability to VL infection, but it also influence the intensity of disease, manifesting as a range of physical abnormalities, many of which involved etiologic pathways of malnutrition (WHO 2023).

Worldwide, VL accounts for 68% of cases in four countries: India, Sudan, Brazil, and Kenya. (Matendechero S, et al. 2016). In Africa, Visceral Leishmaniasis (VL) is one of the most neglected infectious diseases. Reithinger et al, (2019) note that East Africa is one of the world's main endemic areas for VL, which over the last 20 years has seen a dramatic increase in the number of

VL cases, due to a complexity of factors. Kenya, a developing country in Sub-Saharan Africa, is among five East African countries that now bear the largest proportion of the global burden of VL (Ngere I, 2019). Kenya is ranked among the high-burden countries for VL in endemic areas (Njau J 2019). The disease was first described in Kenya in 1935 in the northern districts of Mandera and Wajir. (Njau J 2019). Since then, outbreaks of VL have occurred in various parts of the country (Republic of Kenya Ministry of Health; 2021).

Few clinical studies have elucidated the correlations between low serum micronutrient levels in patients with VL and their effect on the treatment outcomes. (Feleke TE, 2020). There is also, inadequate documentation on the prevalence, supplementation, burden, and spatial distribution of VL (Republic of Kenya Ministry of Health; 2021). Considering this knowledge gap this study may help in developing evidence-based strategies related to malnutrition and trace elements, which may be implemented in the eradication program of VL.

2.0 LITERATURE REVIEW

Theoretical Review

The following theories underpin this study:

Researchers and philosophers have recognized nutrition as one of the essential elements of existence since antiquity. Consequently, it should come as no surprise that one of the essential elements of any global medical science paradigm is nutrition. The history of nutrition theory begins with Aristotle and Galen. They believed that diet had a critical role in performance, illness, recovery, and overall health.

The nutrients that are taken in from the food that is eaten form the blood. The ideas presented in Huangdi Neijing (Yellow Emperor's Classic of Medicine), an ancient Chinese medical literature that is comparable to the Hippocratic Corpus, parallel the nutrition and human physiology theories of ancient Europe. Classical Greek, Roman, and Chinese literature states that cereal grains, legumes, fruits, honey, fish, and milk should make up the majority of a person's diet. It's amazing how those ancient physicians and philosophers, lacking a thorough grasp of human anatomy, could forecast such a crude dietary map.

Nutrition theory has advanced one step in the modern era. Beginning in 1910 with many mineral and vitamin discoveries, nutritional science has developed in tandem with contemporary food production techniques. Additionally, according to some experts, a diet would be deemed optimal if it included the precise ratio of macro and micronutrients required to sustain optimal health.

2.2 Conceptual Framework

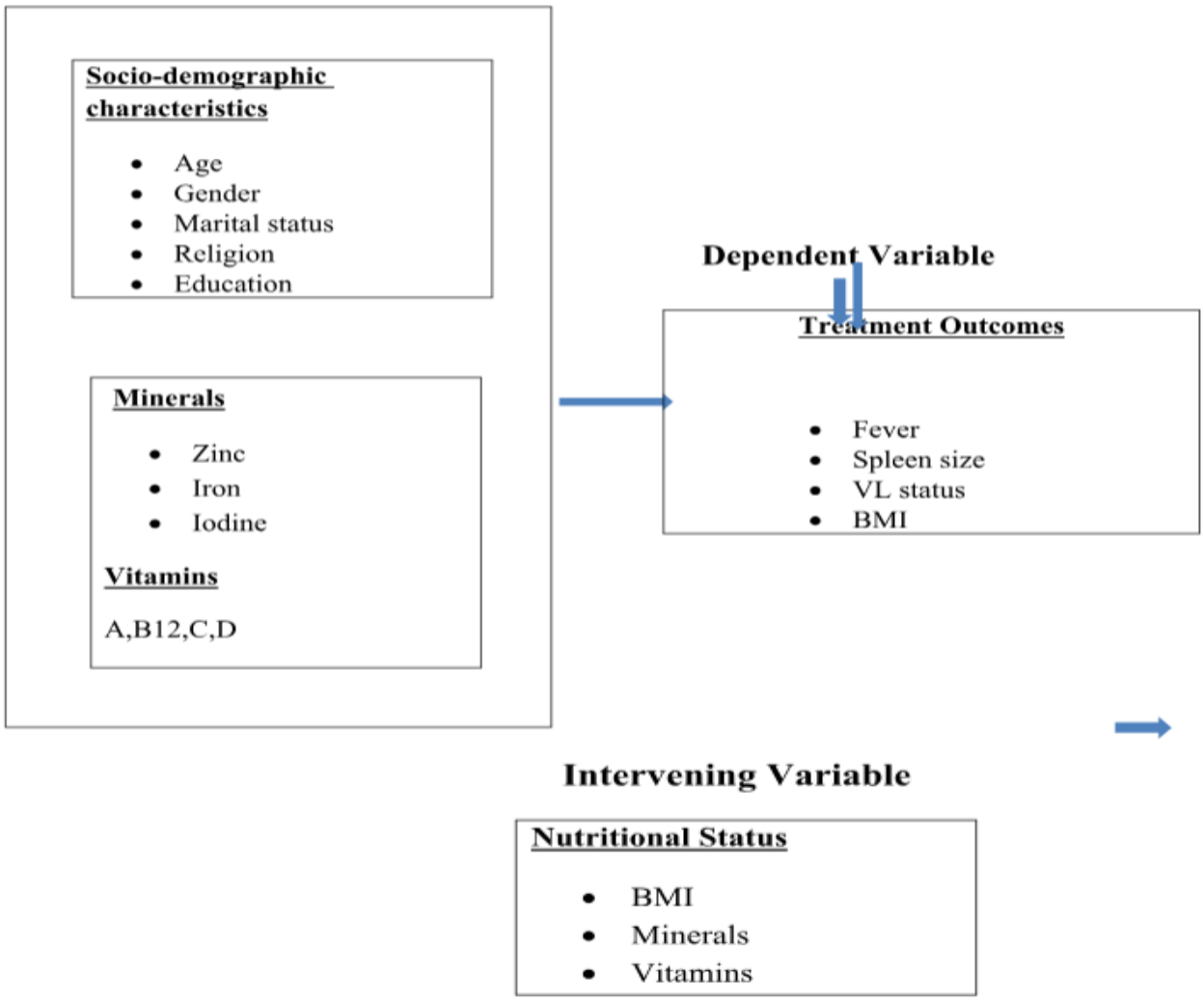

Figure 1: Conceptual Framework

Research Gaps

Although much research has been done on Leishmaniasis disease, the exact understanding of the poor treatment outcomes that lead to the recurrence and reinfection of Visceral Leishmaniasis is not yet fully understood in the endemic Counties in Kenya. A previous researcher's findings (Mashayekhi Goyonlo V, 2020) indicated that administering the anti-leishmaniasis treatment alone will not yield a favorable treatment outcome in Visceral Leishmaniasis patients and a study by Nweze EI (2019) concluded that malnourished patients with VL had an unfavorable outcome. In his study findings, a recurrence of 21.4% of VL, the researcher's finding also recorded that serum micronutrient levels favor good treatment outcomes in Visceral Leishmaniasis. Therefore, there is a need for further studies like the current study, for more evidence-based dietary guidelines and recommendations. A better understanding of the science of nutrition and Leishmaniasis would not

only benefit individual health status but also potentially prevent disease and foster well-being for future generations and better treatment outcomes.

3.0 MATERIAL AND METHODS

Study Design: Quasi - Experimental study design was used in this study.

Study Location: The study was carried out in Kacheliba Sub-County Hospital in West Pokot County and in Chemolingot Sub-County Hospital in Baringo County, Kenya. These two sites have reported high cases of VL patients who visit for diagnosis and treatment services.

Population: The study target population was comprised of children aged 5-12 years with VL who were attending chemolingot and Kacheliba health care facilities in Baringo and West Pokot Counties respectively.

Sample and sampling techniques. The sample size for this study was 204 was. Convenience sampling technique was used. Children attending the selected health facilities were asked if they were willing to participate in the study. A written informed consent (ICF) was obtained from guardians and assent from children willing to participate in the study. They were then tested using R-K39 to determine their VL status. Those who turned positive for VL were admitted to the health facilities and 5-12 year old selected, recruited and enrolled into the study 102 in the intervention group and 102 in the comparison group.The intervention group at Chemolingot Health Facility of 102 patients each received a micronutrient tablet containing vitamins A.B12, C and D and minerals Zinc, Iron and iodine orally for 30 days together with the usual VL treatment.

Data Collection: The trained study team completed the data collection tools. A semi-structured questionnaires were administered to the guardians to collect baseline data of the children in the study. A lab request form was used to collect spot urine samples for the determination of urinary iodine concentration. A data abstraction form was used to assess nutritional status of the children. A 3.5ml blood sample was taken via venipuncture from the selected children in order to determine the micronutrient status.

Anthropometric assessments were taken and used to compare the effect of the supplements before and after the treatment of VL weekly for four weeks and at six month follow-up period. Both the intervention and the comparison groups were reassessed to confirm any reinfection and recurrence of VL. Splenic aspirate was performed to determine the presence of VL parasites in the spleen. Body temperature >37.5 ^{0}C were considered as fever.

Those found with a spleen size more than 15cm or more were considered re-infection or recurrence of VL in the period after treatment to 6 months follow-up period. Splenic aspirate was taken after treatment and at 6 -month follow -up period and compared. Any positive result for VL was considered re-infection or recurrence of VL. Assessment of PKDL was done at 6 -month follow-up period. The presence of PKDL was considered recurrence of VL.

Statistical Analysis: The data from questionnaire and lab request forms was coded and entered into the computer for computation of descriptive statistics. Descriptive statistics such as frequencies, proportions, and means were computed and presented in tables and charts. Kruskal-Walli's test was used to assess the difference between comparison and intervention groups. Chi-square test was used to establish the relationship between the independent and dependent variables. A paired t-test was used to detect whether a significant difference exists between the means within each

group at 5% level of significance. To estimate the impact of the treatment, difference-in-difference was used to compare changes in the outcomes (body temperature,spleen size, BMI, splenic Aspirate and PKDL) over time between the intervention and comparison groups.The effect of the intervention was determined at 5% significance level from the interaction between study groups (intervention and comparison) and the time (pre- and post-intervention).

4.0 FINDINGS

Baseline Characteristics of the Study Participants

The mean age was 8.72 years and 8.72 years in intervention and comparison groups respectively. Age did not differ significantly by group (P>0.05). Children aged 5-9 years were 64.7% in the intervention and comparison groups. Those aged 10-12 years were 35.3% in both the intervention and comparison groups. The age groups did not differ by group.There were more males than females in the study (53.9% in the intervention and 52.9% in the comparison group) All 204 children were single,and from the Christian background.). Grade 4 learners were the majority in both groups, with many in the intervention than comparison group. (Table 1)

Table 1: Baseline Characteristics

Baseline characteristic	Total	Intervention	Comparison	P-value for the difference*
	(N=204)	(N=102)	(N=102)	
AGE				0.9685
Mean (SD)	**8.71** (2.17)	8.72 (2.18)	8.71 (2.18)	
Age group				1
5-9 years	**132** (64.7%)	66 (64.7%)	66 (64.7%)	
10-12 years	72 (35.3%)	36 (35.3%)	36 (35.3%)	
GENDER				1
F	**95** (46.6%)	47 (46.1%)	48 (47.1%)	
M	**109** (53.4%)	55 (53.9%)	54 (52.9%)	
MARITAL STATUS				-
S	**204** (100%)	102 (100%)	102 (100%)	
RELIGION				-
C	**204** (100%)	102 (100%)	102 (100%)	
EDUCATION				1
G1	**30** (14.7%)	15 (14.7%)	15 (14.7%)	
G2	**28** (13.7%)	14 (13.7%)	14 (13.7%)	
G3	**25** (12.3%)	12 (11.8%)	13 (12.7%)	
G4	**33** (16.2%)	17 (16.7%)	16 (15.7%)	
G5	**24** (11.8%)	12 (11.8%)	12 (11.8%)	
G6	**28** (13.7%)	14 (13.7%)	14 (13.7%)	
N 7	12 (5.9%)	6 (5.9%)	6 (5.9%)	
S	**24** (11.8%)	12 (11.8%)	12 (11.8%)	
BMI (kg/m2)				0.8803
Mean (SD)	**13.0** (0.824)	13.0 (0.888)	13.0 (0.758)	
BMI classification				-
Underweight	**204** (100%)	102 (100%)	102 (100%)	
BODY TEMP				0.8987
Mean (SD)	**38.7** (0.916)	38.7 (0.915)	38.7 (0.921)	
Fever				1
No	**24** (11.8%)	12 (11.8%)	12 (11.8%)	
Yes	180 (88.2%)	90 (88.2%)	90 (88.2%)	
RK39				-
NEG	**0 (0%)**	0 (0%)	0 (0%)	
POS	**204** (100%)	102 (100%)	102 (100%)	
SS (cm)				0.09052
Mean (SD)	**37.4** (0.849)	37.4 (0.876)	37.5 (0.816)	
SS				-
Splenomegaly	**204** (100%)	102 (100%)	102 (100%)	

Table 1: Continuation

Baseline characteristic	Total	Intervention	Comparison	P-value for the difference*
NEG	**0 (0%)**	0 (0%)	0 (0%)	
POS	**204** (100%)	102 (100%)	102 (100%)	
Zn				0.2721
Mean (SD)	**65.5** (14.6)	66.1 (14.7)	64.9 (14.6)	
Zn levels				0.8881
Deficient	**92** (45.1%)	45 (44.1%)	47 (46.1%)	
Normal	1**12** (54.9%)	57 (55.9%)	55 (53.9%)	
Fe				P<0.001
Mean (SD)	**8.32** (1.73)	8.83 (1.63)	7.80 (1.68)	
Fe levels				0.805
Deficient	**18** (8.8%)	8 (7.8%)	10 (9.8%)	
Normal	**186** (91.2%)	94 (92.2%)	92 (90.2%)	
IODINE				0.6034
Mean (SD)	**62.3** (20.6)	62.8 (20.7)	61.8 (20.6)	
IODINE				-
Insufficient	**204** (100%)	102 (100%)	102 (100%)	
Sufficient	0 (0%)	0 (0%)	0 (0%)	
Vit A				0.1608
Mean (SD)	**0.795** (0.554)	0.874 (0.751)	0.717 (0.200)	
Vit A levels				0.09162
Deficient	**93** (45.6%)	40 (39.2%)	53 (52.0%)	
Normal	**111** (54.4%)	62 (60.8%)	49 (48.0%)	
Vit B12				0.2647
Mean (SD)	**154** (50.8)	156 (50.4)	152 (51.4)	
Vit B12 levels				0.1189
Deficient	**86** (42.2%)	37 (36.3%)	49 (48.0%)	
Normal	1**18** (57.8%)	65 (63.7%)	53 (52.0%)	
Vit C				0.154
Mean (SD)	**0.163** (0.284)	0.168 (0.285)	0.158 (0.285)	
Vit C levels				0.1662
Deficient	**190** (93.1%)	92 (90.2%)	98 (96.1%)	
Normal	**14** (6.9%)	10 (9.8%)	4 (3.9%)	
Vit D				0.3904
Mean (SD)	**24.5** (3.69)	24.6 (3.67)	24.3 (3.72)	
Vit D levels				0.8869
Deficient	**84** (41.2%)	41 (40.2%)	43 (42.2%)	
Normal	**120** (58.8%)	61 (59.8%)	59 (57.8%)	

SD-standard deviation, F-female, M-male, C-Christian, G-grade, N-nursery, S-single, NEG-negative, POS-positive, cm-centimeter, SS-spleen size, SA- splenic aspirate, Zn-zinc, Fe-Iron, vit-vitamin.

Implications of Micronutrient Supplement on Pre- and Post- Nutritional Status of the Study Participants

Changes in the Average Vitamins Levels (Week 0 to Week 4): Comparing Intervention and Comparison Groups

As shown Table 2, between week 0 and week 4, the levels of all the vitamins rose in both groups, although the intervention group's increase was larger. The statistical analysis revealed that there is adequate evidence to link nutritional supplements to elevated vitamin levels (p-value 0.001, less than the significance level at alpha (α) equal to 0.05).

The minerals zinc,Iron and Iodine differed significantly between the 2 groups. P-values were presented for comparison of the differences in the mineral levels between the intervention and the comparison groups. The $p = 0.001$, $p < 0.05$, confirms that the effect of administering the micronutrient supplement is significant at 5% significance level with the intervention having a positive effect. The intervention led on average to an increase of the minerals levels.

BMI in the entire period of study (week 0 to week 4) was assessed. P-values were presented for comparison of the differences in BMI between the 2 groups. BMI differed significantly between the 2 groups. BMI increased significantly upon administering the intervention. The administration of the micronutrients led on average to an increase in BMI.

Table 2: Trend of Average Vitamins, Minerals and BMI Levels (Week 0 to Week 4): Comparing Intervention and Comparison Groups

Mineral/ vitamin	Total (N=204)	Intervention (N=102)	Comparison (N=102)	P-value*
Vit A				P<0.001
Mean	**0.870** (0.311)	0.904 (0.371)	0.836 (0.232)	
Vit B12				P<0.001
Mean	**223** (131)	283 (156)	163 (52.2)	
Vit C				P<0.001
Mean	**0.705** (0.911)	1.14 (1.10)	0.274 (0.298)	
Vit D				P<0.001
Mean	**46.5** (31.3)	67.6 (32.5)	25.5 (3.80)	
Zn				P<0.001
Mean	**70.4** (15.5)	75.7 (14.3)	65.1 (14.7)	
Fe				P<0.001
Mean	**9.78** (3.97)	11.3 (2.02)	8.26 (4.78)	
IODINE				P<0.001
Mean	**97.8** (49.1)	133 (43.2)	62.2 (20.5)	
BMI				
Mean (SD)	**14.4** (1.77)	15.2 (2.02)	13.6 (0.995)	P<0.001
BMI classification				P<0.001
Underweight	**988** (96.9%)	478 (93.7%)	510 (100%)	
Normal	**31** (3.0%)	31 (6.1%)	0 (0%)	
Overweight/Obese	**1** (0.1%)	1 (0.2%)	0 (0%)	

Vit - vitamin, Zn -zinc, Fe -Iron, I - iodine, BMI -Body Mass Index, SD -Standard deviation

Implications of Micronutrients on Pre- and Post-Visceral Leishmaniasis Treatment Outcomes in the Intervention and Comparison Groups

As shown in Table 3, clinical characteristics in the entire period of study (week 0 to week 4) were assessed. P-values are presented for comparison of the differences in the characteristics between the 2 groups. The clinical characteristics differed significantly between the 2 groups. Since p-value of 0.001 was less than the level of significance at alpha (α) equal to 0.05, the results confirm that, there was a relationship between the intervention and the clinical characteristics. The results indicate that administering micro micronutrients had an effect on the control of the body temperature, reduction of spleen size to an acceptable limits and also the reduction of the *leishmania* parasites to undetectable levels.

Table 3: Trend of Clinical Characteristics in the Entire Period of Study (Week 0 to Week 4). Comparing Intervention and Comparison Groups

Clinical characteristic	Overall (N=204)	Intervention (N=102)	Comparison (N=102)	P-value*
BODY TEMPERATURE				
Mean (SD)	**37.7** (1.49)	36.7 (1.20)	38.7 (0.915)	P<0.001
FEVER				P<0.001
No	**95** (46.4%)	83 (81.0%)	12 (11.8%)	
Yes	**109** (53.6%)	19 (19.0%)	90(88.2%)	
SS				P<0.001
Mean (SD)	**36.2** (1.40)	35.7 (1.49)	36.6 (1.15)	
SS condition				-
splenomegaly	**204** (100%)	102 (100%)	102 (100%)	
SA				0.01849
NEG	**61** (30.0%)	102 (100%)	41 (40.0%)	
POS	**41**(40.0%)	0 (0.0%)	61 (60.0%)	

SD-Standard deviation, SS -Spleen Size, SA Splenic.

The Impact of the Micronutrient Supplement on Recovery Rates of the Study Participants from VL Post Treatment in the Intervention and Comparison Groups

Figure 2 shows changes in the body temperature, BMI and Spleen size between week 0 (pre-treatment) and week 4 (post-treatment) comparing the intervention and the comparison groups. The recovery rates were determined by the control of the body temperature, increase in BMI and reduction in the spleen size. This study's median recovery time from VL was 4 weeks (95% CI = 0–4). The cumulative proportion of recovery was 0.9% and 0,3% at week 1, 17.5%and 9,1% at week 2, 49.5% and 11,1% in week 3, and 78% and 16.3 at week 4. BMI trend showed an increase in the intervention group by 4.2 kg/m2 and 1.5 kg/m2 in the comparison group. Spleen size reduced by 3.7cm in the intervention and by 2.3cm in the comparison group.

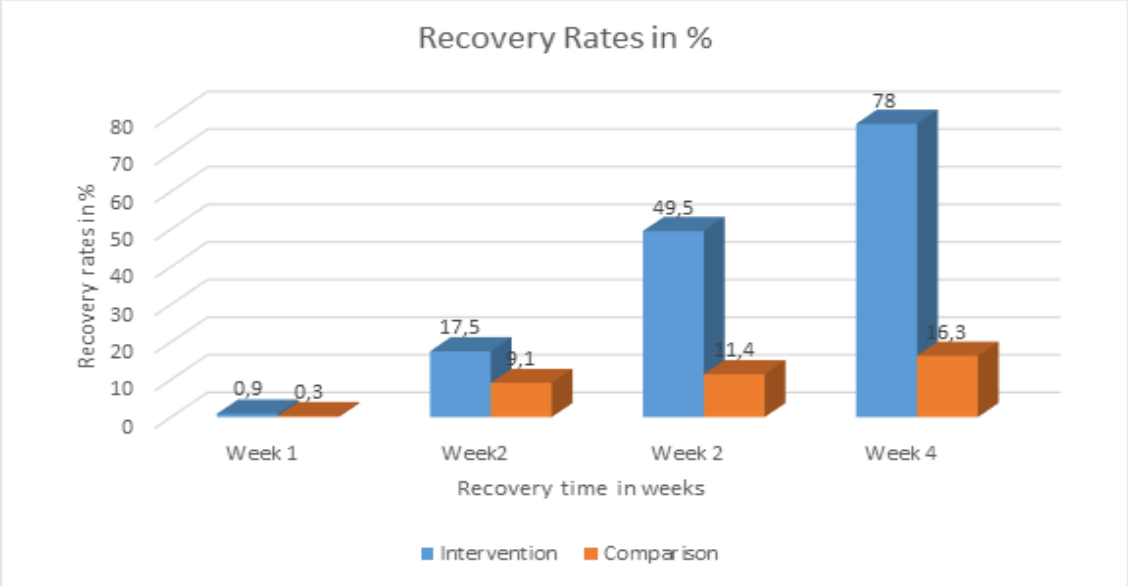

Figure 2: Recovery Rates of Study Participants Week 0 - Week 4 Comparing Intervention and Comparison

Results of the Reinfection and Recurrence of VL among Cured Children Aged 5-12 Years in the Intervention and Comparison Groups

Reinfection of the Study Participants

The table below presents P-values for comparison of the differences in the characteristics between the 2 groups. The clinical characteristics differed significantly between the 2 groups. Fever (body temperature) and spleen size differed significantly between the 2 groups. Splenic aspirate did not differ between the 2 treatment groups.

Table 4: Results of the Reinfection of Study Participants

	Overall (N=204)	**Intervention (N=102)**	**Comparison (N=102)**	**P-value***
Body Temp				
Mean (SD)	**36.5 (0.664)**	36.6 (0.790)	36.4 (0.496)	0.2491
Fever				0.02631
No	**186 (91.2%)**	88 (86.3%)	98 (96.1%)	
Yes	**18 (8.8%)**	14 (13.7%)	4 (3.9%)	
SS				
Mean (SD)	**35.4 (1.19)**	34.5 (0.521)	36.3 (0.934)	P<0.001
SS condition				
Splenomegaly	**204 (100%)**	102 (100%)	102 (100%)	-
SA				
NEG	**204 (100%)**	102 (100%)	102 (100%)	-

Body Temp- Body temperature, SS- spleen size, SA- splenic aspirate

Recurrence of Visceral Leishmaniasis

There was no recurrence of VL in the intervention group at month 6 follow-up period. as shown by the negative PKDL results in the table below. However, there were 2 children (1%) in comparison group who turned positive for VL as shown by the presence of PKDL positive results.

Table 5: Recurrence of Viceral Leishmaniasis

	Overall (N=204)	Intervention (N=102)	Control (N=102)	P-value*
PKDL				0.4773
POS	2 (1.0%)	0 (0%)	2 (2.0%)	
NEG	202 (99.0%)	102 (100%)	100 (98.0%)	

POS-positive, NEG- negative

Testing for Effect of the Treatment

The table below shows the changes between pre and post-treatment in minerals and vitamins levels. P-values were presented for the test of difference in means between pre- and post- treatment (week 0 and week 4 levels) in the intervention and comparison groups.

A paired t-test was used to detect whether a significant difference exists between the means within each group at 5% level of significance. All vitamins, and all minerals had a significant change (positive increase) between pre- and post-treatment periods.

Table 6: Results of the Effect of the Treatment

Mineral/ Vitamin	Intervention (N=102)				Comparison (N=102)			
	Pre-treatment (Week 0)	Post-treatment (Week 4)	Difference (week 4 – week 0)	P-value	Pre-treatment (Week 0)	Post-treatment (Week 4)	Difference (week 4 – week 0	P-value
Zn								
Mean	66.1	81.2	15.1	P< 0.001	64.92	65.22	0.3	P< 0.001
Fe								
Mean	8.83	13.0	4.17	P< 0.001	7.80	8.13	0.33	P< 0.001
I								
Mean	62.8	152.9	90.1	P< 0.001	61.82	62.21	0.39	P< 0.001
Vit A								
Mean	0.874	0.937	0.063	0.3858	0.72	0.99	0.27	P< 0.001
Vit B12								
Mean	156.4	319.3	162.9	P< 0.001	152.1	176.9	24.8	P< 0.001
Vit C								
Mean	0.168	1.28	1.112	P< 0.001	0.158	0.419	0.261	P< 0.001
Vit D								
Mean	24.6	95.8	71.2	P< 0.001	24.34	26.78	2.44	P< 0.001

Zn-Zinc, Fe-Iron, I- Iodine

Assessing the Effect of the Intervention on the Nutritional Status and Treatment Outcomes

To estimate the impact of the intervention, difference-in-difference (DID), was used to compare changes in the outcomes (mineral/ vitamin levels) over time between the intervention and comparison groups. The effect of the intervention was determined at 5% significance level from the interaction term between study groups (intervention and comparison) and the time (pre- and post-intervention). Table 7 shows that the effect of administering the micronutrient supplement is significant at 5% significance level with the intervention having a positive effect. The administration of the micronutrients supplement led on average to an increase of their levels in the body.

Assessing the Effect of the Intervention on Treatment Outcomes

A DID regression model was used to determine the effect of the intervention on the treatment outcomes. The effect of the intervention was determined at 5% significance level from the interaction term between study groups (intervention and comparison) and the time (pre- and post-intervention). Temperatures decreased significantly by 3.2 upon administration of the treatment. Spleen size decreased significantly by 1.3 upon administration of the intervention.

Table 7: Results of the Effect of Intervention on Treatment Outcomes

Nutrition outcome	DID value	P-value
Zinc (ug/dL)	14.8	P<0.001
Iron (g/dL)	3.84	P<0.001
Iodine (mcg/L)	89.71	P<0.001
Vitamin A (µmol/L)	2.1	P<0.001
Vitamin B12 (pmol/L)	138.1	P<0.001
Vitamin C (mg/dL)	0.85	P<0.001
Vitamin D (nmol/L)	68.76	P<0.001
BMI	2.72	P<0.001
Temperature	-3.2	P< 0.001
Spleen size	-1.3	P< 0.001

BMI -Body Mass Index, DID- Difference in Difference

5.0 CONCLUSION AND RECOMMENDATIONS

Conclusion

Based on the findings of this study the following conclusion was made:

The association between the intervention and the nutritional status of the study participants had a statistical significance as seen in the increase in BMI, vitamins and minerals greater in the intervention than in the comparison group. The p-value 0.001 was less than the level of significance at alpha (α) equal to 0.05, this is a sufficient conclusion that the nutritional supplements increased the levels of the vitamins, minerals and BMI

The intervention had a statistical significance in the treatment outcomes as was shown in the results, the control of body temperature, BMI increase and spleen size reduction more in the intervention than in the comparison group. at alpha (α) equal to 0.05 ($P = 0.001$, $P < 0.05$). The

intervention accelerated the recovery of the study participants by accelerating the control of the body temperature from high fever to normal body temperature to below 37.50 C which was below the acceptable limits. This is a statistical significance between the intervention and the treatment outcome variables.

The intervention reduced the likelihood of reinfection and recurrence as shown by the results in the intervention group of all the 102 study participants had no signs and symptoms of VL including the PKDL at the end of treatment and at month 6 follow -up whereas in the comparison group there were 2(2.0%) study participants who turned positive for VL. Therefore, the overall conclusion of this study is that effect of administering the micronutrients was significant at 5% significance level with the intervention having a positive effect. The administration of the micronutrient supplement led on average to an increase of the minerals and vitamins levels in the body. BMI increased significantly upon administering the micronutrients. The administration of the micronutrients led on average to an increase in BMI levels.

Recommendations

The study recommends educating the affected population in this study of the use of the nutrients locally available foods that contain the micronutrients required by the VL patients.

The study also recommends the strategy for the VL elimination Programme in endemic areas through early diagnosis & complete treatment, Integrated Vector Management including Indoor residual spraying (IRS), Advocacy, Communication for Behavioral Impact and Inter-sectoral convergence, Capacity Building, Supervision, Monitoring and Evaluation This study recommends the intergretion of nutritional supplements to all visceral leishmaniasis patients as a routine to hasten recovery and to prevent recurrence and re-infection of VL. The study recommends the surveillance of PKDL to prevent recurrence of VL as PKDL cases serve as a reservoir for disease transmission during the inter-epidemic period and also because treatment of PKDL is prolonged. Also, recurrence of VL may cause spread of drug resistance, especially in anthroponotic leishmaniasis settings. Research should focus on the use of combination therapy in these patients to reduce the number of recurrences, prevent resistance, and reduce toxicity, avoiding the use of the highly cardiotoxic pentavalent antimonials.

REFERENCES

Ahmed, M. A. A., Ahmed, A. A., Omar, S. M., Adam, G. K., Abdallah, T. M., & Ali, A. A. A. (2016). Epidemiology of visceral leishmaniasis among children in Gadarif hospital, eastern Sudan. BMC Public Health, 16(1), 1–4. https://doi.org/10.1186/s12889-016-3875-2

Ali A, Ashford RW. Visceral leishmaniasis in Ethiopia. IV. Prevalence, incidence, and the relation of infection to disease in an endemic area. Annals of Tropical Medicine and Parasitology 1994; 88: 289-293.

Alvar J, den Boer M, Dagne DA. Towards the elimination of visceral leishmaniasis as a public health problem in East Africa: reflections on an enhanced control strategy and a call for action. Lancet Glob Health. 2021;9(12): e1763–e9. pmid:34798033

Amini, Marzyeh, et al. "Biochemical association between essential trace elements and susceptibility to Leishmania major in BALB/c and C57BL/6 mice." *Brazilian Journal of Infectious Diseases* 13 (2009): 83-85.

Arenas, R., Torres-Guerrero, E., Quintanilla-Cedillo, M. R., & Ruiz-Esmenjaud, J. (2017). Leishmaniasis: A review. *F1000Research*, *6*(May), 1–15. https://doi.org/10.12688/f1000research.11120.1

Badaro R, Jones TE, Lorenco R, Cerf BJ, Sampaio D, Carvalho EM, Rocha H, Teixeira R, Johnson Jr. WDA. Prospective study of visceral leishmaniasis in an endemic area of Brazil. Journal of infectious diseases 1986; 154:640649.

Brodskyn, C. I., & Kamhawi, S. (2018). *Biomarkers for Visceral Leishmaniasis in Latin America*. *8*(July), 1–10. https://doi.org/10.3389/fcimb.2018.00245

Difference-in-differences (DiD) is a popular econometric technique used to estimate the causal effect of a treatment on an outcome. One can run a DiD regression in R using the glm() function with Gaussian as the link function.

Diro, E., Lynen, L., Mohammed, R., Boelaert, M., Hailu, A., & van Griensven, J. (2014). High Parasitological Failure Rate of Visceral Leishmaniasis to Sodium Stibogluconate among HIV Co-Infected Adults in Ethiopia. *PLoS Neglected Tropical Diseases*, *8*(5), 14–17. https://doi.org/10.1371/journal.pntd.0002875

Duthie, M. S., Lison, A., & Courtenay, O. (2018). Advances toward Diagnostic Tools for Managing Visceral Leishmaniasis. *Trends in Parasitology*, *xx*, 1–10. https://doi.org/10.1016/j.pt.2018.07.012

Feleke, B.E., Feleke, T.E. Micronutrient levels and their effects on the prognosis of visceral leishmaniasis treatment, a prospective cohort study. *BMC Infect Dis* 20, 867 (2020). https://doi.org/10.1186/s12879-020-05615-1

Ghosh P, Roy P, Chaudhuri SJ, Das NK. Epidemiology of Post-Kala-azar Dermal Leishmaniasis. Indian J Dermatol. 2021;66(1):12–23. pmid:33911289

Grifferty G, Shirley H, McGloin J, Kahn J, Orriols A, Wamai R. Vulnerabilities to and the Socioeconomic and Psychosocial Impacts of the Leishmaniases: A Review. Res Rep Trop Med. 2021; 12: 135–51. Pmid: 34188584 https://rpubs.com/phle/r_tutorial_difference_in_differences

Kumar P, Chatterjee M, Das NK. Post Kala-Azar Dermal Leishmaniasis: Clinical Features and Differential Diagnosis. Indian J Dermatol. 2021 Jan-Feb;66(1):24-33. doi: 10.4103/ijd.IJD_602_20. PMID: 33911290; PMCID: PMC8061484.

Kumar, V., KT, M.F., Sharma, A. *et al.* The Possible Role of Selected Vitamins and Minerals in the Therapeutic Outcomes of Leishmaniasis. *Biol Trace Elem Res* 201, 1672–1688 (2023). https://doi.org/10.1007/s12011-022-03311-6

Leishmaniasis Fact Sheet: World Health Organization; 2022 [Available from: https://www.who.int/news-room/fact-sheets/detail/leishmaniasis.

Malafaia G. Protein-energy malnutrition as a risk factor for visceral leishmaniasis: a review. Parasite Immunol. 2009 Oct; 31(10):587-96. doi: 10.1111/j.1365-3024.2009.01117. x. PMID: 19751470.

Mann S, Frasca K, Scherrer S, Henao-Martinez AF, Newman S, Ramanan P, et al. A Review of Leishmaniasis: Current Knowledge and Future Directions. Curr Trop Med Rep. 2021;8(2):121–32. Pmid: 33747716

Ngere I, Gufu Boru W, Isack A, Muiruri J, Obonyo M, Matendechero S, et al. Burden and risk factors of cutaneous leishmaniasis in a peri-urban settlement in Kenya, 2016. PLoS One. 2020;15(1): e0227697. pmid:31971945

Njau J, editor Leishmaniasis control in Kenya: Current challenges and future strategies. Geneva Health Forum; 2010.

Olaf Müller, M. K. A. (2005). Malnutrition and health in developing countries. *CMAJ*, *279–286*(3), 671–677. https://doi.org/10.1007/s12541-016-0082-0

Pigott DM, Bhatt S, Golding N, Duda KA, Battle KE, Brady OJ, et al. Global distribution maps of the leishmaniases. Elife. 2014;3. pmid:24972829

Prasad, Ananda S. "Zinc in human health: effect of zinc on immune cells." *Molecular medicine* 14 (2008): 353-357.

Singh OP, Hasker E, Sacks D, Boelaert M, Sundar S. Asymptomatic Leishmania infection: a new challenge for Leishmania control. Clin Infect Dis. 2014;58(10):1424–9. pmid:24585564

The Strategic Plan for Control of Leishmaniasis 2021–2025. Kenya: Republic of Kenya Ministry of Health; 2021.

Wasunna, M., Musa, A., Hailu, A., Khalil, E. A. G., Olobo, J., Juma, R., Wells, S., Alvar, J., & Balasegaram, M. (2016). The Leishmaniasis East Africa Platform (LEAP): Strengthening clinical trial capacity in resource-limited countries to deliver new treatments for visceral leishmaniasis. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *110*(6), 321–323. https://doi.org/10.1093/trstmh/trw031

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