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POST IMMUNE RESPONSE TO ZINC SUPPLEMENTATION IN DIABETES (Type II) PATIENTS WITH IMMUNE DYSFUNCTION.

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ABSTRACT: Diabetes mellitus, particularly type 2, is associated with immune dysfunction and zinc deficiency, which exacerbate inflammation and impair glycemic control. This study solely investigated the post-immune response to zinc supplementation in 315 diabetic patients with immune dysfunction within Jaba Local Government Area (LGA), Kaduna State, Nigeria. In a randomized controlled trial, participants received either 30mg/day elemental zinc or placebo for 12 weeks. Immune markers (CD4+ T-cell counts, TNF-α, IL-6) and glycemic indices (fasting blood glucose [FBS], HbA1c) were assessed before and after intervention. Results showed significant improvements in the zinc group: CD4+ counts increased by 25% ($p<0.001$), TNF-α decreased by 32% ($p<0.01$), IL-6 by 28% ($p<0.05$), FBS by 18% ($p<0.001$), and HbA1c by 1.2% ($p<0.001$). No significant changes was observed in the placebo group. Zinc supplementation enhances the immune function and glycemic control in this population, supporting its role as an adjunct therapy in resource-limited settings.

Keywords: *Zinc supplementation, diabetes mellitus, immune dysfunction, cytokines, Nigeria*

Introduction

Diabetes mellitus (DM) affects over 422 million people globally, with sub-Saharan Africa bearing a disproportionate

burden due to rising prevalence and limited healthcare access.[1] In Nigeria, the epicenter of African diabetes cases, type 2 DM (T2DM) is linked to immune dysregulation, characterized by chronic low-grade inflammation, T-cell exhaustion, and elevated pro-inflammatory cytokines like TNF-α and IL-6.[10] Zinc, an essential trace element, plays a pivotal role in immune homeostasis and insulin signaling, yet deficiency is prevalent among Nigerian diabetics, relating with disease severity and complications such as polyneuropathy.[15, 16]

Jaba LGA in Kaduna State shows rural Nigeria's challenges, where malnutrition and infectious comorbidities amplify immune dysfunction in DM patients. This study evaluates the immunomodulatory effects of zinc supplementation in 315 such patients, hypothesizing that it would restore T-cell function, decrease cytokine storms, and improve metabolic outcomes. The findings may perhaps inform cost-effective interventions in similar low-resource environments.

REVIEW OF RELATED LITERATURE

Zinc Deficiency in Diabetes and Immune Implications

Zinc homeostasis is disrupted in T2DM, with serum levels often reduced by 20-30% compared to healthy controls, attributed to urinary losses, oxidative stress, and impaired absorption.[1,3] In Nigerian cohorts, studies from Maiduguri and Lagos report zinc hypozincemia in 60-70% of T2DM patients, associating it with poor glycemic control and heightened infection risk.[1,14] This deficiency impairs antioxidant defenses, as zinc is a cofactor for superoxide dismutase (SOD), exacerbating β-cell damage and insulin resistance.[9]

Immunologically, zinc modulates T-lymphocyte differentiation and cytokine production. Deficiency leads to thymic atrophy, reduced CD4+ T-cell proliferation, and skewed Th1/Th2 balance, raising pro-inflammatory states in DM.[12,20] In diabetics, low zinc correlates with elevated IL-6 and TNF-α, cytokines that promote endothelial dysfunction and neuropathy.[16,10]

Effects of Zinc Supplementation on Glycemic and Immune Parameters.

Meta-analyses confirm zinc's benefits in DM management. A systematic review of 15 trials (n=1,000+) showed 30mg/day supplementation reduced FBS by 12-18 mg/dL

and HbA1c by 0.5-1.0%, via enhanced GLUT4 expression and reduced hepatic gluconeogenesis.[2,4,8] An umbrella review further linked it to lowered HOMA-IR, underscoring anti-insulin resistance effects.[8]

On immunity, zinc restores T-cell function by up-regulating NF-κB signaling and IL-2 production, while suppressing NF-κB-mediated cytokine release.[11,12] In metabolic syndrome patients with DM, supplementation boosted monocyte anticancer activity and reduced TNF-α by 25-40%.[7] A study in T2DM reported increased TNF-α gene expression post-zinc, but overall anti-inflammatory shifts via balanced cytokine profiles.[18] In African contexts, limited data from Ethiopia and South Africa suggest similar immunomodulation, though Nigeria-specific trials are scarce.[13]

JUSTIFICATION

While global evidence supports zinc's role, studies in rural Nigerian settings like Jaba LGA are absent, where comorbidities (e.g., malaria) compound immune deficits.[13]This trial addresses this by focusing on post-supplementation immune dynamics in a large cohort.

MATERIALS AND METHODS

Study Design and Participants

This prospective randomized controlled trial was conducted from March to August 2025 at the Kwoi General Hospital and three primary health centers (in Jaba LGA, Kaduna State, Nigeria. Inclusion criteria: adults (≥18 years) diagnosed with T2DM (per ADA criteria) and immune dysfunction (CD4+ <500 cells/μL or elevated TNF-α >10 pg/mL). Exclusion: pregnancy, acute infections, or zinc allergy. From 450 screened, 315 eligible participants (mean age 52.3 ± 8.7 years; 58% female) were randomized 1:1 to intervention (n=158) or placebo (n=157) groups using computer-generated blocks.

Intervention

The intervention group received 30mg elemental zinc (as zinc gluconate) daily for 12 weeks, alongside standard DM care (metformin/oral hypoglycemics). Placebo was

identical in appearance. Compliance was monitored via pill counts (>85% adherence).

Assessments

Baseline and endpoint (week 12) evaluations included:

- Immune markers: Flow cytometry for CD4+ T-cells; ELISA for serum TNF-α and IL-6.

- Glycemic indices: FBS (glucometer), HbA1c (HPLC).

- Safety: Adverse events, serum zinc (atomic absorption spectrophotometry).

Ethical approval was obtained from Kaduna State Ministry of Health (Ref: KSMH/ERC/2024/045); informed consent was secured.

Statistical Analysis

Data were analyzed using SPSS v.26. Between-group differences: independent t-tests/Mann-Whitney U. Within-group: paired t-tests. Significance: $p<0.05$. Power calculation (80%, $\alpha=0.05$) ensured n=315 detected 15% CD4+ change.

Results

Baseline characteristics were comparable: mean FBS 168 ± 32 mg/dL, HbA1c 8.2 ± 1.4%, CD4+ 420 ± 85 cells/μL, TNF-α 14.5 ± 3.2 pg/mL, IL-6 12.1 ± 2.8 pg/mL, serum zinc 65 ± 12 μg/dL (all $p>0.05$).

Post-intervention:

Parameter	**Zinc Group (n=158) pre**	**Zinc Group post**	**Placebo Group (n=157) Pre**	**Placebo Group post**	**p-value (Zinc vs. placebo change)**
CD4+ (cells/μL)	418±84	523±92*	422±86	415±88	<0.001
TNF-	14.6±3.1	9.9±2.4*	14.4±3.3	14.1±3.2	<0.01

α(pg/mL)					
IL-6(pg/mL)	12.2±2.7	8.8±2.1*	12.0±2.9	11.8±2.8	<0.05
FBS (mg/dL)	169±31	139±28*	167±33	165±32	<0.001
HbA1c (%)	8.3±1.3	7.1±1.1*	8.1±1.4	8.0±1.3	<0.001
Serum Zinc (µg/dL)	66±11	92±14*	64±13	63±12	<0.001

* p<0.001 vs. baseline (paired t-test). No serious adverse events; mild GI upset in 5% zinc group.

Subgroup analysis revealed greater benefits in females (CD4+ +28%) and those with baseline zinc <60µg/dL (TNF-α -38%).

Discussion

Zinc supplementation elicited robust immunomodulation, aligning with literature: elevated CD4+ reflects restored thymic output and T-cell signaling.[12] Cytokine reductions mirror zinc's NF-κB inhibition, mitigating DM's inflammatory milieu.[11] Glycemic gains corroborate meta-evidence, likely via insulin-mimetic actions.[17,2]

In Jaba LGA, baseline deficiencies (mirroring Nigerian data) underscore nutritional vulnerabilities.[14] Limitations include short duration and lack of dietary zinc assessment; future studies should explore long-term neuropathy outcomes.

Conclusion

Zinc supplementation significantly ameliorates immune dysfunction and hyperglycemia in Nigerian diabetic patients, offering a feasible adjunct in rural settings. Integrating zinc into DM protocols could reduce complications and healthcare costs.

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