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Original Research Article

Marijuana Smoke Inhalation and Potential Micronutrient Deficiencies among Nigerian Smokers

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ABSRTACT

The impact of marijuana use on the micronutrient status remains largely unexplored. This knowledge gap may hinder the development of comprehensive public health strategies and interventions aimed at promoting optimal nutritional status among marijuana users. This study aimed to determine serum levels of vitamins E and C, magnesium, zinc, copper, and copper-to zinc ratio among marijuana smokers. Serum zinc, copper, magnesium, vitamin E, and C were assayed in 60 regular marijuana users and 60 non-users of marijuana using Atomic Absorption Spectrophotometric and spectrophotometric methods respectively. Only individuals who tested positive for the presence of cannabinoids in their urine using cannabis test strips were recruited. The data generated were compared using Students' paired t-test and Analysis of Variance (ANOVA) at 95% confidence intervals and at a 5% level of significance ($p<0.05$). Serum zinc, vitamin C, and E were significantly lower ($p<0.001$), while copper was higher among marijuana smokers than non-smokers. Copper-to- zinc ratio was significantly higher ($p<0.001$) in marijuana smokers compared to non-smokers. There was no significant difference in serum levels of magnesium between marijuana smokers and non-smokers. Serum zinc, vitamins C and E decreased while serum copper increased with increasing duration of marijuana usage ($p<0.05$), but the differences in magnesium levels were insignificant. Findings indicated significant differences in micro-nutrient levels among marijuana consumers compared to non-users, with lower zinc, vitamin C, and E and increased copper levels. The increased copper-to-zinc ratio in marijuana users suggests an imbalance that could have broader health implications.

Keywords: Marijuana, Smokers, Micronutrients, Humans

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Introduction

Marijuana is the most widely used illicit drug globally and has been associated with various health effects. Marijuana ranked third among the most popularly used drugs in Nigeria apart from alcohol and cigarettes especially among young adults because of the low cost, availability, and ease of cultivation [1]. Despite being illegal, marijuana production, distribution, and consumption rates remain high and are still growing among Nigerians [1]. Although marijuana is used for medicinal purposes as an antioxidant, anticonvulsant, anti-inflammatory, and neuroprotective, its harmful effects are also well known [2]. Studies have indicated that acute and chronic use of marijuana is associated with several harmful health consequences, including marijuana dependence, severe respiratory illnesses, impaired coordination and performance, anxiety, suicidal/tendencies, cardiovascular, cerebrovascular, and high occurrence of other psychiatric disorders [3,4]. Apart from being linked with many complications related to some organs of the human body and social effects, there is growing interest in understanding the impact of marijuana consumption on the nutritional status of individuals, particularly about micronutrients[5]

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Micronutrients, which include vitamins and minerals, are essential for various physiological functions[6]. They play crucial roles in several processes, from energy production and immune function to bone health and blood clotting[6] . However, many people do not get enough of these essential nutrients in their diet[6]. This can lead to micronutrient deficiencies, which can have serious health consequences.

Copper, zinc, vitamin C, and E are essential elements required by the human body for many biological reactions. Copper and zinc act as cofactors in enzymatic reactions and also play a vital role in several biochemical and metabolic processes. Magnesium is essential for adequate immune function and regulating inflammation. Magnesium deficiency may result in temporary or long-term immune dysfunction[7,8]. The main line of defense against potentially dangerous oxidation processes is vitamin E and vitamin C, is a crucial component that supports the antioxidant defense system by preventing lipid peroxidation. Also, copper, zinc, and magnesium are important for lipid metabolism[9].

Interestingly, the impact of marijuana consumption on the micronutrient status of consumers remains largely unexplored. Deficiencies in these micronutrients can lead to serious health consequences. This knowledge gap may hinder the development of comprehensive public health strategies and interventions aimed at promoting optimal nutritional status among marijuana users. Furthermore, the method of marijuana consumption may influence nutrient absorption and utilization, adding another layer of complexity to this issue[10,11]. Therefore, there is a clear and urgent need to evaluate the micronutrient status among marijuana consumers to inform potential therapeutic interventions for this population. This study aimed to determine serum levels of vitamins E and C, magnesium, zinc, copper, and copper-to zinc ratio among marijuana users.

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Materials and Methods

Study Design/Population
This is a case-control study designed to determine some micronutrient status among marijuana consumers. The subjects include smokers of marijuana in Benin City, Edo State, Nigeria. The control subjects were non-smokers of marijuana or cigarettes in the same locality. Evidence of marijuana smoking was confirmed at smoking joints where volunteers were certified by co-smokers as consumers for at least one year. Only subjects who gave consent and met inclusion criteria were enrolled in the study. A total of 120 participants were recruited for this study. The participants include 60 marijuana smokers and 60 nonmarijuana smokers. Their age, sex, and duration of consumption of marijuana were obtained by a semi-structured questionnaire. Participants were notified several days before the commencement of the study and given appropriate instructions. The age and sex of the participants were recorded. All subjects were interviewed to establish their level of literacy and assisted in filling out the questionnaire to minimize errors.

Sociodemographic Data
Sociodemographic data were collected by an interviewer who administered a structured questionnaire to determine the age, educational levels, socioeconomic status, duration of marijuana use, and quantity of marijuana consumed. Information on general health and history of past disease(s) and habits like consumption of alcoholic beverages and addictions were collected[12].

Inclusion Criteria
Adult human marijuana consumers and non-marijuana smokers above the age of 18 years were included. Only individuals who tested positive for the presence of cannabinoids in their urine using cannabis test strips (ACRO BIOTECH diagnostics) were recruited. The control group was non-smokers of marijuana/cigarettes, who tested negative for the presence of cannabinoids and gave consent to participate in this study.

Exclusion Criteria
Human marijuana consumers below the age of 18 years and above the age of 65 years those with abdominal or gastric pain, and individuals with nausea or vomiting were excluded. Also excluded are individuals who are infected with HIV, Hepatitis B and C, Cancer patients, Diabetes patients, individuals with Sickle Cell Disease, and Chronic Liver Disease. Also excluded are individuals who smoke cigarettes and marijuana.

Ethical Approval
Ethical approval was obtained from the Research Ethics Committee, College of Medical Sciences, University of Benin, Benin City via letter ref. CMS/REC/01/VOL.2/403 dated 20th August 2023. Informed consent was obtained from each participant.

Sample Size
The sample size for this study was determined using the sample size determination formula ($n= Z^2 P(1-P)/d^2$) for health studies[13] and 2.5% worldwide annual prevalence of marijuana use[14]. The calculated sample size was 38. However, 60 adults were recruited for the study while 60 healthy subjects who do not smoke marijuana or cigarettes were enrolled as controls.

Sample Collection
Before the collection of blood specimens, random urine specimen was collected and tested for the presence of cannabinoids using cannabis test strips (ACRO BIOTECH diagnostics). Only those with positive strip tests were further evaluated. About five (5 mL) of venous blood was withdrawn from the antecubital vein of each subject using a sterile needle and syringe and dispensed into a labeled and dry plain tube. The specimen was allowed to clot at room temperature and was centrifuged at 3000 rpm for 15 minutes. The serum was separated into another clean labeled tube and kept frozen at -80ºC until analyzed.

Sample Analysis
Determination of zinc, copper, and magnesium levels was done using an Atomic Absorption spectrophotometer (AAS), while vitamins E and C were assayed by the spectrophotometric method as previously described[15,16].

Statistical Analysis
Data obtained from the study were analyzed using the statistical software SPSS for Windows, version 17.0 (SPSS. Chicago, IL, USA). Values obtained in this study are presented as the mean standard error of mean (SEM). The data generated were compared using Students' paired t-test and Analysis of Variance (ANOVA) at 95% confidence intervals and at 5% level of significance (p-value 0.05).

Results and Discussion

Table 1 shows the sociodemographic and lifestyle characteristics of study participants (marijuana smokers). Male participants were 54 (90%) while the female was 06 (10%). The mean ± SD age of study participants was 34.33±11.57 with a minimum age of 19 years and a maximum of 58 years. Most of the participants (46.7%) were between 19-30 years followed closely by age group 31-45 (40%). The age group 46-60 had the lowest participation (13.3%). For the lifestyle characteristics related to marijuana consumption, participants who had been smoking marijuana for 1-10 years were the most frequent (66.7%), followed by 11-20 years (20%), and lastly 21-30 years (13.3%). It was also observed that 90% of participants consumed between 1-5 wraps of marijuana daily while the other 10% consumed between 6-10 wraps daily.

Table 1: Sociodemographic and Lifestyle Characteristics of Marijuana Smokers

Variables	Category	Frequency	Percentage (%)
Gender	Male	54	90.0
	Female	06	10.0
Age Range (Years)	19-30	28	46.7
	31-45	24	40.0
	46-60	08	13.3
Smoking Duration (Years)	1-10	40	66.7
	11-20	12	20.0
	21-30	08	13.3
Quantity (Wraps/day)	1-5	54	90.0
	6-10	6	10.0

Table 2 shows the mean levels of copper, zinc,copper-to-zinc ratio, and vitamins C and E among Adults Marijuana Smokers. Serum zinc, vitamin C, and E were significantly lower ($p<0.001$), while copper was higher among marijuana smokers than non-smokers. Copper-to- zinc ratio was significantly higher ($p<0.001$) in marijuana smokers compared to non-smokers. There was no significant difference in serum levels of magnesium when compared between marijuana smokers and non-smokers.
Table 3 shows that serum zinc, vitamins C and E decreased while serum copper increased with increasing duration of marijuana usage ($p<0.05$), but the differences in magnesium levels were not significant.

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Table 2: Comparison of mean levels of copper, zinc, and copper-to-zinc ratio among Adults Marijuana Smokers (Mean ± SD)

Measured Serum Parameters	Marijuana Smokers (n=60)	Non-Smokers (n=60)	p-Value
Zinc (µg/dL)	88.36±2.84	115.6±2.10	0.001
Copper (µg/dL)	135.18±2.80	112.06±2.50	0.001
Magnesium(µg/dL)	2050±10.50	2056±9.80	0.820
Cu/Zn ratio	1.53±0.02	0.96±0.03	0.001
Vitamin C (mg/dL)	0.90±0.21	1.62±0.23	0.001
Vitamin E (µg/mL)	11.02±0.18	15.82±0.70	0.001

Cu/Zn ratio=Copper-Zinc ratio

Table 3: Comparison of Measured micronutrient levels based on the Duration of Marijuana consumption

Duration	1-10 Yrs	11-20Yrs	21-30Yrs	F-value	P-value
No of Subjects	40	12	08		
Zn (µg /dL)	87.2±0.10	86.2±0.05	84.1±0.08	3.51	0.05
Cu (µg /dL)	132±0.04	133±0.05	138±0.08	3.82	0.05
Mg (µg /L)	2042.2±0.10	2045.2±0.05	2056.1±0.08	2.23	0.20
Cu/Zn ratio	1.51±0.04	1.54±0.02	1.64±0.04[a]	3.19	0.05
Vitamin C (mg/dL)	1.00±0.01	0.88±0.02	0.82±0.03	3.20	0.05
Vitamin E (µg/mL)	11.45±0.18	11.00±0.05	10.60±0.08	3.51	0.05

Zn-Zinc; Cu-Copper; Mg=magnesium; Cu/Zn ratio-Copper-Zinc ratio

Deficiencies in essential micronutrients such as zinc, magnesium, vitamin C, and E could lead to health risks among marijuana smokers. Most marijuana smokers in our setting may not get enough of these essential nutrients in their diet due to adverse dietary habits. Previous data indicated that marijuana use influences food intake, appetite, and metabolism, yet human study on the impact of marijuana consumption on the micronutrient status among Nigerians remains largely unexplored. The widespread use of marijuana worldwide indicates that developing evidence of its harmful effects is already a critical global health issue[17]. This study was designed to assess serum levels of vitamins E and C, magnesium, zinc, and copper and calculate the copper-to zinc ratio among marijuana users. It may help in the development of public health strategies and interventions aimed at promoting optimal nutritional status among marijuana users.

In this study, most of the participants are male (90%), with a small proportion being female (10%). The high percentage of male participants is indicative of the higher prevalence of marijuana use among males, which is consistent with global patterns of substance use. Hormonal and metabolic differences between genders can impact micro-nutrient levels. Research consistently shows higher rates of marijuana use among men than women[17-19]. It was reported that males are more likely to use marijuana and other substances compared to females[17,20]. Data from the 2019 National Cannabis Survey in Canada showed that more men than women have used marijuana in the past three months. Also, more men than women reported greater frequency of marijuana in Canada[20]. Furthermore, evidence from the US and Europe also showed that more boys and men reported a greater prevalence of marijuana use than girls and women[20]. Reports elsewhere also indicated that males are more likely to use marijuana and other substances compared to females[19], and men and women may have different nutrient requirements and metabolisms, affecting how marijuana use influences micro-nutrient levels[18].

Also, participants are primarily in the 19-30 age group (46.7%), followed by 31-45 (40%), and 46-60 (13.3%). Younger individuals (19-30 years) form the largest group, which is typical as this age group tends to have higher rates of marijuana use. This is consistent with previous studies. Age can affect nutrient metabolism, with younger individuals potentially having different dietary habits and metabolic rates compared to older individuals. Younger adults often have higher substance use rates. Gelfand and Tangney[21] reported that young adults (18-25 years) have the highest rates of marijuana use. Nutrient metabolism also changes with age, as seen in studies by Smith *et al* [22] which found that nutrient absorption and metabolism can decline with age, potentially influencing the impact of marijuana on nutrient status. On the contrary, more middle-aged (50-64 years) and older adults (≥65 years) were more likely to engage in marijuana use than younger adults, but the age differences in marijuana use patterns suggest that middle-aged and older adults are more likely to engage in less risky marijuana use patterns (consumption of highly potent concentrates) when compared to younger adults[23].

Furthermore, most participants have been smoking marijuana for 1-10 years (66.7%), with fewer participants in the 11-20 years (20%) and 21-30 years (13.3%) categories. The duration of marijuana use is crucial for understanding its long-term impact on micro-nutrient levels. Longer duration correlated with more significant alterations in nutrient levels due to cumulative exposure. Long-term marijuana use has been linked to various health effects, including changes in nutrient levels. Yuan, *et al*[24] found that chronic marijuana users had altered levels of several nutrients. The duration of use can exacerbate these effects, with longer use potentially leading to more pronounced nutrient imbalances.

In addition, the participants smoke 1-5 wraps per day (90%), while a small fraction smoke 6-10 wraps per day (10%). The quantity of marijuana consumed daily can influence micro-nutrient levels, with higher consumption potentially leading to more significant nutrient imbalances due to increased exposure to marijuana compounds that can affect nutrient absorption and metabolism. Higher consumption of marijuana has been associated with greater health impacts. It was reported that heavy marijuana use could lead to more significant metabolic disturbances and nutrient imbalances compared to lighter use[25]. This is important when analyzing data, as higher daily intake might correlate with lower levels of certain nutrients.

Similarly, the study correlates the blood zinc, copper, and magnesium levels with duration of marijuana use. The results on the mean zinc level in marijuana smokers are significantly lower compared to non-smokers. This suggests that chronic marijuana use may lead to zinc deficiency, impacting various physiological functions including immune response and metabolism. This result is consistent with previous findings by Vidot *et al*[26], which indicated lower serum zinc levels in chronic marijuana users due to potential depletion and altered dietary intake. The mean copper level in marijuana smokers was significantly higher than in non-smokers. Elevated copper levels could be attributed to metabolic changes or liver function alterations associated with chronic marijuana use. Deficiencies in some micronutrients such as zinc and vitamins were associated with health challenges[8,27]. Copper and zinc are particularly important because they play a vital role in physiological processes and suboptimal levels in the circulation may have significant effects on the pathogenesis of

metabolic diseases[8]. Some authors have reported that an imbalance in serum zinc and copper homeostasis was linked with an increased risk of cardiovascular diseases and diabetes, while an imbalance between Zn and Cu concentrations resulted in oxidative stress and insulin resistance[28]. One study suggested that deficiencies in copper and zinc were the strong risk factor for metabolic syndrome (MetS) among adult Iranian subjects with normal weight[29]. On the contrary, a meta-analysis of several studies observed an inverse relationship between cannabis smoking and diabetes mellitus[30].

In this study, participants were individuals who were regular marijuana users who smoked 1 -5 wraps per day. Hall and Degenhardt[31] defined regular marijuana use as taking marijuana 10 to 19 times monthly, while heavy use was characterized as using it 20 times a month. It is interesting to note that both regular and heavy use of marijuana are associated with several health challenges. Over 420 chemicals are reported to be present in marijuana and more than 60 of the chemicals are cannabinoids[3]. About 20%-70% of tetra-hydro cannabinoids (THC) are delivered through smoking, which is rapidly absorbed and reaches high blood concentration quickly after inhalation through the lungs[32]. THC has a long biological half-life of 18 h to 4 days because of its high lipid solubility and a large volume of distribution[3]. It reaches the various tissues and organs such as adipose tissue, liver, lung, and spleen. Cannabinoids communicate directly with the human body via the endocannabinoid system (CB1 and CB2) which is involved in the regulation of various metabolism, intercellular communication, appetite, memory, immune, and pain responses[33].

Findings from this study also indicated that the mean serum levels of both vitamin C and E were significantly lower in cannabis smokers than in non-smokers. This is consistent with previous study[34]. Marijuana may influence the metabolism of vitamins and trace elements ranging from their intestinal absorption to their bioavailability and elimination[3]. The reasons for the lower levels of Vitamin C and E among marijuana smokers are multifactorial. One plausible reason is the observation that marijuana smokers tend to eat less healthy diets when compared with non-smokers and may be prone to eating fewer fruits and vegetables than non-smokers[35]. It should be noted that data on dietary consumption was not gathered in this study. Even exposure of cigarette smoke to plasma in-vitro was reported to deplete vitamin C present in the plasma[36]. The formulation of Dietary Reference Intakes (DRIs) for marijuana smokers is imperative to prevent micronutrient deficiencies, maximize health, and improve the quality of life of consumers similar to that of the Institute of Medicine, Food and Nutrition Board in the USA[37]. Marijuana smokers may require supplementation of essential micronutrients to avoid the risk of chronic diseases.

Data from this study revealed no significant difference in mean magnesium levels between marijuana smokers and non-smokers. This suggests that marijuana use may not directly influence serum magnesium levels in this study population. This result is consistent with the inconclusive findings on magnesium levels in marijuana users[38].

The copper-to-zinc ratio is significantly higher in marijuana smokers compared to non-smokers. This imbalance could indicate potential health risks associated with altered nutrient ratio in chronic marijuana users. Similar findings were noted in individuals with acute and chronic conditions[39], highlighting the importance of evaluating nutrient ratios alongside individual micro-nutrient levels. An imbalance in the copper/zinc homeostasis in young adults is a risk factor for marijuana psychosis. It was found in an animal investigation that copper enhanced the ability of marijuana to intensify barbiturate hypnosis. For one to two weeks, the administration of a single dosage of copper significantly postponed the development of tolerance to the hypothermic activity of marijuana and partially suppressed tolerance to barbiturate hypnosis-potentiation activity. Maintaining a proper copper/zinc balance might be challenging for many mentally unstable people. Adverse reactions to substances and foods are exacerbated by this significant homeostatic imbalance. In addition to blocking key fatty acid pathways, deficiencies in vitamin B groups, omega-6 and omega-3 fatty acids, and zinc and copper can further raise the risk of psychosis[40].

A comparison of the micronutrient levels based on the duration of marijuana consumption indicated a gradual depletion of zinc, vitamin C, and E levels with prolonged marijuana consumption. Chronic use may affect zinc metabolism or absorption, leading to lower levels over time. This observation aligned with that of Smith *et al.*[22], which indicated lower serum zinc levels in chronic marijuana users due to potential depletion and altered dietary intake. On the other hand, copper levels increased with a longer duration of marijuana use. This result supported findings from Bidwell *et al*[41] who noted increased copper levels in long-term marijuana users. Magnesium levels did not show significant variation with different durations of marijuana use. The stability of magnesium levels suggests that marijuana use duration does not significantly impact magnesium status in this study population. This could be due to homeostatic mechanisms maintaining magnesium levels. This result is in consistent with Bidwell *et al*[41] who reviewed inconclusive findings on magnesium levels in marijuana users. The Cu/Zn ratio increases with the duration of marijuana use, which may indicate a growing imbalance between copper and zinc levels with prolonged marijuana use. This imbalance could affect immune function and oxidative stress regulation.

Conclusion

The study highlights significant differences in micro-nutrient levels among marijuana consumers compared to non-users, with lower zinc, vitamin C, and E and increased copper levels. The elevated copper-to-zinc ratio in marijuana users suggests an imbalance that could have broader health implications.

Conflict of interest

The authors declare no conflict of interest

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them

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