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Original Article

Biochemistry Section

Magnesium Imbalance before and during Concomitant Chemoradiation in Cervical Cancer Patients: A Prospective Interventional Study

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ABSTRACT

Introduction: Cervical cancer is a major health concern, especially in developing countries. It is the second most common cancer among women in India, largely due to limited access to advanced screening and Human Papilloma Virus (HPV) vaccination. Despite significant advancements in cervical cancer prevention and treatment, the disease remains a major health burden, particularly in low-resource settings. Magnesium (Mg), an essential mineral involved in immune function, inflammation and Deoxyribonucleic Acid (DNA) repair, has been linked to various cancers, including colorectal and breast cancers, but its role in cervical carcinoma is underexplored.

Aim: To investigate the association between magnesium levels and cervical carcinoma and to explore the association of hypomagnesemia with concomitant chemotherapy using cisplatin during chemoradiation.

Materials and Methods: This was a hospital-based prospective interventional study, in which a total of 322 subjects were included in the study, of which 161 were healthy controls and 161 were diagnosed cases of cervical carcinoma. The magnesium levels were estimated before and after treatment using the Xylidyl blue complexing method on an autoanalyser. The data were compared between the two groups using appropriate statistical analysis with Statistical Package for the Social Sciences (SPSS) software version 20.0.

Results: The mean magnesium levels were 2.08±0.24 mg/dL in controls and 1.56±1.02 mg/dL in cancer patients (p-value <0.001). Mean serum levels decreased in cancer patients postchemoradiation to 0.74±0.39 mg/dL. During concomitant chemoradiation with cisplatin, hypomagnesemia was observed as grade I in 62 (38.5%), grade II in 25 (15.5%), grade III in 12 (7.5%) and grade IV in 36 (22.4%). A significant correlation was found between hypomagnesemia and hyponatremia, hypokalemia and cumulative cisplatin dose toxicity.

Conclusion: The study demonstrated a high prevalence of hypomagnesemia in cervical cancer patients, especially those undergoing cisplatin-based chemotherapy, with levels declining further during treatment. Routine magnesium monitoring and proactive management are essential to prevent complications and improve outcomes.

Keywords: Biomarker, Cisplatin, Kidney, Platinum-based treatment

INTRODUCTION

Carcinoma of the cervix is the second most common cancer in females in India, following breast cancer. In developing nations like India, where screening and vaccination programs are limited, cervical carcinoma poses a significant health burden [1]. Science has made significant progress in the diagnosis and prevention of cervical cancer with the discovery of HPV vaccine and the ThinPrep cytologic test, resulting in a decrease in the incidence of cervical cancer. However, the high cost of these tests has contributed to the continued prevalence of cervical cancer as the predominant malignancy among women in low-resource countries. Although advancements in early detection and treatment have improved outcomes, the intricate interplay between various physiological factors in the progression and prognosis of cervical carcinoma remains an area of intense research [2].

Among various factors, the role of magnesium has garnered increasing attention due to its diverse biological functions and potential implications in cancer pathogenesis. Magnesium is an essential mineral that plays a crucial role in numerous cellular processes, such as cell proliferation, immune function, inflammation, apoptosis, DNA repair and nucleic acid metabolism, all of which are integral to cancer development and progression [3]. Perturbations in magnesium homeostasis have been associated with various malignancies, including cervical carcinoma [4]. Previous studies have linked low intakes of magnesium to the risk of colorectal cancer [5,6], adenomas [7] and breast cancer [8]. Low levels of magnesium are also associated with a high infection rate. Magnesium is essential for the activation and function of T cells, which are a crucial component of the immune system responsible for recognising and eliminating abnormal or infected cells [9]. Studies have shown that T cells are capable of effectively eliminating abnormal or infected cells only when they are in an environment with adequate magnesium levels [9-11].

Despite being the second most abundant intracellular cation in the human body and playing a critical role in numerous physiological processes, magnesium remains a relatively under-recognised element in overall health [12]. The kidneys meticulously regulate magnesium homeostasis through controlled reabsorption. However, chemotherapy disrupts electrolyte balance, including magnesium. These drugs either enhance renal excretion of magnesium or impede its intestinal absorption, resulting in a decline in serum magnesium levels [13]. Cisplatin demonstrates a predilection for accumulation within the renal cortex, thereby inducing degenerative alterations in the proximal tubules. Cisplatin-induced nephrotoxicity presents with a diverse spectrum of manifestations, with Acute Tubular Necrosis (ATN) being the most commonly observed form [14]. This phenomenon is demonstrably linked to a concomitant elevation in the urinary excretion of proximal tubular proteins, specifically β2-microglobulin and N-acetyl-β-glucosaminidase (NAG). Intriguingly, a robust correlation is observed between NAG excretion and

magnesium levels, suggesting a potential mechanistic link between cisplatin-mediated tubular injury and the depletion of magnesium stores [13].

The relationship between magnesium levels and cervical carcinoma has been relatively underexplored. This study aims to bridge this gap by investigating the association between magnesium levels and cervical carcinoma, as well as exploring the association of hypomagnesemia with concomitant chemotherapy using cisplatin during chemoradiation. Understanding the role of magnesium in cervical cancer pathogenesis could offer valuable insights into potential diagnostic biomarkers, therapeutic targets and preventive strategies.

MATERIALS AND METHODS

This is a hospital-based, prospective interventional study conducted in the Department of Radiation Oncology and the Department of Biochemistry at Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India, from May 2024 to October 2024, after obtaining approval from the Institutional Ethical Committee (IEC) (BREC/24/648). Consent was obtained from study participants following the approval from the IEC.

Inclusion criteria: Adult patients (≥18 years) with histopathologically confirmed cervical carcinoma were included in the study. Age- and gender-matched apparently healthy individuals were enrolled as control subjects.

Exclusion criteria: Cases with a known history of any chronic disease, such as diabetes, cardiac, renal, hepatic, or endocrine diseases, patients who were on any type of dietary supplements were excluded from the study.

Sample size calculation: The sample size was calculated based on a prevalence of 7.0% for cervical cancer, with a 5% margin of error at a 95% confidence level [15]. Using an online sample size calculator, the initial calculation yielded 97 participants. To account for a 20% attrition rate, the sample size was adjusted by multiplying by a factor of 1/(1-0.20)=1.25, resulting in a final sample size of 122 participants. However, to ensure statistical robustness and improve the generalizability of the findings, a final sample size of 161 patients was included in the study.

Study Procedure

Clinical histories were recorded and clinical examinations were conducted. The diagnosis and staging of cervical cancer were established through routine biopsy, X-ray and, when necessary, advanced imaging techniques such as Computed Tomography (CT) scans or combined Positron Emission Tomography (PET)/CT and Magnetic Resonance Imaging (MRI) were used to determine the extent of the disease. A standard treatment protocol was followed for patients with locally advanced cervical cancer (FIGO (International Federation of Gynaecology and Obstetrics) stage II-IVA), involving Concurrent Chemoradiation Therapy (CCRT) with cisplatin [16]. As part of the concomitant chemoradiation, chemotherapy was administered with injection cisplatin at a dose of 40 mg/m^2 intravenously on a weekly basis for five cycles, along with external beam radiation therapy administered at a dose of 50 Gy in 25 fractions over five weeks, with five fractions per week. Therefore, the scheduled number of chemotherapy cycles was five for each patient. Chemotherapy was administered after ensuring that complete blood count, liver function tests and kidney function tests were within normal limits. The maximum tolerable dose of weekly cisplatin was 70 mg to minimise toxicity [17].

The study population was divided into 2 groups:

Group I: Healthy controls (n=161);

Group II: Cervical cancer (n=161), with IIa representing before treatment and IIb representing after treatment.

Analysis of biochemical parameters: A 5 mL venous blood sample was collected from all participants under proper aseptic conditions. Samples were collected at the time of diagnosis, after every chemotherapy cycle and two weeks after the completion of treatment. Serum was separated and analysed for routine parameters and magnesium levels. Magnesium levels were estimated using the Xylidyl blue complexing method on a Beckman Coulter AU 700 autoanalyser. In this method, magnesium ions react with Xylidyl blue-I in an alkaline medium to form a red-purple coloured complex. The intensity of the colour produced is directly proportional to the concentration of magnesium in the sample [18]. The baseline was defined as the period from 30 days before to the day of the first chemotherapy administration and the treatment course was defined as the period from 1 day after the first administration of chemotherapy to 30 days after the last cycle of chemotherapy [19]. The normal serum magnesium level is 1.6-2.5 mg/dL [20]. Hypomagnesemia was defined according to the CTCAE (Common Terminology Criteria for Adverse Events) or magnesium reduction level [21,22]. Grade 1 hypomagnesemia was defined as magnesium levels between 1.6 mg/dL (lower limit of normal) and 1.2 mg/dL, Grade 2 as levels from <1.2 mg/dL to 0.9 mg/dL, Grade 3 as <0.9 mg/dL to 0.7 mg/dL and Grade 4 as <0.7 mg/dL. The frequency of hypomagnesemia refers to the number of instances in which hypomagnesemia occurred during the study [22].

STATISTICAL ANALYSIS

All data were collected using Microsoft Office Excel worksheets and analysed using SPSS software version 20.0. Values shown in the text, tables and figures are presented as mean±SD. Descriptive statistics were used to analyse the frequencies, medians, means and standard deviations of the study variables for the cohort. Student's t-test and the Mann-Whitney rank sum test were used to assess the statistical significance of continuous variables, while the Chi-squared test was employed for categorical variables. Correlation between clinical factors was evaluated using the Pearson product moment correlation or Wilcoxon signed-rank test. A p-value <0.05 was considered statistically significant.

RESULTS

The study included a total of 322 subjects, comprising 161 cervical cancer patients and 161 healthy controls. The median age was 54 years for the cases and 52 years for the controls, while the median Body Mass Index (BMI) was 27.5 kg/m^2 for the cases and 25 kg/m^2 for the controls. The mean age of the cases was 28.08±3.01 years (range: 19-75 years) and that of the controls was 27.87±1.5 years (p-value=0.08). All subjects in both groups were females. A majority of the participants, 124 (77.01%), resided in rural areas. The distribution of FIGO stages revealed that 80 patients (49.69%) were in stage II, 61 patients (37.89%) were in stage III and 20 patients (12.42%) were in stage IVA [23]. Hypomagnesemia was present in 83 (51.55%) patients at the time of diagnosis. Key median values included heart rate (84 bpm), systolic blood pressure (128 mmHg), glucose (108 mg/dL), haemoglobin (9.7 g/dL), creatinine (0.9 mg/dL) and magnesium (1.56 mEq/L). The frequency of hypomagnesemia occurred a median of three times, while hyponatremia and hypokalemia had median occurrences of zero and one, respectively [Table/Fig-1].

At the time of diagnosis, Group I (cases) had a mean magnesium level of 2.08±0.24 mg/dL, while Group II (controls) had a significantly lower mean magnesium level of 1.56±1.02 mg/dL. This difference was statistically highly significant (p<0.001) [Table/Fig-2]. Magnesium levels declined significantly after treatment, from 1.56±1.02 mg/dL in Group IIa (cases before treatment) to 0.74±0.39 mg/dL in Group IIb (cases after treatment) (p<0.001), indicating treatment-related impacts of platinum-based chemotherapy [Table/Fig-3].

Characteristics	Value (%) or (IQR)
Total no. of cases	161
Median age for cases (years)	54 (43-61)
Median BMI for cases (kg/m^2)	27.5 (21–33)
Residence	
Rural	124 (77.01%)
Urban	37 (22.99%)
FIGO stage	
II	80 (49.69%)
III	61 (37.89%)
IVA	20 (12.42%)
Baseline hypomagnesemia	83 (51.55%)
Median baseline heart rate, beats per minute	84 (76-91)
Median baseline systolic blood pressure (mmHg)	128 (116-141)
Median glucose (mg/dL)	108 (98-122)
Median haemoglobin (g/dL)	9.7 (9.2-10.7)
Median creatinine (mg/dL)	0.9 (0.7-1.1)
Mean magnesium (mEq/L)	1.56 (0.54-2.58)
Median frequency of hypomagnesemia	3 (1–5)
Median frequency of hyponatremia	0 (0–2)
Median frequency of hypokalemia	1 (0–3)

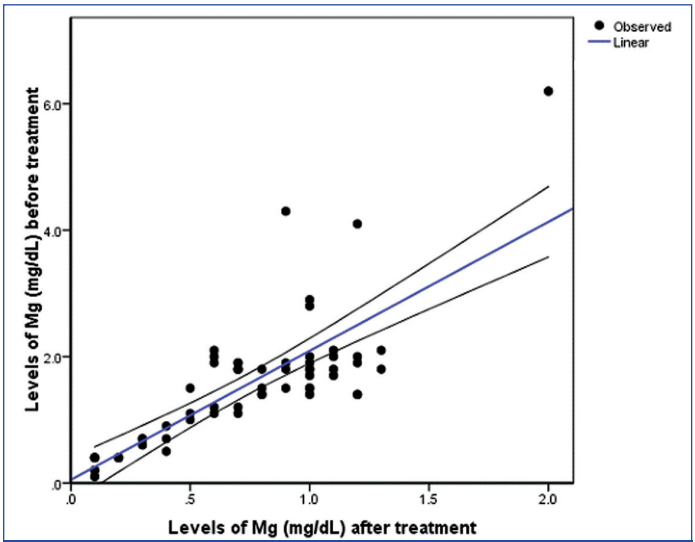
[Table/Fig-1]: Demographics and clinical characteristics of cases.
Value in N (%) or IQR (inter quartile range)

Parameter	Group I (Controls)	Group II (Cases)	p-value
Mg (mg/dL)	2.08±0.24	1.56±1.02	<0.001**

[Table/Fig-2]: The results of unpaired t-test in controls and cases at the time of diagnosis.
Unpaired t-test **Highly Significant; all values are in mean±SD

Parameter	Group IIa (before treatment)	Group IIb (after treatment)	p-value
Mg (mg/dL)	1.56±1.02	0.74±0.39	<0.001**

[Table/Fig-3]: The results of paired t-test in cervical cancer cases before and after treatment.
Paired t-test **Highly Significant; all values are in mean±SD



[Table/Fig-4]: Logistic regression analysis showing levels of magnesium (m/dL) in cases before and after treatment.

Logistic regression analysis revealed a positive correlation between magnesium levels before and after treatment [Table/Fig-4].

[Table/Fig-5] shows the distribution of hypomagnesemia in patients before and during/after treatment. There was a worsening trend in magnesium levels post-treatment.

Patients with hypomagnesemia commonly reported symptoms such as fatigue, muscle weakness and cramps. Among the

Hypomagnesemia	Magnesium levels (mg/dL)	Before treatment	During/after treatment
Grade I	<1.6-1.2	33 (20.49%)	62 (38.50%)
Grade II	<1.2-0.9	13 (8.07%)	25 (15.52%)
Grade III	<0.9-0.7	8 (4.96%)	12 (7.45%)
Grade IV	<0.7	29 (18.01%)	36 (22.36%)

[Table/Fig-5]: Hypomagnesemia grading seen in patients before and during/after treatment.
Hypomagnesemia grading according to CTCAE (Common Terminology Criteria for Adverse Events) version 5, N (%)

161 patients analysed, 135 (83.85%) experienced at least one episode of hypomagnesemia during the treatment course, with magnesium levels monitored throughout. The median frequency of hypomagnesemia was three episodes. Additionally, 119 patients (73.91%) experienced early onset of hypomagnesemia, occurring before the third cycle of cisplatin.

The median cumulative cisplatin dose was 230 mg, with a range from 180 to 320 mg. A significant positive correlation was observed between the cumulative cisplatin dose (median) and the severity of hypomagnesemia (r-value=0.22, p-value=0.03). The reduction in magnesium levels from baseline to post-treatment was also statistically significant (r-value=0.32, p-value <0.01), as determined by Pearson's correlation test. During treatment, hypomagnesemia showed a significant correlation with hypokalemia (r-value=0.35, p-value=0.02) and hyponatremia (r-value=0.24, p-value=0.03). However, hypomagnesemia showed no correlation with baseline heart rate (r-value=-0.06, p-value=0.6) and baseline systolic blood pressure (r-value=-0.05, p-value=0.6). [Table/Fig-6].

Correlation	Strength (r)	Significance (p)
Cumulative dose of cisplatin and severity of hypomagnesemia	0.22	0.03*
Magnesium levels (before and after treatment)	0.32	<0.01*
Hypomagnesemia and hypokalemia	0.35	0.02*
Hypomagnesemia and hyponatremia	0.24	0.03*
Hypomagnesemia and baseline heart rate	-0.06	0.6
Hypomagnesemia and baseline systolic blood pressure	-0.05	0.6

[Table/Fig-6]: Pearson's correlation between various parameters.
*Significant

DISCUSSION

The present study evaluated the prevalence and progression of hypomagnesemia in cervical cancer patients undergoing cisplatin-based chemoradiation. A significant portion of patients, 83 (51.55%), had hypomagnesemia at baseline and this prevalence increased to 135 (83.8%) during treatment, with the severity of magnesium depletion worsening over successive cycles. Furthermore, 119 (74%) patients experienced early onset hypomagnesemia before the third chemotherapy cycle. These findings underscore the substantial risk of magnesium depletion in this patient population and its potential implications for treatment outcomes. The results of the present study align with previous studies that reported high rates of hypomagnesemia in patients receiving cisplatin-based chemotherapy for various cancers. For instance, Buckley JE et al., found that 41% of patients developed hypomagnesemia after just one course of cisplatin, with 100% affected after six cycles [24]. Similarly, Hodgkinson E et al., observed a 43% incidence of hypomagnesemia at any point during cisplatin therapy [25] and Schilsky RL and Anderson T, reported that hypomagnesemia occurred in 52.3% of patients, emphasising that most individuals receiving cisplatin would experience some degree of magnesium depletion [26]. These studies collectively highlight the susceptibility of patients undergoing cisplatin treatment to hypomagnesemia, consistent with the trends observed in the current study.

However, the findings of the present study contribute novel insights specific to cervical cancer patients. While previous research has documented hypomagnesemia in patients receiving platinum-based chemotherapies, specific data on magnesium levels in cervical cancer patients remain limited [24-26]. Notably, a recent case report by Komoda J et al., detailed a 76-year-old woman who developed hypomagnesemia following nedaplatin chemotherapy for cervical cancer [27]. This underscores the need for further investigation into magnesium homeostasis in this patient population. Unlike previous studies, this study provided a detailed breakdown of hypomagnesemia progression across grades (I-IV) and identified early onset hypomagnesemia as a prominent feature in this cohort [24-27]. Moreover, this study uniquely demonstrated significant correlations between cumulative cisplatin doses and the severity of hypomagnesemia (r-value=0.22, p-value=0.03). Hypomagnesemia during treatment was also significantly associated with other electrolyte imbalances, such as hypokalemia (r-value=0.35, p-value=0.02) and hyponatremia (r-value=0.24, p-value=0.03), emphasising its systemic impact.

Progressive cancers frequently present with anorexia (loss of appetite) and cachexia (wasting syndrome), potentially contributing to early declines in magnesium levels, a critical micronutrient [28]. Reduced dietary intake associated with appetite loss may be a key factor. Furthermore, Gastrointestinal (GI) fluid losses can be significant due to the adverse effects of cancer itself, such as nausea, vomiting and diarrhoea [12]. Cancer treatment can also contribute to these losses, with inflammatory diarrhoea being a common side-effect. Additionally, pelvic or abdominal radiation therapy can lead to both acute and chronic enteritis, further exacerbating diarrhoea [12]. Notably, research suggests a significant association between the use of Proton-Pump Inhibitors (PPIs) in cancer patients and a 43% increased Relative Risk (RR) of developing hypomagnesemia [13].

In the present study, no significant correlation was found between baseline hypomagnesemia and baseline heart rate or systolic blood pressure. A high baseline heart rate is significantly associated with shorter survival, as resting heart rate is a strong predictor of cardiovascular morbidity and mortality [19]. Hyponatremia and hypokalaemia are strongly associated with hypomagnesemia in the present study, which was in accordance with a study by Liu et al., conducted on head and neck cancer and ovarian cancer [19,29]. Maintaining adequate magnesium homeostasis is paramount during oncological therapy, encompassing both chemotherapy and radiotherapy, to effectively manage a constellation of treatment-related symptoms. These symptoms, including muscle cramps, fatigue, nausea and vomiting, neuromuscular changes, mental status changes and cardiac arrhythmias, can significantly impact the quality of life and can interfere with adherence to therapy in cervical cancer patients [30].

In the present study, hypomagnesemia was strongly correlated with the cumulative dose of cisplatin chemotherapy, which was in line with previous studies [19,29]. Notably, a recent critical evaluation of magnesium supplements suggests that magnesium citrate exhibits superior bioavailability compared to other formulations, potentially making it a preferred choice for supplementation [31]. To further bolster magnesium stores and enhance overall nutritional wellbeing during therapy, cervical cancer patients should be frequently encouraged to adopt a dietary pattern rich in magnesium-replete sources. Leafy green vegetables, nuts, seeds and whole grains are prime examples of such dietary inclusions. This nutritional strategy serves as a complementary approach to supplementation, aiming to synergistically support magnesium homeostasis and optimise overall nutritional status throughout the treatment [32].

Oncological interventions for cervical cancer, particularly those incorporating cisplatin-based chemotherapy, present a substantial risk of hypomagnesemia. Cisplatin demonstrates the highest risk of hypomagnesemia, affecting roughly 90% of patients [28]. Notably, carboplatin, a structurally similar chemotherapeutic agent, has a lower propensity for both nephrotoxicity and hypomagnesemia (10% of patients), potentially offering a valuable alternative in select clinical scenarios [33,34]. Emerging evidence suggests that the frequency and severity of hypomagnesemia during treatment with cisplatin-based regimens can serve as a prognostic marker for survival in patients with head and neck cancers and ovarian cancers [19,29]. Given this potential impact on treatment outcomes, early detection and management of hypomagnesemia become crucial. To optimise patient outcomes during therapy, meticulous monitoring and management of electrolyte balance, with particular emphasis on magnesium homeostasis, are essential. This comprehensive approach to supportive care aligns with the overarching goal of maximising patient wellbeing while minimising the iatrogenic burden associated with oncological therapy.

Limitation(s)

It was a single-centre study, so the findings may not apply to a broader population. There was no long-term follow-up to assess whether hypomagnesemia persisted or resolved after treatment. Additionally, magnesium supplements were not provided to patients during the study, which could have influenced the results and prevented an evaluation of how supplementation might help manage or prevent hypomagnesemia.

CONCLUSION(S)

The study reveals a high prevalence of hypomagnesemia in cervical cancer patients, especially those receiving cisplatin-based chemotherapy. Magnesium levels were significantly lower in patients compared to healthy controls and declined further during treatment, correlating with cumulative cisplatin doses and associated electrolyte imbalances. These findings underscore the necessity of routine magnesium monitoring in cervical cancer patients undergoing treatment. Incorporating proactive magnesium management into standard supportive care can help prevent complications and enhance treatment outcomes and quality of life for these patients. Future studies with multi-centre designs and long-term follow-up should be conducted to explore the impact of magnesium management on clinical outcomes, including treatment toxicity, patient quality of life and overall survival in cervical cancer patients.

REFERENCES

[1] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-63.
[2] Wang Z, Wang W, Yang A, Zhao W, Yang J, Wang Z, et al. Lower dietary mineral intake is significantly associated with cervical cancer risk in a population-based cross-sectional study. J Cancer. 2021;12:111-23.
[3] de Baaij JH, Hoenderop JG, Bindels RJ. Magnesium in man: Implications for health and disease. Physiol Rev. 2015;95(1):01-46.
[4] Yavuz O, Ekmekci H, Basar M, Buyukberber S, Camci C, Evliyaoglu O, et al. Serum magnesium levels in patients with cervical intraepithelial neoplasia and invasive cervical cancer. Gynecol Oncol. 2005;99(3):922-55.
[5] Cheng GC, Pang Z, Liu QF. Magnesium intake and risk of colorectal cancer: A meta-analysis of prospective studies. Eur J Clin Nutr. 2012;66:1182-86.
[6] Wark PA, Lau R, Norat T, Kampman E. Magnesium intake and colorectal tumor risk: A case-control study and meta-analysis. Am J Clin Nutr. 2012;96:622-31.
[7] Dai Q, Shrubsole MJ, Ness RM, Schlundt D, Cai Q, Smalley WE, et al. The relation of magnesium and calcium intakes and a genetic polymorphism in the magnesium transporter to colorectal neoplasia risk. Am J Clin Nutr. 2007;86:743-81.
[8] Huang WQ, Long WQ, Mo XF, Zhang NQ, Luo H, Lin FY, et al. Direct and indirect associations between dietary magnesium intake and breast cancer risk. Sci Rep. 2019;9(1):5764.
[9] Bird L. Magnesium: Essential for T cells. Nat Rev Immunol. 2022;22:144-45.
[10] Ashique S, Kumar S, Hussain A, Mishra N, Garg A, Gowda BHJ, et al. A narrative review on the role of magnesium in immune regulation, inflammation, infectious diseases, and cancer. J Health Popul Nutr. 2023;42:01-14.
[11] Lotscher J, Lindez AAM, Kirchhammer N, Kin C, Zippelius A, Hess C, et al. Magnesium sensing via LFA-1 regulates CD8+ T cell effector function. Cell. 2022;185(4):585-602.E29.
[12] Workeneh BT, Uppal NN, Jhaveri KD, Rondon-Berrios H. Hypomagnesemia in the cancer patient. Kidney360. 2020;11:154-66.
[13] Swaminathan R. Magnesium metabolism and its disorders. Clin Biochem Rev. 2003;24:47-66.

[14] Miller RP, Tadagavadi RK, Ramesh G, Reeves WB. Mechanisms of cisplatin nephrotoxicity. Toxins (Basel). 2010;2:2490-518.
[15] Sankaranarayanan R, Nene BM, Dinshaw KA, Mahe C, Jayant K, Shastri SS, et al. A cluster randomized controlled trial of visual, cytology and human papillomavirus screening for cancer of the cervix in rural India. Int J Cancer. 2005;116:617-23.
[16] Bhatla N, Aoki D, Sharma DN, Sankaranarayanan R. Cancer of the cervix uteri: 2021 update. Int J Gynecol Obstet. 2021;155:28-44.
[17] Katke A, Nanda R, Thejaswini B, Pasha T, Giri GV, Babu G, et al. Weekly vs. tri- weekly cisplatin based chemoradiation in carcinoma cervix: A prospective randomized study of toxicity and compliance. Rep Pract Oncol Radiother. 2021;26(6):948-94.
[18] Tietz NW, editor. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 5th ed. Elsevier; 2012.
[19] Liu W, Qdaisat A, Soliman PT, Ramondetta L, Lopez G, Narayanan S, et al. Hypomagnesemia and survival in patients with ovarian cancer who received chemotherapy with carboplatin. Oncologist. 2019;24:e312-e317.
[20] Odusan OO, Familoni OB, Odewabi AO, Idowu AO, Adekolade AS. Patterns and correlates of serum magnesium levels in subsets of type 2 diabetes mellitus patients in Nigeria. Indian J Endocrinol Metab. 2017;21(3):439-42.
[21] Hsieh MC, Wu CF, Chen CW, Shi CS, Huang WS, Kan C. Hypomagnesemia and clinical benefits of anti-EGFR monoclonal antibodies in wild-type KRAS metastatic colorectal cancer: A systematic review and meta-analysis. Sci Rep. 2018;8:2047.
[22] National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) v5.0 Quick Reference [Internet]. Bethesda (MD): National Institutes of Health; 2017 [cited 2024 Nov 21]. Available from: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf.
[23] Bhatla N, Berek JS, Cuello Fredes M, Denny L, Grenman S, Karunaratne K, et al. Revised FIGO staging for carcinoma of the cervix uteri. Int J Gynaecol Obstet. 2019;145(1):129-35.
[24] Buckley JE, Clark VL, Meyer TJ, Pearlman NW. Hypomagnesaemia after cisplatin combination chemotherapy. Arch Intern Med. 1984;144(12):2347-48.
[25] Hodgkinson E, Neville-Webbe HL, Coleman RE. Magnesium depletion in patients receiving cisplatin-based chemotherapy. Clin Oncol (R Coll Radiol). 2006;18:710-18.
[26] Schilsky RL, Anderson T. Hypomagnesaemia and renal magnesium wasting in patients receiving cisplatin. Ann Intern Med. 1979;90:929-31.
[27] Komoda J, Hori T, Sato K, Kusajima K, Shimizu T. Hypomagnesemia because of nedaplatin for cervical cancer: A case report. J Gen Fam Med. 2023;24(4):257-60.
[28] Lajer H, Daugaard G. Cisplatin and hypomagnesemia. Cancer Treat Rev. 1999;25:47-58.
[29] Liu W, Qdaisat A, Ferrarotto R, Fuller CD, Guo M, Meyer LA, et al. Hypomagnesemia and survival in patients with head and neck cancers who received primary concurrent chemoradiation. Cancer. 2021;128:528-34.
[30] Saif MW. Management of hypomagnesemia in cancer patients receiving chemotherapy. J Support Oncol. 2008;6:243-48.
[31] Rylander R. Bioavailability of magnesium salts – A review. J Pharm Nutr Sci. 2014;4:57-59.
[32] Rude RK. Magnesium. In: Ross AC, Caballero B, Cousins RJ, Tucker KL, Ziegler TR, editors. Modern Nutrition in Health and Disease. 11th ed. Baltimore: Lippincott Williams & Wilkins; 2012.
[33] Adams M, Kerby IJ, Rocker I, Evans A, Johansen K, Franks CR. A comparison of the toxicity and efficacy of cisplatin and carboplatin in advanced ovarian cancer. The Swons Gynecological Cancer Group. Acta Oncol. 1989;28:57-60.
[34] Foster BJ, Clagett-Carr K, Leyland-Jones B, Hoth D. Results of NCI-sponsored phase I trials with carboplatin. Cancer Treat Rev. 1985;12:43-49.

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