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ORIGINAL ARTICLE

Carcinogenic risk associated with dietary and non-dietary exposure to pesticide residues around Hirakud Command Area, Odisha, India

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Abstract

Objective The present study investigated the level of pesticide residues in soil, water, and rice grain samples in various agricultural zones under Hirakud command area and evaluated associated human health risks.

Methods Pesticide residues in various matrices were quantified using LCMSMS. Human health risks associated with exposure to pesticide residues through dietary as well as non-dietary routes were estimated using the USEPA method. Cancer burden was assessed using hospital-based survey and correlated to pesticide exposure as well as health risk.

Results Out of 13 pesticides detected in soil, water and rice grain, 8 were compounds with higher carcinogenic potential. Carcinogenic pesticides such as Aldrin, Dieldrin, Heptachlor epoxide, αHCH and βHCH ranged from 0.313–1.084 (µg/g), 0.112–0.877 (µg/g), 0.035–0.135(µg/g), 0.020–0.838(µg/g) and 0.113–0.957(µg/g) in soil, αHCH, DDT, Chlorpyrifos 0.118–0.773 (µg/L),0.05–1.39(µg/L) and 0.309–1.172 (µg/L) in water and αHCH, βHCH, Chlorpyrifos 0.008–0.557 (µg/g), 0.045–0.212(µg/g) and 0.058–0.106 (µg/g) in rice grain across different agricultural zones. Carcinogenic risk of pesticide residues through dietary sources was found to be high compared to non-dietary sources. Dietary exposure to Heptachlor epoxide, dieldrin, aldrin and αHCH through rice grain and water posed high carcinogenic risk respectively while non-dietary exposure to Aldrin, and Dieldrin through soil ingestion and dermal root showed moderate to low carcinogenic risk.

Conclusions Enhanced Incidence of cancer in intense agricultural areas reporting higher concentrations of carcinogenic pesticides in water and rice grains indicated a closer association of pesticide exposure with cancer incidence.

Keywords Pesticides · Bargarh · Agricultural intensity · Carcinogenic risk · Cancer incidence

Introduction

To protect and safeguard crop loss due to pest infestation, chemical pesticides have been used in various concentrations in modern agriculture across the globe. Due to the emergence of pesticide resistance among pest species, new classes of more potent pesticides are being added to the market every year. Global pesticide production has grown by 11% annually, rising from 0.2 million tons in the 1950s to over 5 million tons by the year 2000 [1]. The global agricultural use of pesticides is expected to increase from approximately 4.3 million metric tons in 2023 to about 4.41 million metric tons by 2027. India ranks as the world's fourth largest producer of agrochemicals, following the United States, Japan, and China, and has become the 13th largest exporter of pesticides globally. State-wise pesticide used in India during 2022–2023 was reported to be 1348 Million Tons for a total cultivated area of 108,216 Hector [2]. Previous reports

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indicate that pesticide residues can accumulate over time on crops, soil, and other surfaces, some might be captivated into the soil or leached into groundwater [3]. Due to their higher persistence and bio-accumulative nature, these pesticide residues built over time in different environmental compartments eventually reach to the human being in elevated concentration through trophic transfer [4]. The toxicity of these pesticides to the non-target species including human being is a matter of serious distress and are widely reported to be associated with numerous detrimental diseases in the community [5, 6]. As several pesticide residues widely used in agriculture and disease control programmes in developing nations are potent carcinogenic agents, there is utmost necessity to assess the risk associated with their exposure through dietary as well as non-dietary sources.

A diversity of health issues, including cancer, reproductive diseases, neurotoxicity, and developmental disorders have been associated with pesticide exposure through food or water polluted with pesticide residues [7]. Health risk assessments for fourteen organochlorines in Nigeria have indicated potential dangers for humans exposed to contaminated water, sediment, and fish through ingestion, inhalation, and skin contact [8]. The study of pesticides residues in the Thamirabarani River in Tamil Nadu, India found that exposure to pesticides through ingestion and dermal exchange could lead to greater cancer risks than inhalation [9]. Several studies indicate association of prostate cancer with organochlorines, triazines, and organophosphates [10] while chronic exposure to DDT, DDD ethylene, and pendimethalin is implicated in the development of pancreatic cancer [11]. Recent report indicates closer correlation between the onset and progression of breast cancer with organochlorine pesticides like Aldrin, dieldrin, hexachlorocyclohexane, and endosulfan [12]. Exposure to organochlorine pesticides (OCPs) like endosulfan, DDT, heptachlor, and aldrin have been reported to be associated with cervical cancer as indicated in a pilot study of Delhi [13]. Farmers are exposed to pesticide-contaminated soils through various pathways, including dermal contact, direct ingestion, and inhalation [14]. The increased likelihood of humans developing cancer and non-cancer diseases due to pesticide exposure can be assessed using USEPA standard risk models. Health risk assessments commonly utilize indices such as the hazard quotient (HQ) and the hazard index (HI) [15–17]. However, there is a lack of comprehensive monitoring of pesticide residues in soils and assessment of their potential health risks in India.

With the commissioning of Hirakud Dam the world's longest earthen dam—the Hirakud Command Area in Odisha transformed into the state's rice bowl due to assured irrigation and fertile land. However, over the past 65 years, Bargarh district, once an agricultural stronghold, has become one of India's most cancer-prevalent regions. Of its 471,000 hectares of cultivated land, 149,400 hectares are irrigated by canal water from the Hirakud reservoir. The dominant crops paddy and vegetables require intensive use of pesticides, with usage rising sharply from 440.7 tonnes in 2016 to 713.9 tonnes in 2017. The major crop grown in this area includes paddy and vegetable which require increased consumption of hazardous insecticides and fungicides to protect the crop from pest infestation [18, 19]. Pesticide use in this district jumped from 440.702 tonnes in 2016 to 713.867 tonnes in 2017 [20]. People residing in Hirakud Command area have been exposed to pesticide residues via various pathways such as non-dietary ingestion, dermal route and soil particle inhalation as most of them depend on farming for their livelihood. Several studies across the globe report increased human health risk due to pesticide application in agrarian activities [21–24]. Preliminary survey in the Hirakud Command area showed that many of the hazardous pesticides banned in Europe and other developed nations are still in use. Personal protective equipment and safety practices are not followed by the farmers in this region due to their poor socio-economic status making them more susceptible to pesticide toxicity. Recent study from our laboratory reports the higher prevalence of non-cancer diseases such as chronic kidney disease in intense agricultural zones of Bargarh district and their association with exposure to pesticides residues [25]. However, the carcinogenic risks from pesticide residues through dietary and non-dietary exposure in this region remain unexplored. This study aims to assess pesticide residues in soil, water, and rice grains, evaluate their carcinogenic risk through exposure modelling, and correlate these findings with regional cancer incidence using retrospective hospital data.

Materials and methods

Study area

Bargarh district in Odisha, India, falls within the agro-climatic zone VII, known as the Eastern Plateau and Hills Region. Agriculture is the predominant land use, covering 70.4% of the district's geographical area, followed by forests at 12.48% and pastures at 3.4%. The average cropping intensity is 133%, with the net sown area making up to 86.10% of the total agricultural land (CGWB). Out of the 12 blocks, Attabira (31,288 ha), Bheden (31,640 ha), Bargarh (24,975 ha), and Bhatli (21,793 ha) which support multiple cropping cycles with net irrigation exceeding 60% are designated as high intense agricultural blocks. Ambabhona (1,979 ha), Barpali (16,676 ha), Sohela (15,848 ha), and Bijepur (8,575 ha), are primarily single-cropped with 35–60% net irrigation categorised as moderately intense agricultural blocks. In contrast, Padampur (18,926 ha), Gaisilat (13,103 ha), Paikmal (21,546 ha), and Jharbandh (12,553 ha) also follow single-cropping practices but have less than 35% net irrigation coverage are classified as low intensity agricultural blocks [26].

Procedure followed in sampling of water, soil and rice grain from crop field

Top soil sample (n = 144) from 10 to 15 cm depth were collected from high, moderate and low agricultural blocks of Bargarh district as shown in Fig. 1. The soil samples were air-dried, grounded into a fine powder, and sieved through a 2 mm mesh. Triplicate samples of 20 gm each were placed in 100 mL polypropylene centrifuge tubes. Soil samples collected from the experimental fields without the application of pesticides were used as a control for comparison [27, 28]. Water samples (n = 144) were collected from different sources in the study area with pre-cleaned glass bottle. Harvested rice seeds were collected from the same agricultural fields for analysis of pesticide residues (Fig. 2).

Determination of pesticide residues in water, soil & rice grain

Chemicals

Analytical standards for all pesticides were obtained from Sigma Aldrich (USA). Acetonitrile, Methanol, and Formic Acid of LC grade were procured from Merck Life Science (Germany). Reagents such as Sodium Acetate (anhydrous; 99% purity), Magnesium Sulphate (99.8% purity; anhydrous), and PSA 40 mm were provided by J.T. Baker (Japan). Purified water obtained from Milli-Q filtration system (Millipore, Bedford, MA, USA) was used for analysis of sample.

Solutions

Stock solutions for all pesticides and sulfamethoxazole (used as the surrogate standard) were individually prepared at concentrations of 1000 mg L^{-1} in acetonitrile and stored at 4 °C. A mixture of these pesticides, with varying concentrations according to the MRL of each, was then prepared in water. This mixture was used to prepare working standard solutions

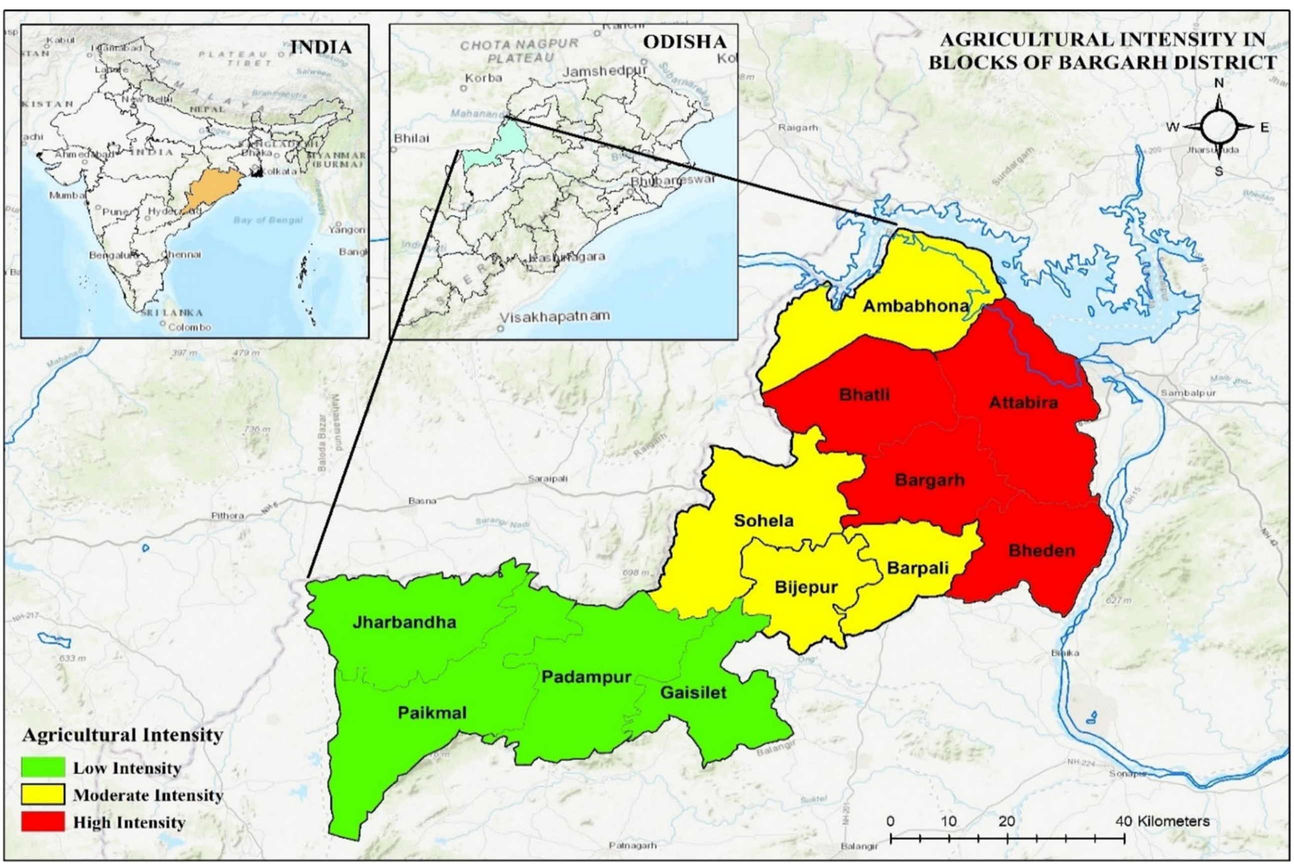

Fig. 1 Sampling villages of four blocks of Bargarh District

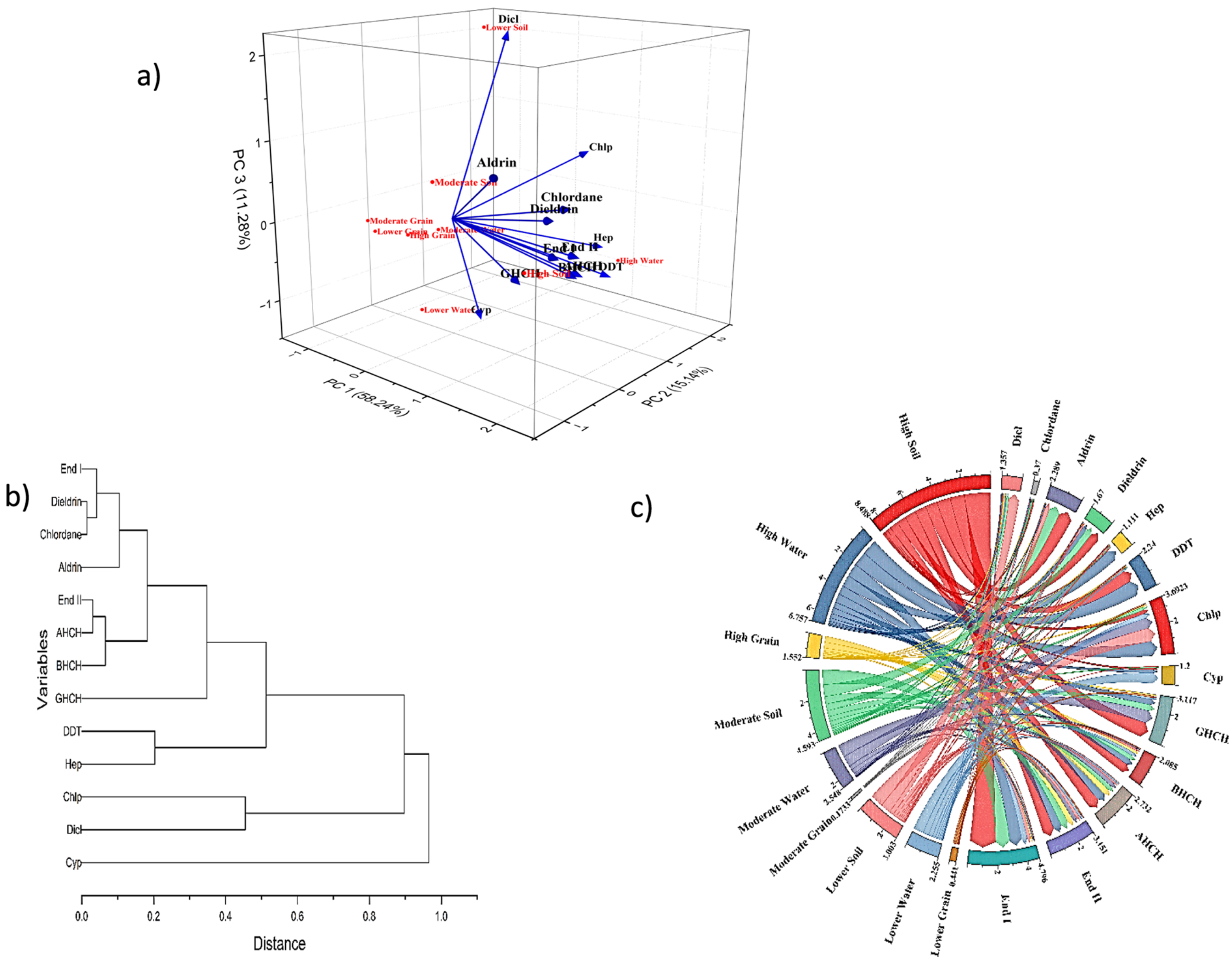

Fig. 2. 3D PCA plot showing pesticide distribution across different matrices of agricultural intensities. Dendrogram illustrating hierarchical clustering of pesticide residues by similarity and Chord diagram illustrating interconnections between pesticide residues and environmental factors across agricultural zones

in acetonitrile, which included the analytical standards and were also used for spiking the blank matrix extract.

Blank control

To develop the current method, rice grain samples obtained from EPAGRI were used as the blank control. The cultivation and harvesting processes were closely monitored by professional workers to ensure the matrices were free of pesticides. The rice grains were harvested, peeled, and ground into particles ranging from 0.2 to 1.0 mm, which were then used for all studies.

Analytical methods

Modified QuEChERS method was used to determine the chlorpyrifos and TCP residues in rice samples [29, 30]. The analysis was performed using an Agilent HPLC series 1200 system, equipped with a quaternary pump, a membrane degasser, and an auto-sampler (Agilent Technologies, Palo Alto, CA). Pesticide separation was achieved on a Synergi Polar RP column (150 mm × 2.0 mm i.d., 4 µm particle size, Phenomenex). The mobile phase consisted of acetonitrile–water (95/5, v/v) as solvent A and 0.1% formic acid as solvent B, operated in gradient mode. The column was maintained at 40 °C, with a mobile phase flow rate of 400 µL min^{-1} and an injection volume of 10 µL. The LC was coupled to a mass spectrometry system comprising a hybrid triple quadrupole/linear ion trap mass spectrometer QTrap 3200 (Applied Biosystems/MDS Sciex, Concord, Canada). Analyst software version 1.5.1 controlled the LC–MS/MS system and performed data analysis. Experiments utilized a Turbo Ion Spray source (electrospray-ESI) in positive ion mode, with the capillary needle set at + 5500 V. MS/MS parameters included: curtain gas (N_2) at 10 psi, temperature at 600 °C, gas 1 (Ar) at 18 psi, gas 2 off, and CAD gas (N_2) set to high. Analytes were monitored and quantified using multiple reaction monitoring (MRM), with the MS optimized through direct infusion of solutions containing each analyte examined in this study.

QuEChERS analytical method for estimation of pesticide residues in water and soil

A 10 mL water sample was placed in a 15 mL centrifuge tube, and 2.5 mL of acetonitrile (1% acetic acid) was added. After capping, the tubes were frozen at –18 °C for 15 min, followed by the addition of 4 g of $MgSO_4$ and 1 g of NaCl. The tubes were vigorously hand-shaken for 1 min and then centrifuged at 4400 rpm for 5 min under cooling (5 °C). One millilitre of the upper layer was transferred into a 2 mL vial containing 500 mg of $MgSO_4$. After shaking and subsequent centrifugation at 4400 rpm for 2 min at 4 °C, the supernatant was transferred into a PTFE-capped vial for GC–MS analysis.

Twenty grams of soil samples were placed into 100 mL polypropylene centrifuge tubes. To this, 30 mL of Mass grade acetonitrile: water (2:1, v/v) was added and vortexed for 2 min. The tubes were then centrifuged at 10,000 rpm for 10 min. The acetonitrile layer was carefully transferred into a measuring cylinder containing 10 mL of saturated sodium chloride solution and mixed thoroughly. Six milliliters of the upper acetonitrile layer were extracted and subjected to dispersive solid-phase extraction (d-SPE) using 900 mg of $MgSO_4$ and 300 mg of PSA. One milliliter of the sample was then filtered through a 0.2 µm PTFE membrane filter prior to LC–MS/MS analysis.

Modified QuEChERS method to determine pesticide residues in rice grains

For the extraction, 14 mL of acetonitrile with 1.0% acetic acid and 1.0 mL of a solution containing sulfamethoxazole (142 mg L^{-1}, as the surrogate standard) were added to a 50 mL PTFE tube containing 5 g of previously ground sample. After a 30-min incubation period, 2.0 g of anhydrous magnesium sulfate and 0.5 g of sodium acetate were introduced into the mixture, followed by vortex stirring for 1.0 min and centrifugation at 4000 rpm for 1.0 min. For the cleanup step, 1.5 mL of the liquid phase was extracted and transferred into a 15 mL Falcon tube. Then, 150 mg of anhydrous magnesium sulfate and 50 mg of PSA (primary and secondary amines) were added. The Falcon tubes were vortexed for 1.0 min and centrifuged for 1.0 min at 4000 rpm. Finally, 1.0 mL was collected from the supernatant and placed directly into vials for automatic injection into the chromatographic system. All procedures were carried out in triplicate.

Human health risk estimations

To evaluate the health risks associated with exposure to pesticide residues from rice grain consumption, drinking contaminated water (dietary intake), and contact with contaminated sediment samples (non-dietary intake), guidelines provided by the US Environmental Protection Agency (USEPA) were employed. The USEPA has established an acceptable risk range for known or suspected carcinogens, spanning from 1×10^{-6} to 1×10^{-4}. Risks below 1×10^{-6}, equivalent to one additional cancer case in 1,000,000 individuals, are typically considered negligible. Conversely, risk levels exceeding 1×10^{-4}, representing one additional cancer case in 10,000 individuals, are generally deemed unacceptable [31].

Human health risk assessment of pesticide residues in rice grain (dietary)

Carcinogenic risk was estimated by multiplying Estimated Daily Intake (EDI) and multiplying with slope factor (SF). THQ was calculated following methods used by previous researchers [32, 33]and used to determine health risk in target populations: adults and children, according to the following and Eqs. 1 and 2:

$$EDIing = \frac{CF \times IR \times EF \times ED}{BW \times AT} \tag{1}$$

$$CRing = EDIing \times SF \tag{2}$$

where CF is residual pesticide concentration (mg/kg^{-1}), IR is consumption rate of food (kg/day), EF stands for exposure frequency (days/year), ED is exposure duration (years). In addition, BW refers to average body weight and AT is average exposure time for carcinogens effect (EF × ED) [34].

Human health risk assessment of pesticides in water samples

To evaluate the risk of exposed pesticides to humans (adults) through ingestion of contaminated water, the hazard quotient (HQ) model was employed [35].

$$HQ = \frac{ECDI}{RfD} \tag{3}$$

$$EDI(ingestion) = \frac{Cw \times IR(water) \times EF \times ED}{BW \times AT} \tag{4}$$

$$CRing = EDIing \times SF \quad (5)$$

where the concentration of water samples is Cw, the ingestion rate of water is IR (water), EF and ED are the exposure frequency, and the exposure duration respectively, BW is the body weight, and AT is the average life Span. The values for each of these constraints are provided in Table S1.

Human health risk assessment of pesticides in soil samples (non-dietary)

Non-Dietary exposure refers to pesticide residues exposure through other routes apart from dietary. Non-dietary consumption can be assessed using the chronic daily intake (CDI). Three routes of exposures were considered which comprise dermal contact, ingestion, and inhalation route. Chronic daily intake is a model, designed by US Environmental Protection Agency (USEPA, 1992, 1997) to estimate the non-carcinogenic risks for adults from non-dietary exposure to contaminants [36]. The CDI was enumerated using the following formulae adapted from Huang et al. [37] (Eqs. 6–11).

$$CDI\text{ing} = C\text{soil} \times \frac{IR \times CF \times EF \times ED}{BW \times AT} \quad (6)$$

$$CRing = CDI\text{ing} \times \text{SF} \quad (7)$$

$$CDI\text{inh} = C\text{soil} \times \frac{IAR \times EF \times ED}{PEF \times BW \times AT} \quad (8)$$

$$CRinh = CDI\text{inh} \times \text{SF} \quad (9)$$

$$CDI\text{derm} = C\text{soil} \times \frac{IAR \times EF \times ED}{PEF \times BW \times AT} \quad (10)$$

$$CRderm = CDI\text{derm} \times \text{SF} \quad (11)$$

where CS represents the concentration of the contaminant in sediment samples, IR (sediment) denotes the ingestion rate of sediment, CF stands for the carcinogenic slope factor, EF signifies the exposure frequency, ED indicates the exposure duration, BW represents body weight, FE denotes the dermal exposure ratio, AF signifies the dermal surface factor, ABS represents the dermal absorption factor, AT denotes the average lifespan, SA stands for surface area, and PEF represents the particle emission factor. Detailed values for each parameter are listed in Table S1.

Study population and assessment of cancer incidence rate

The present study includes all diagnosed cancer cases from 2020 to 2022 and is based on a hospital-based retrospective cohort design. Data were collected from the District Headquarters Hospital, Bargarh; Veer Surendra Sai Institute of Medical Science and Research (VIMSAR), Burla; and Acharya Harihara Cancer Hospital, Bhubaneswar, Odisha. All newly diagnosed cancer cases from Bargarh district in each respective year were included in the study, while follow-up cases were excluded. Patient information, including age, sex, cancer type, history of tobacco and alcohol use, and occupation, was obtained from hospital records or through direct communication with the patients or their family members. Individuals engaged in farming or farming-related activities were classified as farmers, while those involved in other occupations such as government service, construction labor, and similar non-agricultural work were categorized as non-farmers. The population data of Bargarh district was taken from 2011 census of India. Cancer incidence was estimated using the formula suggested by National Cancer Institute (NCI), Surveillance, Epidemiology and End Result Program SEERP [38] as follows:

$$\text{Incidence rate} = (\text{New cancers} / \text{Population}) \times 100,000$$

Statistical analysis

All the data of pesticide residues presented in table were expressed as Mean ± Standard Deviation. PCA, Chord diagram and cluster analysis was performed using Origin software 2023. IBM SPSS was used to perform MANOVA and post-hoc test.

Results

High intensity agricultural zones reported elevated concentration of carcinogenic pesticide residues in soil, water and rice grain

Carcinogenic pesticide residues classified as Class B2 and Class C were detected in soil, water, and rice grains across high-, moderate-, and low-intensity agricultural zones of Bargarh District. In high-intensity zones, α-HCH was most prevalent in both soil (0.695–0.955 µg/g) and rice grains (0.257–0.557 µg/g), while DDT dominated water samples (0.79–1.39 µg/l). Chlordane consistently showed the lowest levels across all matrices. In moderate-intensity areas, Aldrin was the dominant soil contaminant (0.722–0.902 µg/g), DDT remained highest in water (0.87–1.27 µg/l), and α-HCH led in rice grains (0.303–0.505 µg/g). In low-intensity zones, Dichlorvos was most abundant in soil (0.629–0.771 µg/g), α-HCH in water (0.118–0.122 µg/l), and Heptachlor epoxide in rice grains (0.010–0.024 µg/g). Chlordane and Aldrin were typically found in the lowest concentrations (Table 1).

These findings underscore the widespread contamination of agricultural products and environmental matrices with carcinogenic pesticide residues.

Endosulfan, lindane, DDT, aldrin and dieldrin are the principal pesticide residues in environmental sample across the matrix and intensity of agricultural activity

The Principal Component Analysis (PCA) of pesticide residues in Bargarh District revealed significant contamination patterns related to agricultural practices. The first three principal components (PCs) collectively accounted for 84.66% of the total variance. PC 1 had the highest eigenvalue (7.57), explaining 58.24% of the variance, predominantly influenced by residues like End I, End II, α-HCH, β-HCH, γ-HCH, DDT, Dieldrin, and Aldrin. PC 2 explained 15.14% of the variance with major contributions from Chlp and Hep, while PC 3 accounted for 11.28% of the variance, primarily driven by Dichlorvos. Aldrin was notably associated with soil samples from lower and moderate agricultural intensity areas along PC1. Chlordane and Dieldrin exhibited distinct distribution patterns in water samples, aligning more with PC2 and PC3, respectively. High and low agricultural intensity areas showed higher prevalence of Hep, Endosulfan, and DDT in water samples. Additionally, Aldrin and Dieldrin clustered together along PC1 for rice grain samples from moderate and lower agricultural intensity regions, highlighting potential risks linked to varying agricultural practices (Fig. 2).

Pesticide residues are distributed unequally across matrices and intensities of agricultural activity

The circular chord diagram illustrates the relationships and interactions between various environmental matrices (soil, water, and rice grains) and pesticide residues. Pesticides such as Dieldrin, Chlordane, and Aldrin exhibited strong associations with soil in areas with high and moderate agricultural activity indicated by thicker arcs, reflecting their prevalence, low water solubility, and strong adsorption to soil particles. Compounds like DDT, Chlp, and Hep showed varied connections to both soil and water, with DDT displaying multiple links, suggesting a broader distribution across different matrices. Pesticides such as γ-HCH, Cyp, and DDT were associated with water compartments, indicating their mobility in aqueous environments. Additionally, Cyp, γ-HCH, β-HCH, and α-HCH were linked to water from areas with high and moderate agricultural intensity, highlighting their potential for water contamination due to easier transport through water. Endosulfan I and Endosulfan II was

Table 1 Concentration of pesticides residues in soil (µg/g), water sample (µg/L) and rice grain (µg/g) sample collected from different villages of Bargarh District

Agricultural Intensity	Sample	End I	End II	α-HCH	β-HCH	γ-HCH	Cyp	Chlp	DDT	Hep	Dieldrin	Aldrin	Chlordane	Dicl
High	Soil	1.92 ± 0.21	0.829 ± 0.20	0.**825** ± 0.13	0.627 ± 0.33	1.032 ± 0.23	0.129 ± 0.035	0.288 ± 0.11	0.868 ± 0.21	**0.085** ± 0.05	0.667 ± 0.21	1.014 ± 0.07	0.117 ± 0.1	0.087 ± 0.027
	Water	0.916 ± 0.12	0.611 ± 0.25	0.613 ± 0.16	0.411 ± 0.13	0.415 ± 0.11	0.227 ± 0.10	1.022 ± 0.15	1.09 ± 0.3	0.819 ± 0.11	0.316 ± 0.10	0.094 ± 0.01	0.077 ± 0.01	**0.146** ± 0.017
	Grain	0.111 ± 0.028	0.409 ± 0.13	0.407 ± 0.15	0.209 ± 0.003	0.108 ± 0.002	ND	0.105 ± 0.001	0.036 ± .012	0.021 ± 0.01	0.027 ± .014	0.017 ± 0.00	0.012 ± 0.01	**0.09** ± 0.017
Moderate	Soil	1.030 ± 0.14	0.526 ± 0.20	0.323 ± 0.10	0.327 ± 0.12	0.430 ± 0.20	0.087 ± 0.009	0.187 ± 0.027	0.673 ± 0.16	**0.070** ± 0.025	0.465 ± 0.21	0.812 ± 0.09	0.096 ± 0.05	0.173 ± 0.24
	Water	0.713 ± .05	0.703 ± 0.03	0.412 ± 0.02	0.309 ± 0.03	0.304 ± 0.01	0.130 ± 0.09	0.719 ± 0.10	**1.07** ± 0.2	ND	0.307 ± 0.11	0.073 ± 0.017	0.061 ± 0.01	0.133 ± 0.025
	Grain	0.097 ± 0.034	0.307 ± 0.14	0.304 ± 0.001	0.106 ± 0.025	0.087 ± 0.016	ND	0.075 ± 0.017	0.023 ± 0.009	0.017 ± 0.01	0.023 ± 0.012	0.012 ± 0.007	0.009 ± 0.002	**0.03** ± 0.013
Low	Soil	0.250 ± 0.18	0.201 ± 0.16	0.120 ± 0.1	0.126 ± 0.013	ND	0.027 ± 0.011	0.93 ± 0.25	0.601 ± 0.017	0.065 ± 0.03	0.124 ± 0.012	0.313 ± 0.00	0.037 ± 0.01	0.75 ± 0.021
	Water	0.413 ± .15	0.17 ± 0.003	0.120 ± 0.002	0.219 ± 0.003	0.14 ± 0.001	0.73 ± 0.009	0.319 ± 0.010	**0.07** ± 0.02	ND	0.016 ± 0.01	0.015 ± 0.01	0.012 ± 0.006	0.031 ± 0.013
	Grain	0.019 ± 0.003	0.093 ± 0.043	0.016 ± 0.008	0.052 ± 0.007	0.116 ± 0.016	ND	0.09 ± 0.005	0.013 ± 0.009	0.017 ± 0.007	0.009 ± 0.001	0.006 ± 0.001	ND	**0.01** ± 0.006

Endosulphan -I and II: Endosulphan-II; Cyp: Cypermethrin; Hep: Heptachlor Epoxide; Chlp: Chlorpyrifos; Dicl: Dichlorvos; ND: Not detected found to be connected to both soil and rice grains in regions with lower agricultural activity (Fig. 2).

The dendrogram organizes pesticides into clusters based on their similarity in distribution across environmental matrices and agricultural practices. Persistent organochlorine pesticides, such as Endosulfan I, Dieldrin, Chlordane, and Aldrin, were closely grouped together while Endosulfan II, α-HCH, β-HCH, and γ-HCH were clustered together as another group across matrices and agricultural intensity (Fig. 2).

Agricultural intensity and environmental matrices significantly influence pesticide residue distribution

Multivariate Analysis of Variance (MANOVA) revealed a significant impact of agricultural intensity and environmental matrices on pesticide residues. Pillai's Trace and low Wilks' Lambda value (0.069, $p = 0.01$) indicated a strong multivariate effect for both agricultural intensity (High, Moderate, Low) and environmental matrices (soil, water, rice grain). Significant differences in pesticide residues were observed between high and low agricultural intensity groups for α-HCH and Heptachlor epoxide, and between high and low as well as high and moderate groups for DDT and Aldrin. However, no significant differences were noted for Endosulfan I, Endosulfan II, β-HCH, γ-HCH, Cypermethrin, Chlorpyrifos, Chlordane, and Dichlorvos (Table S2, S3).

Significant variations in pesticide residues between matrices were also identified. α-HCH residues significantly differed between soil and grain, and soil and water, while differences between water and grain were less pronounced. Strong significant differences for Cypermethrin and Chlorpyrifos were observed across all matrices. For DDT and Dieldrin, significant differences existed between soil and grain, and water and grain. Similarly, significant differences were found for Heptachlor epoxide and Aldrin between soil and grain, and water and grain. The analysis underscores the influence of agricultural intensity and environmental matrices on pesticide residue distribution, with notable variations among specific pesticides (Table S4).

Dietary carcinogenic risk for exposure to carcinogenic pesticide residues via *water and grains predominates in high intensity agricultural areas*

In regions with high agricultural intensity, the soil ingestion pathway demonstrated significant non-dietary carcinogenic risks, particularly from Dieldrin (1.83E-05) and Aldrin (2.95E-05). Dermal exposure also posed substantial risks from Aldrin (1.53E-05) due to its higher carcinogenicity. However, carcinogenic risk through Inhalation route was comparatively lower for all pesticides. Dietary carcinogenic risk through water was particularly alarming, with Heptachlor epoxide (1.8E-04) and Dieldrin (1.22E-04) identified as major contaminants. Additionally, α-HCH (6.19E-05) and Dieldrin (1.04E-05) in rice grains posed risks, though within the acceptable range defined by the USEPA. However, dietary carcinogenic risks from water and rice grain consumption remained higher compared to non-dietary risks from soil ingestion, dermal contact, and inhalation pathways (Table 2).

Hospital based retrospective cohort study indicates higher cancer incidence among farming communities in high intensity agricultural area

From 2020 to 2022, cancer incidence varied notably with agricultural intensity. In 2020, 777 cases were reported 53.02% from high, 33.72% from moderate, and 13.26% from low-intensity zones, with incidence rates of 76, 87, and 40 per 100,000, respectively. Most patients were farmers (82.6%), and tobacco use exceeded alcohol use. Mean age ranged from 44.98 to 47.78 years. In 2021, 985 cases followed a similar pattern wherein 53.33% from high, 31.07% from moderate, and 15.59% from low-intensity zones, with incidence rates of 87, 92, and 54 per 100,000 individuals. Farmers constituted 94.2% of cases, and female cases exceeded males in high and moderate zones. In 2022, 995 cases were recorded 56.48% from high, 29.05% from moderate, and 14.47% from low-intensity areas, with incidence rates of 104, 97, and 57 per 100,000 individuals. Most cases were among farmers especially in high intensity areas, and the average age rose reaching 56 years in low-intensity zones. Males dominated in high-intensity areas, while females were more affected in moderate and low zones.

Analysis of cancer type distribution using hospital based retrospective study across agricultural intensity zones revealed significant site-specific patterns. Breast cancer predominated across all zones, followed by gastrointestinal malignancies. Cervical cancer showed higher prevalence in moderate-intensity regions compared to high and low zones. Ovarian cancer was most frequent in high-intensity areas and lowest in moderate zones. Haematological malignancies maintained relatively uniform distribution, while head and neck cancers were more prevalent in low-intensity and moderate areas than high-intensity regions. Lung cancer incidence increased progressively from high to low-intensity areas. Multiple myeloma and gall bladder cancers showed higher proportions in low-intensity zones compared to high-intensity areas. Male reproductive and oral cancers exhibited similar distributions across zones, with slight increases in low-intensity areas. Liver and uterine carcinomas were highest in high-intensity regions and lowest in low-intensity areas. Kidney cancer showed an increasing gradient from high to low-intensity zones. Brain and pancreatic cancers were observed only in high and moderate-intensity regions, while bone cancers were infrequent throughout. The "others" category demonstrated a notable increase in low-intensity areas compared to high and moderate zones (Fig. 3)

Discussion

The intensive application of pesticides is prevalent in almost every agricultural state of India. As per the statistical data from the Ministry of Agriculture & Farmers Welfare, Uttar Pradesh accounted for the highest consumption of chemical pesticides in 2022–23 followed by Maharashtra and Punjab [39]. Further, this usage is determined by the variety of crops being grown, pest prevalence, climatic conditions, and the attraction towards growing high-yielding varieties. However, the overreliance on these harmful agrochemicals has raised concerns about their potential impacts on the environment and human health. Present study identified 13 pesticide residues in soil, water and rice grains collected from intense agricultural zones under Hirakud Command Area, Odisha, out of which eight are known carcinogens and found above permissible limits. Exposure to these pesticide residues through dietary route was found to pose higher carcinogenic risk over non-dietary routes. Hospital based survey indicated higher cancer burden in the regions showing elevated pesticide concentrations in soil, water and rice grains.

The detection of carcinogenic pesticide residues (Class B2 and C) in soil, water, and rice grains across Bargarh District's agricultural zones highlights significant contamination and public health risks. In high-intensity agricultural zones, α-HCH was the predominant contaminant in both soil and rice grains, while DDT levels peaked in water. This pattern reflects findings from Thailand and China, where historical use and persistence of HCHs and DDT have led to their continued presence in rice ecosystems. Despite being banned under the Stockholm Convention, these persistent organic pollutants (POPs) remain in the environment for decades. In moderate-intensity zones, Aldrin concentrations were notably high in soil, and DDT remained prominent in water, indicating ongoing use of legacy pesticides despite regulatory restrictions. The consistent presence of α-HCH in rice grains across all zones indicates its bioaccumulation potential, aligning with studies that demonstrate the transfer of OCPs from soil to crops. Unexpectedly, low-intensity zones exhibited significant levels of Dichlorvos in soil, suggesting a shift toward organophosphate use or variations in soil organic carbon (TOC) influencing degradation rates. These findings underscore the urgent need for continuous monitoring, stricter pesticide regulations, and the adoption of sustainable agricultural practices to mitigate long-term health risks.

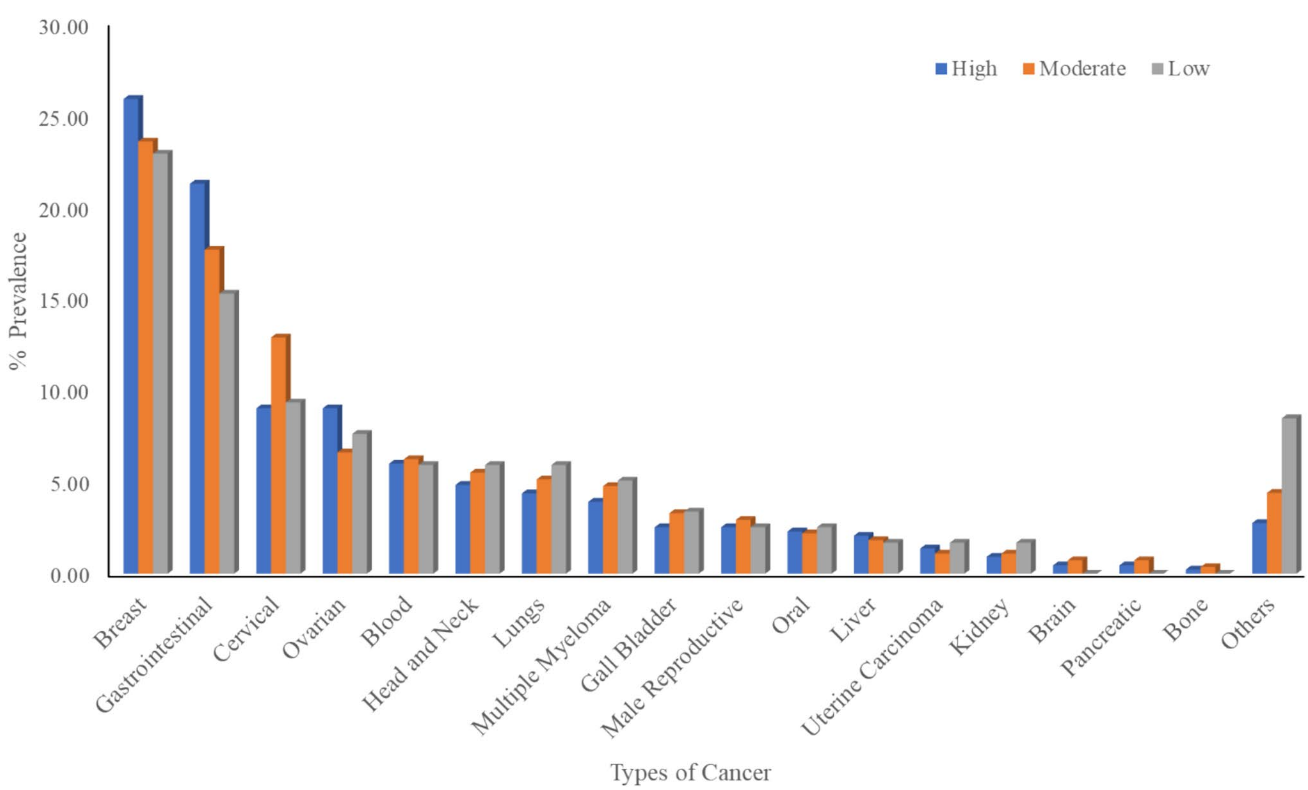

Fig. 3 Prevalence of different types of cancer across agricultural intensity in Bargarh District

Table 2 Non-dietary and dietary carcinogenic risk of pesticide exposed through soil, water and rice grain in Adult population

Agricultural Intensity	Root of Exposure		αHCH	βHCH	DDT	Heptachlor epoxide	Dieldrin	Aldrin	Chlordane	Dichlorvos
High	Non-Dietary Carcinogenic Risk Soil	Ingestion	8.9E-06	1.93E-06	5.05E-07	1.32E-06	1.83E-05	2.95E-05	7.01E-08	4.32E-08
		Dermal	4.62E-06	1E-06	2.62E-07	6.87E-07	9.48E-06	1.53E-05	3.64E-08	2.24E-08
		Inhalation	6.54E-09	1.42E-09	3.72E-10	9.74E-10	1.34E-08	2.17E-08	5.16E-11	3.18E-11
	Dietary Carcinogenic Risk	Water	9.32E-05	1.79E-05	8.95E-06	0.00018	0.000122	3.86E-05	6.51E-07	1.02E-06
		Grain	6.19E-05	9.08E-06	2.96E-07	4.61E-06	1.04E-05	6.98E-06	1.01E-07	6.30E-07
Moderate	Non-Dietary Carcinogenic Risk Soil	Ingestion	3.48E-06	1.01E-06	3.9E-08	1.09E-06	1.27E-05	2.36E-05	5.75E-08	8.59E-08
		Dermal	1.81E-06	5.23E-07	2.02E-08	5.66E-07	6.61E-06	1.23E-05	2.98E-08	4.46E-08
		Inhalation	2.56E-09	7.41E-10	2.87E-11	8.02E-10	9.37E-09	1.74E-08	4.23E-11	6.32E-11
	Dietary Carcinogenic Risk	Water	6.27E-05	1.34E-05	8.78E-06	–	0.000119	3E-05	5.15E-07	9.31E-07
		Grain	4.62E-05	4.61E-06	1.89E-07	3.74E-06	8.88E-06	4.93E-06	7.61E-08	2.1E-07
Lower	Non-Dietary Carcinogenic Risk Soil	Ingestion	1.29E-06	3.88E-07	3.49E-08	1.01E-06	3.4E-06	9.11E-06	2.22E-08	3.72E-07
		Dermal	6.71E-07	2.01E-07	1.81E-08	5.25E-07	1.76E-06	4.73E-06	1.15E-08	1.93E-07
		Inhalation	9.52E-10	2.86E-10	2.57E-11	7.45E-10	2.5E-09	6.7E-09	1.63E-11	2.74E-10
	Dietary Carcinogenic Risk	Water	1.83E-05	9.52E-06	5.75E-07	–	6.18E-06	6.16E-06	1.01E-07	2.17E-07
		Grain	2.43E-06	2.26E-06	1.07E-07	3.74E-06	3.48E-06	2.46E-06	–	7E-08

Water samples from areas with lower and moderate agricultural intensities showed moderate concentrations of pesticide residues compared to highly intensive agricultural regions, where DDT and chlorpyrifos were the most prevalent. Intensive agricultural practices, along with leaching and evaporation during the pre-monsoon and surface runoff during the monsoon, contributed to the increased presence of pesticide residues in surface water [40]. Organochlorine Pesticides (OCPs) like aldrin, dieldrin, endrin, chlordane, DDT, and heptachlor epoxide are commonly used for pest management, especially during the flowering season of paddy to optimize crop yield [41]. However, pesticides applied during this period tend to accumulate in rice grains due to their lipophilic nature, as observed in both high and moderate intensity agricultural areas. Similar studies have reported the accumulation of OCPs, such as Endosulfan I, II, and Hexachlorocyclohexanes (α, β, and γ), in rice grains, particularly in areas with high agricultural activity [42]. Studies from Dehradun and Punjab state also reported pesticide residues, indicating their potential for bioaccumulation in rice grains [43, 44].

Endosulfan, Aldrin, Dieldrin, and HCH exhibit significant grouping, indicating similar hydrophobicity and a strong tendency to bioaccumulate in the environment [45]. DDT and Heptachlor epoxide, known for their chemical stability and lipophilic nature, persist in soil and aquatic environments and share structural similarities, leading to comparable degradation products and bioaccumulation patterns [46]. Chlorpyrifos and Dichlorvos are identified as organophosphate pesticides, while Cypermethrin stands out for its long-term persistence in soil. Posthoc tests (Tukey HSD and LSD) reveal significant differences in pesticide residues between high and low agricultural-intensive regions, particularly for DDT, HCH, Heptachlor epoxide, and Aldrin, highlighting the impact of varying agricultural practices. In contrast, Endosulfan I and II show no significant differences, suggesting homogeneity in residue levels across regions.

Among the pesticides, the highest carcinogenic risk via ingestion was observed for Dieldrin and Aldrin, attributed to their persistence in soil and bioaccumulation potential in high agriculturally intensive areas (Table 3). Their low volatility and water solubility result in long residence times, with Dieldrin persisting for over seven years [47]. Additionally, Aldrin and Heptachlor epoxide posed significant carcinogenic risks through dermal contact, underscoring the need for protective measures when handling contaminated surfaces. Inhalation exposure posed minimal risk, likely due to lower airborne concentrations and limited respiratory absorption, especially from coarse particles [48]. In lower agriculturally intensive areas, Aldrin posed elevated carcinogenic risks through soil ingestion, potentially linked to prolonged pesticide usage [49]. Similarly, Dieldrin and Heptachlor epoxide presented significant risks via dermal contact, reflecting residual levels in soils despite their phase-out decades ago. These findings align with global cancer risk assessments, emphasizing ingestion and dermal exposure as primary risk routes [50].

The dietary carcinogenic risk associated with pesticide ingestion through rice grains is the most significant exposure route, followed by water ingestion [51, 52]. In agriculturally intensive areas, the primary contributors to dietary carcinogenic risk via rice grains are Dieldrin, Heptachlor epoxide, and Aldrin, while in moderately to less intensive areas, Dichlorovos leads, followed by Heptachlor epoxide [53, 54]. High agriculturally intensive areas also pose the greatest carcinogenic risk through water consumption due to elevated levels of Dieldrin and Aldrin, both classified as category B2 carcinogens and persistent organic pollutants (POPs) [55]. In contrast, moderately intensive areas show a lower dietary carcinogenic risk due to reduced pesticide concentrations [56]. Lower agriculturally intensive areas exhibit the highest risk through rice grain intake, primarily due to high Chlordane levels, a POP known for its bioaccumulation and carcinogenic potential. Despite regulatory efforts, these pollutants persist in the environment, emphasizing the need for stringent food safety measures and continuous monitoring to minimize long-term health risks [57]. In contrast, DDT exposure shows negligible carcinogenic risk, with no substantial long-term cancer effects reported [58].

This study reveals significant carcinogenic risks linked to pesticide exposure, especially in high-intensity farming areas, where pesticides like Dieldrin and DDT persist in the environment (Fig. 4). Non-dietary exposure pathways, such as ingestion and dermal contact, pose health threats to farmworkers and nearby communities, while dietary risks from rice and water suggest long-term implications for consumers. Immediate action is needed through integrated pest management, stricter pesticide regulations, and public health initiatives to raise awareness and promote safer practices. Future research should prioritize long-term studies to evaluate health impacts and the effectiveness of alternative pest management methods.

The study highlights a strong link between high-intensity farming and increased cancer prevalence in Bargarh District, with occupational exposure to pesticides being a significant risk factor. While lifestyle factors like tobacco and alcohol use are relevant, agricultural practices play a more critical role in cancer risk. Protective measures, such as safe pesticide use training and monitoring, are essential, along with targeted health interventions for younger adults and public awareness campaigns on carcinogenic exposure and addiction cessation.

Cancer incidence shows a higher prevalence among middle-aged adults, indicating increased susceptibility within this age group. Studies, such as the Agricultural Health Study (AHS), also suggest that younger age groups involved in farming may be at risk [59]. Farmers appear more affected by cancer than non-farmers, although a significant number of non-affected farmers indicates potential variability due to sample size differences [60, 61]. Addictions, particularly tobacco and alcohol, are significantly higher among cancer patients, underscoring their role as potential risk factors [62, 63]. Elevated mortality risk is observed among oral and pharyngeal cancer patients with high alcohol intake. Pesticide exposure, especially in agricultural zones, is associated with increased cancer risk. Pesticides like Dieldrin, Heptachlor epoxide, aldrin, DDT, chlordane, cypermethrin, and chlorpyrifos show carcinogenic potential, linked to cancers of the lungs, gastrointestinal tract, and breast [64–66]. Organochlorine pesticides, particularly DDT metabolites, are prevalent in breast milk samples of women with breast cancer, suggesting a link between pesticide exposure and elevated cancer risk [67].

Cancer incidence in agricultural-intensive areas is influenced by multiple factors, including lifestyle, environmental exposures, genetic predispositions, and healthcare access. However, pesticide exposure stands out as a significant risk factor, with organochlorine pesticide residues detected in a vast majority of cancer cases [68]. In Karachi, 98% of cancer patients and 94% of those with other health issues showed organochlorine residues in their blood serum [69]. Breast cancer emerged as the most prominent cancer type in the study areas, strongly associated with insecticides such as malathion, chlordane, dieldrin, and chlorpyrifos [70]. The International Agency for Research on Cancer (IARC) classifies chlordane and dieldrin as probable carcinogens [71]. Studies have linked elevated dieldrin levels to breast cancer, and it has even been detected in breast milk and adipose tissues of affected individuals [12]. Gastrointestinal cancer prevalence was higher in areas with intensive agriculture, supporting a link between pesticide exposure primarily through dietary exposure and increased cancer risk [72, 73]. Multiple studies and mechanistic evidence suggest that dietary pesticides exposure can disrupt gut microbiota, damage intestinal barriers, and induce oxidative stress and genotoxicity, all contributing to carcinogenesis [74, 75].

Cervical cancer was the third most prevalent type, particularly in agricultural zones where endocrine-disrupting pesticides like chlorpyrifos were linked to hormonal alterations [76]. Stomach cancer incidence remained constant across all regions, with agricultural workers showing a higher risk of mortality [77]. Ovarian cancer cases were the least common, but exposure to endocrine-disrupting chemicals like DDT and chlorpyrifos was associated with reproductive dysfunction [78]. Lung cancer prevalence was also low, but long-term studies on pesticide applicators indicated a positive correlation between pesticide exposure and lung cancer risk, especially for chemicals like chlorpyrifos, diazinon, and dieldrin [79, 80]. Despite the challenges in

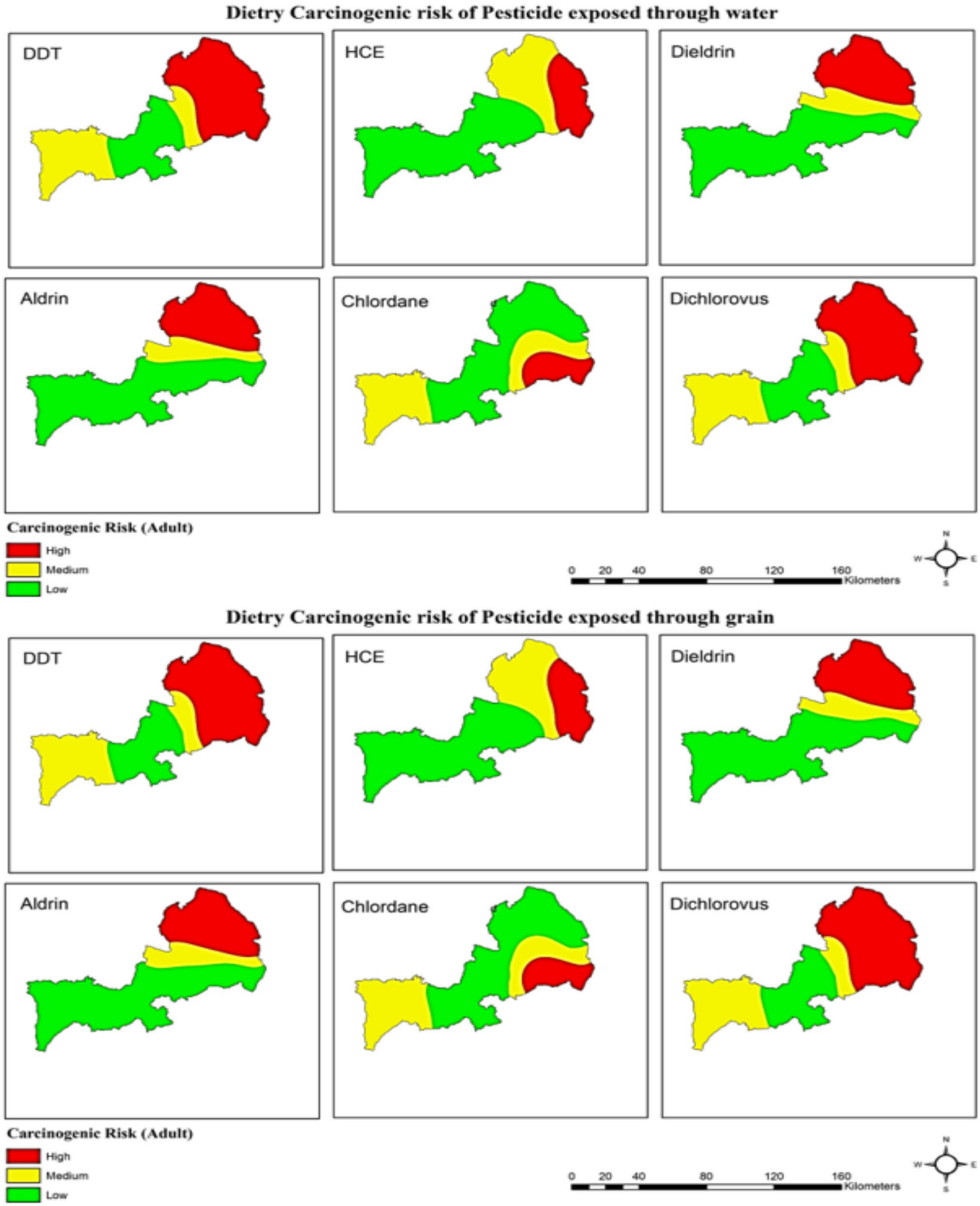

Fig. 4 Regions in Bargarh District showing higher carcinogenic risk due to exposure to pesticide residues through dietary route (Water and grain)

Table 3 Demographic distribution of cancer cases in study area

Year	Agricultural Intensity	Population	No. of Cancer patients n(%)	Occupation		Addiction		Age (Mean ± SD)	No. of Affected Males	No. of Affected Females	Incidence (n per 100,000 population)
				Farmer	Non-Farmer	Tobacco	Alcohol				
2020	High	539,148	412 (53.024)	389	23	225	128	47.78 ± 15.38	224	188	76.417
	Moderate	298,505	262 (33.719)	165	97	56	32	47.67 ± 16.25	139	123	87.771
	Low	254,287	103 (13.256)	88	15	33	28	44.98 ± 15.78	46	57	40.505
2021	High	539,148	472 (53.333)	452	20	109	88	51.30 ± 27.20	207	265	87.546
	Moderate	298,505	275 (31.073)	258	17	69	34	49.87 ± 27.29	136	139	92.126
	Low	254,287	138 (15.593)	124	14	12	09	47.73 ± 26.27	73	65	54.269
2022	High	539,148	562 (56.482)	508	54	267	21	52.07 ± 21.41	356	206	104.239
	Moderate	298,505	289 (29.045)	278	11	65	16	51 ± 16.93	93	196	96.816
	Low	254,287	144 (14.472)	114	30	15	07	56 ± 22.25	119	25	56.629

interpreting data due to confounding factors like smoking, the overall findings underscore the significant health risks posed by pesticide exposure in agricultural settings [81].

Conclusion

The study is the first report that evaluated pesticide residues in soil, water, and rice grain samples, and assessed carcinogenic health risk using established methodologies around Hirakud Command Area, Odisha. Mass spectrometric analysis of different matrices indicated presence of eight potent carcinogenic pesticides residues such as DDT, Dieldrin, Dichlorvos, Chlordane, Heptachlor epoxide, Chloropyrifos in water, soil and rice grain across different agricultural zones. Pesticide such as Dieldrin and Heptachlor epoxide were reported to be above the maximum residue level in soil and rice grain. Maximum pesticide residues were noted in the highly intense agricultural areas in soil, water, and rice grains. Carcinogenic risk of pesticide residues through dietary sources was found to be high compared to non-dietary sources. Dietary exposure to Heptachlor epoxide and dieldrin through rice grain and water posed high carcinogenic risk of 3.00E-04 and 2.51E-02 respectively while non-dietary exposure to Aldrin, and Chlordane through soil ingestion and inhalation showed moderate to low carcinogenic risk. Higher prevalence of cancer in areas reporting higher concentrations of carcinogenic pesticides in water and rice grains indicated a closer association of pesticide exposure with cancer incidence. Farmers were found to be more affected by cancer compared to non-farmers, highlighting a potential association between farming occupation and cancer incidence. Continuous monitoring of pesticides residues in different environmental compartments is necessary to ensure long-term safety of community coming in direct and indirect contact to pesticide residues above MRLs.

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Author contributions All the authors have read, written and approved the final version of the manuscript. AKS performed the experiments, drafted the original manuscript, analysed the data, PB and SRN performed hospital-based survey, documented and edited the manuscript, SKS performed statistical analysis and edited the manuscript, SNA conducted hospital-based survey and edited manuscript, KMM involved in investigation, data curation and methodology. BS and PKN involved in supervision, conceptualisation and review, IB involved conceptualisation, fund acquisition, supervision, editing and review of manuscript.

Data availability The data that support the findings of this study are available in manuscript and supplementary material.

Declarations

Conflict of interest Ashish Kumar Sahu, Pralaya Biswas, Sawan Kumar Sahoo, Syed Nikhat Ahmed, Soumya Ranjan Nath, Kabita Manjari Majhi, Bikram Sen Sahu, Pradeep Kumar Naik, and Iswar Baitharu declare that they have no conflict of interest.

Human and animal rights The retrospective hospital-based survey for assessment of prevalence of cancer cases in Bargarh district was approved by the Institutional Ethical Committee, Sambalpur University (20/IEC-SU/2024). All the study procedures adhered to the principles of the Declaration of Helsinki revised version (2013) and institutional ethics guidelines.

Ethical Approval All the procedure followed in the present study for assessing cancer prevalence in Bargarh District was approved by the Institutional Ethical Committee, Sambalpur University vide Ethical Clearance No. 20/IEC-SU/2024 and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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