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A REVIEW ON INTEGRATED APPROACH IN CHILDHOOD MALIGNANCIES-PREVENTION AND CONTROL

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ABSTRACT

Introduction: Cancer has become a huge concern since it is the second-leading cause of death in poor nations and the primary cause in economically developed countries. According to the WHO, cancer has become the deadliest killer in the world and is one of the deadliest diseases of the twenty-first century. According to the World Health Organization, India accounts for at least 20% of the world's burden of paediatric cancer, with about 75,000 children diagnosed with the disease annually. According to the Indian Council for medical research, 5.5% of all cancer cases in India include youngsters. Paediatric cancer may primarily be examined under three categories: before conception, throughout pregnancy, and after delivery, according to the adhyatmika vyadhi categorization of illness. According to the current paradigm, DNA alterations that occur early in a child's life cause cancer, which is caused by inherited mutations from parents that raise the chance of cancer in children. Some preventative methods, including dinacharya, rasayana, shodhana, and garbhini paricharya, are explained by Ayurveda. The condition that resembles cancer is described as Granthi and Arbuda in the classical texts of Ayurveda. The purpose of this study to find out the integrated approach in childhood malignancies-prevention and control.

Keywords: Childhood malignancies, Ayurveda, Integrated approach, Adhyatmika vyadhi.

INTRODUCTION

Cancer is one of the leading causes of death for children and teenagers. The majority of children with cancer are treated in high-income countries (more than 80%), less than 30% of patients in several LMICs (low middle income countries) receive a cure, hence likelihood of surviving a childhood cancer diagnosis varies by the nation where the child lives. ¹⁻² The 6th most typical reason of all cancers worldwide and the 9th most typical disease affecting children worldwide is paediatric cancer. In the present GBD (global burden of disease) framework, unclassified cancers made about 26.5 percent (26.5-26.5) of all children cancers worldwide DALYs (disability-adjusted life year). ³ According to the World Health Organization, India accounts for at least 20% of the world's burden of paediatric cancer, with about 75,000 children diagnosed with the disease annually.⁴ It is extremely practical, affordable, and can increase survival in all settings to provide access to key paediatric cancer treatments, such as lifesaving medications and technologies. 5 According to the most recent data, 10% of all cancer cases in adolescents are genetically predisposed.⁶ Families and qualified primary healthcare professionals can identify a variety of early symptoms of childhood cancer, including fever, severe and persistent headaches, bone pain, and weight loss. 7

The global initiative on childhood cancer was established after WHO held first international conference on childhood cancer held in Geneva (August 29–30, 2018). Its goal is to save an additional one million lives by 2030 while increasing the existence rate of paediatric age with cancer to at least 60%. Standard cancer treatments include medication, resection, and radiation treatment. Teenagers also necessitate specialised care for their ongoing nutritional status, as well as their intellectual and

physical growth, which require for a committed, interdisciplinary group. 8 Since it is typically not possible to prevent childhood cancer, the best way to minimize its impact and enhance results is to emphasize in early, definitive diagnostic procedures, then efficient, scientific proof treatment and customized support services. Resolution on cancer prevention and control through an Integrated Approach of the World Health Assembly (WHA70.12), which concentrates on reducing early mortality from NCDs and achieving universal health coverage, is being addressed in part through the global initiative to combat paediatric cancer. The most frequent form of paediatric cancer, acute lymphocytic leukaemia (ALL), represents for 1/4th of all juvenile cancers and 3/4th of all newly diagnosed leukaemia cases.9 Other top five paediatric cancers in children are retinoblastomas, lymphomas, central nervous system cancers, leukaemia's, and lymphomas for both boys and girls. Hodgkin's disease (65%) had the greatest 5-year absolute survival rate, followed by Acute lymphoid leukaemia (39%), Wilms tumour (64%), retinoblastomas (48%), non-lymphomas Hodgkin's disease (47%), osteosarcomas (44%), and astrocytoma's (39%) are the most prevalent cancers. 10

Causes of Paediatric Cancer

Paediatric cancer is described as *Granthi* (cystic swelling) and *Arbuda* (tumour) in the classical texts of *Ayurveda*. The three *doshas* (*Vata*, *Pitta*, and *Kapha*) are involved in the illness, while the main *dushyas* (liable to be spoilt) are *mansa* (muscle), *rakta* (blood), and *medas* (fat). According to *Ayurveda*, it is related to *sahaja roga* (hereditary disease). It has been challenging to identify potential environmental causes of childhood cancer because the disease is rare and it may be challenging to ascertain what exposures children may have experienced during their early

development. But in Ayurveda, the diseases and their causes are all explicitly stated. Trividha vyadhis (three types of disease), particularly aadhyatmika vyadhis (spiritual disease), can be used to correlate childhood cancer. 11 There are 3 different types of adhyatmika vyadhis i.e., adibala pravritta vyadhis (hereditary disease) (pitruja (from father) and matruja (from mother)), janmabala pravritta vyadhis (congenital disease) (rasakrita (nutritional) and apacharaja dauhruda (full cravings of the mother during period of pregency)), and doshabala pravritta vyadhis (humoral disease) (kalabalapravrutta (ecological disease), daivabalapravrutta (supernatural disease), and svabhavabala pravrutta (natural disease). The causes of Arbuda are mostly based on the Vata, Pitta, and Kapha doshic theories. Moreover, such as mithya ahara and vihara (wrong diet and lifestyle) and vitiated involving different dhatus (mamsa, meda, rakta, etc), its leading to the administration of Arbuda. Sushruta has stated that due to an overabundance of Kapha, Arbuda does not suppurate. 12

Pathophysiology of Arbuda

The ailment known as Arbuda is caused by aggravated doshas that lead to tissue vitiation in the muscles and cause muscle to swell any place in the body It is spherical, immobile, somewhat painful, large, firmly ingrained, and steadily expanding, and not ripening (malignant tumour). 13 When Vata and other doshas connected to Kapha become inflamed, they contaminate the fat, blood, and muscle tissues and create what is known as granthi, a bulging, hard swelling (benign tumour). 14 Arbudas can develop in any area of the body and eventually grow to large sizes, have globular shapes, are fixed with deeper structures, rarely suppurate, and occasionally cause discomfort. Due to the vitiation of the tridosha, mamsa and rakta may be included. 15 Vagbhata also explained that large granthis are known as Arbuda (malignant tumours); they occur in six varieties and are spurred on by doshas, among other things. They do not ripen because of the general dominance of medas (fat) and Kapha as well as because of their deep roots. 16 There is mentioned the three different types of metastases i.e., Raktarbuda (a tumour that has smaller tumours surrounding it), Adhyarbuda (When a tumour forms over an existing one or when one develops over an alreadyexisting location) and Dviarbuda (when two tumours develop simultaneously). 17

It is tough to treat tumours that secrete a lot of liquid at the adjacent tissue, are localized in crucial aspects or canals (such as the blood vascular and lymphatic systems), and are diligently linked to those tissues. The tumours which cause large discharge of liquid in the adjacent tissue, situated in vital sites or canals, persistently attached to the adjacent tissues are tough to treatment. ¹⁸ The following disease can be linked to the pathology of cancer like *Pandu* (anaemia), *rakatajkrimi* (worms due to vitiated blood), *dustashotha* (spoiled inflammation), *dustagranthi* (spoiled cystic swelling), *dustaviserpa* (spoiled erysipelas), *dustanadivarana* (spoiled sinus in anal region), *dustamansa pradosaj vikara* (spoiled muscle tissue pathology). ¹⁹

Prevention of Paediatric cancer

According to *Adhyatmika vyadhi's* concept, the causes and prevention of paediatric cancer can be divided into three categories.

- 1. Preconception
- 2. During pregnancy
- 3. After birth

Preconception

Adhibala Pravritta Vyadhis: Adibalapravritta vyadhis are the disorders that result from sperm and/or ovum morbidity. This category includes the disorders that are passed on from parents and are hereditary. They are also called by other names i.e. sanchari vyadhi (communicable disease) (Yagnavalka), kulaja (hereditary) (Charaka), sahaja vyadhi (Vagbhata) and praktibhava vyadhi (constitutional disease) (Bhela). 20 Sahaja (congenital/genetic/hereditary) diseases arise for five reasons i.e. beejadosha (chromosomal abnormality), atma karma dosha (self deed misconduct), aashya dosha (space vitiation), kaala dosha (seasonal vitiation) and maatru aahara vihara dosha (maternal dite and lifestyle misconduct). Beeja doshaja (adibalapravrittamaatrija, pitruja) diseases develop due to abnormality in beeja (sperm) or beejabhaaga (genes). Arsha (piles), Kushtha (skin conditions), Rajayakshma (tuberculosis), Madumeha (diabetes), Shwitra (lecoderma), and Apasmara (Epilepsy) are examples of Adibalapravritta disorders. 21 According to contemporary science, heritable (germline) mutations, which can be transferred from parents to their children, account for up to 10% of all childhood malignancies. ²² The risk of paediatric cancer is further increased by inherited mutations linked to von Hippel- Lindau and Beckwith-Wiedemann syndrome. In comparison to children without the disease, those with Down syndrome, a genetic defect caused by the presence of an extra copy of chromosome 21, have a 10 to 20-fold higher risk of acquiring leukaemia. ²³

Preventative interventions: Aahara and vihara should be in good condition. Cancer risk factors should be avoided; shodhana (purification); rasayana (rejuvenation); vajeekarana (vrishya chikitsa).

During pregnancy

Janmabalapravritta: Janmabala pravritta vyadhis are diseases that arise in the kid as a result of the mother's incorrect dietary and lifestyle choices during the foetus developmental stages. When a pregnant woman consumes a certain flavour or food in excess, the child is more likely to have certain disorders. These diseases are known as rasakrita vyadhis 25 Modern science has also established that a foetal development in the womb may have genetic abnormalities that cause cancer. Studies of monozygotic (identical) twins who both acquired leukaemia due to the same leukaemia initiating gene mutation provide evidence for this. 26 However, it has been revealed that kids whose moms endured scanning while pregnant and kids that were shown to computed tomography (CT) scan diagnostic medical radiation after delivery have a higher risk of developing leukaemia, brain tumours, and probably other malignancies. 27

Preventive interventions: A healthy diet; avoiding radiation and cell phone use; Follow *garbhini paricharya* (anti natal care) ^{28;} *agnihotra homa* ²⁹.

After birth: Adults who have been exposed to carcinogenic ecological elements like smoke from cigarettes, asbestos, and solar electromagnetic radioactivity frequently get these DNA abnormalities. According to one study, malignancy in kids and teenagers (ages 11 to 20) shares a lot of genetic features with melanoma in adults, such as an enrichment of UV-induced mutations.³⁰ In actuality, environmental exposures are not regarded to be the primary cause of the majority of children malignancies. However, a number of environmental factors have been connected to paediatric cancer. One is ionising radiation, which can cause leukaemia and other cancers in children and teenagers who were exposed to radiation from world war II bombs dropped on Japan and from the Chernobyl nuclear facility

disaster had an elevated risk of thyroid cancer.³⁰ Certain solvents, which are organic chemicals found in several household items and are used by parents at work or around the house, outdoor air pollution, and fathers smoking tobacco as well as pesticides have all been linked to certain kinds of juvenile leukaemia. 32,33 Studies on paediatric brain cancers have shown a potential link to pesticide exposure in and around the house 34 and intake of cured meats by mothers.35 When niraama (devoid of ama) dosha (the dhatuleena condition of dosha/visha) develops after the suppression of infectious diseases or antibiotic therapy and is not eliminated, it lodges in tissue. The first and most important event in the aetiology of cancer is the lodging of saama (with association of ama) or nirama dosha or visha (poisonous) in tissue (according to susceptibility), which over time creates ojo dushti (vitality vitiation) and grade 3rd bala vyapat (strength derangement) of the tissue or cells. ³⁶ The usage of excessive electromagnetic fields (EMF) is one of the causes of childhood cancer, according to current studies. These exposures, which are relatively recent (within the last 20 years), may be a new potential neurotoxic and carcinogen that, when exposed repeatedly and without consideration, may have long-term negative effects on health. 37

Preventive interventions: Encourage sensible eating practises; steer clear of electronics, *medhya* drugs (Intellect drugs) advice; *deepana*, *pachana* (when required to maintain proper *agni*).

Principles of Ayurvedic Management

Ayurvedic herbs and their constituent parts may mediate their effects by influencing a number of the above-mentioned recently discovered therapeutic targets, according to a number of recent studies. However, the following 3 factors can clarify the molecular foundation for the Ayurvedic medicines method of action in cancer ³⁸:-

Anti-angiogenesis: Anti-angiogenesis is a type of targeted therapy that prevents tumours from growing new blood vessels by using *Ayurveda* medications.

Apoptosis: It means programmed cell death. Suicidal tendency is induced by cancer cells. Apoptosis is a mechanism that *Ayurvedic* medicines cause in cancer cells.

Destroying stem cells: *Ayurvedic* medicines eliminate cancer stem cells, which stops metastasis. Anxiety, depression, fatigue, decreased appetite, hair loss, excess salivary secretion, ascites, pleural effusion, pericardial effusion, ascites, weight loss, sexual dysfunction, and liver and kidney issues are the side effects of cancer treatment. It has been demonstrated that *Ayurvedic* medications work well for treating these adverse effects and enhance nutritional status. There are four categories that make up *Ayurveda's* therapeutic approach for health preservation, cure for illness, return to execution process, and spiritual perspective. ³⁹

Ayurvedic Management of Childhood Cancer

Most commonly, the three doshas can be lessened by all of the medications used in rasayana treatment. Triphala (Terminalia chebula Retz., Emblica officinalis Gaertn., and Terminalia bellirica Roxb.), Guduchi (Tinospora cordifolia Willd), and Punarnava (Boerhavia diffusa Linn.) are the rasayana medications most frequently recommended in alopecia, nausea, constipation, anorexia, and vomiting which are some of the adverse effects of chemotherapy and radiotherapy. Due to the ability to maintain haematological levels at a normal range while receiving Ayurvedic treatment along with chemotherapy, patients have demonstrated more consistency in sustaining chemotherapy

cycles. *Ayurvedic* remedies are highly successful as chemo- and radio-preventive agents, according to more than 50 cancer research investigations.

For a better understanding and widespread acceptance of the *Ayurvedic* herbs, they must be rediscovered in light of contemporary chemistry, physics, and biology advances with its inherent therapy methods including herbal medicines, dietary changes, spiritual support, and acceptance of the way of life as outlined in *Ayurvedic* texts.

Tridoshasamak medicines

Triphala: Strengthens the body's various tissues, delays ageing, and fosters health and immunity. 40

Guduchi: The justification behind the use of Guduchi preparations in numerous Ayurvedic medications for immunomodulation has been strengthened by the confirmation of an immunomodulatory protein in Guduchi stem that exhibits lymphoproliferative and macrophage-activating activities. ⁴¹ A study on Tinospora cordifolia (Willd) shows that the plant's extract has anti-tumour potential in a two-stage skin carcinogenesis mice model. ⁴²

Yashtimadhu: Most well-known for its ability to heal inflammatory mucous sheaths in the throat, to intestines and lungs; it also calms *Pitta* and *Vata* while aggravates *Kapha*. Two enzymes that break down prostaglandin E are selectively inhibited by the glycoside glycyrrhizin, which is present in around 8% of liquorice plants. Both antibacterial and anticancer properties are present in liquorice. ⁴³

Organ Specific

Lung Cancer: Vasa (Adhatoda vasica Nees.), Kantakari (Solanum surrattense Burm.f.). Vasicinone demonstrated significant cytotoxic effect *in vitro* against the lung cancer cell line A549. 44

Uterus Cancer: *Talispatra Bhed (Taxus baccata* Linn.) known that *Taxus baccata* Linn. contains taxane or taxol, which has an anticancer effect. ⁴⁵

Liver Cancer

Kalamegh (Andrographis paniculate Burm.f.):- The separated diterpenes (andrographiside and neo-andrographolide) and extract from this plant have been shown to be effective against tumour angiogenesis due to their increased carcinogen detoxification and anti-lipo peroxidative properties. 46

Bhumyamalaki (Phyllanthus niruri Linn.): In research, the antitumour effect of Phyllanthus niruri Linn. was evaluated in 7–9-week-old male Swiss albino mice. The findings showed a considerable reduction in the incidence, yield, burden, and total number of papilloma's q23 due to tumours. When compared to carcinogen-treated controls, Additionally the PNE-treated group's average latent period dramatically increased. ⁴⁷

Breast Cancer

Matulunga (Citrus medica Linn.): Citrus plants are thought to have anti-tumour and due to the presence of flavonoids and limonoids, they have anti-inflammatory qualities ⁴⁸

Haridra (Curcuma longa Linn.): Curcumins affected various cancer development phases.⁴⁹

Colon cancer

Shunti (Zingiber officinale Rosc.): In recent studies found that shunti possess free radical scavenging, antioxidant, inhibition of lipid peroxidation properties. This have contributed to the gastroprotective effects of shunti.⁵⁰

Bilwa (Aegle marmelos Corr.): Swiss albino mice having Ehrlich ascites cancer, the hydro-alcoholic extract of *Aegle marmelos* Corr.)- was investigated for its potential anticancer properties. ⁵¹

New Tissue Proliferation

Punarnava (Boerhavia diffusa Linn.): The development of metastases by B16F10 melanoma cells was reported to be decreased by administration of the *B. diffusa* Linn. aqueous methanol (3:7) extract, In contrast to untreated control mice. ⁵²

Amalaki (Emblica officinalis Gaertn.): The fruits of Amlaki have a reputation for being a tonic that promotes longevity, health, and youth. The fruits are used as an expectorant and an antidote to "mineral" toxins, notably vermillion and sulphur. ⁵³ Human cancer cell lines A549 (lung), HepG2 (liver), HeLa (cervical), MDA-MB-231 (breast), SKOV3 (ovarian), and SW620 were employed to investigate potential anticancer effects of *P. emblica's* aqueous fruit extract (Colorectal). At dosages of 50–100 g/ml, *P. emblica* extract dramatically slowed the growth of a number of human cancer cell lines. At dosages of 25 and 50 g/ml, *P. emblica* extract prevented the invasion of MDA-MB-232 cells in the *in vitro* matri gel invasion assay. ⁵⁴

Enhance Vigor and Vitality

Ashwagandha (Withania somnifera Linn.): Ashwagandha, usually recognized as Indian ginseng, or Ashwagandha, lowers Vata/Kapha dosha (with additional Pitta), aids in the retrieval of general weariness and neurological problems, and generally regenerates tissues. As an in vivo test, Sarcoma-180 that formed on the dorsum of mature BALB/c mice was used subjects for the alcohol root extract of W. somnifera's antitumor and radio sensitising properties, as well as their alteration by heat. 55

Tulsi (Ocimum Sanctum Linn.): Its anticancer effect has been demonstrated in studies using biological models such fibrosarcoma cell culture, albino mice with papilloma's on their skin, 180 solid tumour-bearing animals etc. ⁵⁶ *Ocimum sanctum* Linn. ethanolic extract caused cytotoxicity in A549 cells, raised the sub-G inhabitants, and caused to see cytotoxic cells. ⁵⁷

Other

Aahar (food): The spices have anti-cancer properties.

Kesar (Crocus sativus L.): In Crocus sativa the carotenoid crocetin has antitumor properties. 58

Haridra (*Curcuma longa* Linn.): Curcumin contains antiproliferative and proapoptotic properties. ⁵⁹

Lavanga (Syzygium aromaticum Linn.): Eugenol contains antitumor properties. $^{60}\,$

Lashuna (Allium sativum Linn.): Organosulfur compounds in Allium sativum have anti-cancer and anti-tumor effects. ⁶¹

Methika (Trigonella foenum-graecum Linn.): In a research conducted in vitro, fenugreek seeds are harmful to cancer cells. 62 Sunthi (Zingiber officinale Rosc.): The extract of Sunthi significantly slows the growth of a variety of prostate cancer cells. 63

Kali marich (Piper nigrum Linn.): There are anti-inflammatory, antioxidant, and anti-cancer effects in piperine, which is found in Piper nigrum. ⁶⁴

Jatiphala (Myristica fragrans Houtt.): Human leukaemia T cells respond well to methanol extracts from Myristica fragrans. 65

Vihar (daily routine): It consists of *aachar rasayan* (specific code of conduct), *rutucharya* (seasonal behaviour), *dincharya* (daily routine) and *adharaniya vega* (non-suppression of urges).

Yoga: It can be used to manage complicacy, decrease of cost intricate, improve quality of life, lessen mental illness, and prevent repetitions. Techniques to assist the patient in achieving internal control over the concentration and vitality that aid in restoring the inequity include *asan (physical posture), pranayam* (breath control), meditation etc. ⁶⁶ A single positive thinking has the power to balance everything out. ⁶⁷ Deep inhalation breath holding is beneficial in patients with breast cancers. ⁶⁸

Panchkarma Therapy: Sesame oil, which is used in *panchkarma* for massage and Basti, has also been shown to have antineoplastic effects. ⁶⁹

Shaman Therapy: Triphala, Ashwagandha, and other major shamak dravya are significant shaman chikitsa. According to studies conducted on animals, Ashwagandha has a calming impact on the central nervous system and exhibits antioxidant effects on the brain. The plant's roots exhibit cytotoxic effects on H-460, and Ashwagandha boosts the generation of cytotoxic T lymphocytes. 70 Brahmi, Liquorice, Tulsi, Terminalia Chebula Retz., Tribulus terrestris Linn., Elettaria cardamomum Maton., Centella asiatica Linn., Nardostachys jatamansi DC, and Asparagus racemosus Willd, are the best cancer treatments. 71 According to a report by CCRAS (The Central Council for Research in Ayurvedic Sciences) and ACTREC (Advanced Centre for Treatment Research and Education in Cancer, Arka (Calotropis procera Ait) and Bhallataka (Semecarpus anacardium Linn.), both of which were tested for their cytotoxicity against tumours, appeared to have the strongest cytostatic activity. The *Indian leadwort*, winter cherry, Ballataka, Apamarga, Asoka tree, Indian sarsaparilla, Pandan, Guduchi, and Guggul are further herbal plants with anti-cancer properties. 72

Satvavjaya treatment: It serves as a form of counselling. Fear is sometimes brought on by the patient's emotional distress related to the cancer diagnosis and its treatment. Physical and psychological deficits brought on by the fear of recurrence include sadness, alteration disorder, nervousness, attitude instability, melancholy, and terror of the future. ⁷³

Rasayan Therapy: It is known as reconstruction rehabilitation. This sort of treatment gives the patient more power so they can battle the sickness. It also stops the illness from dispersion and reduces the negative things of radiotherapy and chemotherapy. Indian gooseberry, Semecarpus anacardium Linn., Withania somnifera Linn., Asparagus racemosus Willd., swarna bhasma, diamond bhasma, and coral calx are the drugs used as rasayanas. 74

Sadvritta (code of good behaviour): The *Sadvritta* are the guidelines for behaviour designed to advance his own wellbeing. It should be observed cautiously and in a variety of ways. *Sadvritta's* primary function is to stop external illness (*aagantuj vikar*). ⁷⁵

Naisthiki Chikitsa: This is the best action, barren of allure. The main source of misery is allurement. Elimination of all allures and the abode of misery will end all sorrows. This *dharmic kriya* results in a calm mind, which eventually yields harsh behaviour (joy). ⁷⁶

CONCLUSION

Present paper reveals that Ayurvedic medications may provide people fresh hope for the treatment and prevention of cancer as well as for leading healthy lives. Modern medications fall short in preventing new cancer cases and recurrence of the illness despite enormous advancements in diagnostic technology and rising awareness of the condition. The side effects of chemotherapy occur in patients of cancer and quality of life decreases. Ayurveda medication helps to management of chemotherapy induced illnesses and improve the quality of life of patients. With Ayurveda medication, there are some other concepts like aahar (diet), vihar (routine), yoga, panchakarma, samshaman, satwavajaya, rasayan therapy, satvritta, and naisthiki chikitsa would undoubtedly enhance their quality of life as they approach death.

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