

Biomarkers of Hope: The Effects of Exercise Intervention on Inflammatory and Metabolic Pathways in Cancer Prevention.

Prof. (Dr) Suresh P.R ¹, Mrs. Priyanka Shukla ², Mrs. Tabish Aliya Khan ³, Ms. Deepti Lodhi⁴

¹Dean Faculty, Peoples University, Bhopal,

Email ID : prs.pcps@gmail.com

²Assc. Professor, Peoples University, Bhopal

Email ID : priyankaj725@gmail.com

³Asst Professor, Peoples University, Bhopal

Email ID : aliyakhan.tabish@gmail.com

⁴Faculty, Peoples University, Bhopal

Email ID : deeptilodhi145@gmail.com

ABSTRACT

BACKGROUND: The Prevalence of cancer around the world is hiking due to sedentary lifestyle and poor diet habits. The awareness related to preventive factors and other side strong evidence regarding the preventive risk factor are at to explore. The effective physical activity in relation to the biomechanical relationship concern to cancer reduction is not yet evident. So it could be hypothesized and studied that Physiotherapy and or structured exercise can regulate inflammatory response, oxidative stress and immunological function which are then further provide the cancer for help in the recovery face.

OBJECTIVE: To conduct a scientific examination of know data related to biomechanical process broad down by exercise intervention based on structured exercise/Physiotherapy, its effect on adult on adult cancer prevention. **METHOD:** The study had followed the logistic approach by systematically scouting, following PICO format and applying PRISMA protocol. The studies between 2000 to 2025 has be explore through electronic databases. Full text English article published with mainly RCTs and Cozy Experimental study design were considered for the studies. Participants were only humans with adult categories, No gender specific. PRISMA 2020 protocol has been applied to scrounging and 12 studies were finally included for the systematic review. **RESULT:** The qualitative analysis of 12 studies listed on a customized data extraction table highlighted that structured exercise regiment can bring about variations in biochemical markers that can reduce the cancer risk. **CONCLUSION:** Based on the careful systematic review of 12 articles it can be concluded that structured exercise/Physiotherapy intervention can modulates biochemical pathways including inflammation, oxidative stress, metabolic and antioxidant capacity; leading to the prevention or postponing the cancer

Keywords: Exercise, Physiotherapy, Biochemical Pathways, Inflammatory Markers, Oxidative Stress, Cancer Prevention

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1. BACK GROUND:

Uncontrolled proliferation and spread of aberrant cells is the cause of a wide variety of disorders that are collectively referred to as "cancer." Through a process known as metastasis, these cells have the ability to infiltrate nearby tissues and migrate to distant areas of the body. Cancer can develop in any region of the body, and if it is not treated, it has the potential to be lethal. The formation of tumors, the tendency to infect other tissues, and the inability of cells to stop dividing are all important characteristics of cancer. Cancers that are commonly encountered are categorized based on the place in the body where they first appeared. Sarcomas, which start in connective tissues, and carcinomas, which develop in epithelial tissues, are a few of examples of these classifications. On the other hand, blood malignancies such as leukemia and lymphoma have an impact on both the blood and the immune system. Cancer is caused by a variety of factors, including environmental exposures and genetic changes. However, the survival rates for those who are diagnosed with cancer are improving due to the fact that the tools for detection and treatment are becoming more advanced.

Cancer is categorized according to the type of tissue from which it originates, as follows: Carcinoma is a kind of cancer that can develop in the skin or in tissues that line or cover internal organs. Sarcoma is a form of cancer that originates in connective or supportive tissue, which includes bone, cartilage, fat, muscle, and blood vessels, as well as other forms of tissue. Among the diseases that affect the blood are leukemia, which originates in tissues that produce blood, such as bone marrow, and lymphoma, which originates in the immune system.

Cancer can arise when the DNA of a cell is damaged in this way. This can be ascribed to a number of different factors, including the accumulation of genetic abnormalities that have been passed down through the generations, lifestyle decisions such as the intake of tobacco products, environmental variables such as exposure to radiation, or infections. The normal cell cycle is disturbed by these mutations, which allows cells to continue to survive, develop, and divide in an abnormal manner. Following a series of steps, a tumor that is both malignant and capable of invading other organs and tissues, in addition to spreading to other regions of the body, will eventually emerge as a result of this process. Variations in Genes: In its essence, cancer is a genetic illness that is defined by changes in DNA that lead to uncontrolled cellular proliferation. Environmental Factors: Exposure to hazardous compounds at work or in the environment, such as asbestos, can increase the risk of developing cancer. A tumor is formed when a cell's DNA is damaged, which results in a gene mutation. This gene mutation causes the cells to divide and expand at an uncontrollable rate, which eventually leads to the formation of a tumor.

A sore that does not heal, trouble swallowing or inexplicable indigestion, changes in bowel or bladder habits, a lump or swelling, unusual bleeding or discharge, a persistent cough or hoarseness, and a noticeable change in a mole or skin growth are seven of the most prevalent warning symptoms of cancer. It is essential to make an appointment with a physician for a professional assessment if you have been experiencing any of the following symptoms and they do not seem to be going away.

2. CANCER STATISTICS:

The statistics that are related to cancer are just appalling. Approximately 10 million people died from cancer in the year 2020. Twenty-eight million new cases will be reported each year by the year 2040. By addressing issues such as a poor diet, a lack of physical activity, and being overweight, it is possible that approximately forty percent of malignancies could be avoided. Lung cancer was the most common type of cancer that was newly diagnosed in people all over the world in 2022. Additionally, the incidences of breast cancer, colon and rectum cancer, and prostate cancer were exceedingly high.

Statistical data from a variety of countries throughout the globe

A Large Number of Fatalities: According to the World Health Organization (WHO), cancer was the leading cause of death across the globe in 2020, and it resulted in the deaths of approximately ten million people.

Increasing Incidence: The number of cancer cases is anticipated to climb to 28 million by the year 2040, a significant increase from the 18.1 million cases that were reported in the year 2020.

According to the World Cancer Research Fund, approximately 40% of all cancer cases may be averted if people made changes to their lifestyles, such as improving their diet, increasing the amount of exercise they get, and maintaining a healthy weight.

The Most Frequently Diagnosed Cancers: The Most Common Diagnoses in 2022 According to the American Cancer Society, lung cancer, breast cancer in women, colorectal cancer, and prostate cancer were the most common new malignancies that were diagnosed in people all throughout the world. The number of new instances of lung cancer in 2022 was around 2.5 million, which accounts for 12.4 percent of all malignancies diagnosed that year on a global scale. Pancreatic Cancer: The five-year survival rate for this kind of cancer is rather low, particularly if the cancer is discovered at a later stage of its progression. Breast Cancer: According to Breast Cancer.org, women who do not have a family history of breast cancer are the ones that develop the disease in approximately 85% of cases. Nevertheless, hereditary gene abnormalities are the cause of approximately 5 to 10 percent of breast cancers. Cervical cancer is the second most common condition among women in India, according to Cancer Research UK. On the other hand, it is the most prevalent type of cancer among women in nations with higher median incomes.

3. EXERCISE AND CANCER RISK:

The chance of developing several different types of cancer, including breast cancer, colon cancer, endometrial cancer, and prostate cancer, is reduced by exercising on a regular basis. This decreased risk is due to the fact that it aids in weight management, hormone balancing, immune system strengthening, and chronic inflammation reduction. To reduce your chances of developing cancer, one should engage in at least 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous-intensity aerobic activity each week, or a combination of the two. Some of the activities that can help you achieve this goal include walking at a brisk pace, riding a bike, dancing, and lifting weights.

Exercise reduces the likelihood of developing cancer through various mechanisms. There are a variety of mechanisms via

which exercise reduces your chances of developing cancer:-

Weight Management: It is essential since it assists you in maintaining a healthy weight. Being overweight increases your likelihood of developing several different cancers, including breast, colon, and liver cancer.

Hormonal balance: When hormone levels, such as those of estrogen and insulin, are excessively high, the likelihood of developing cancer increases. Exercise assists in maintaining control over these hormone levels. Engaging in physical activity strengthens our immune system, which in turn makes it easier for it to identify and eliminate cancerous cells.

Reduced inflammation: It contributes to the reduction of chronic inflammation, which has been linked to the development of cancer.

Improved Digestion: Exercise assists in accelerating the passage of food through the digestive system, which in turn reduces the amount of time that potentially carcinogenic substances spend in the digestive tract.

Exercise assists the body in repairing DNA, which lowers the risk of mutations that could lead to the development of cancer.

Methods That Can Be Used to Reduce the Likelihood of Developing Cancer

a. **Exercise that involves the use of oxygen:** Engaging in activities such as brisk walking, running, cycling, and swimming are all ways to increase your heart rate.

b. **Training for strength:** In order to build up your strength, you should incorporate activities like yoga and Pilates into your daily regimen. Participation in active recreation Enjoy our self while participating in sports, dancing, or other activities that involve physical movement. Active Transportation: Travel to our destination by walking or cycling. Recommendations for Increasing the Amount of Physical Activity we engage in.

c. **Moderate Activity:** Strive to engage in aerobic exercise of moderate intensity, such as walking at a brisk pace, for a total of 150 minutes per week. If we want, we can engage in 75 minutes of intense aerobic activity, such as running.

d. **Exercises involving a combination of movements:** To achieve our weekly goal, we have the option of combining workouts of moderate intensity with those that are more demanding.

Be consistent: Any amount of exercise is beneficial, but more exercise can help prevent cancer even more.

Rationale:

While some research has examined the relationship between exercise and cancer incidence, there is a scarcity of systematic reviews specifically addressing the biochemical pathways through which physiotherapy-based exercise facilitates cancer risk reduction. To use physiotherapy, biochemistry, cancer, and preventative medicine together, you need to know how these pathways work.

4. RESEARCH QUESTION:

In adults, what biochemical pathways are responsible for the contribution of exercise therapies that are based on physiotherapy to cancer prevention?

5. OBJECTIVES:

Primary Objective

To conduct a systematic evaluation of the evidence concerning the impact of exercise based on physiotherapy on biochemical pathways that are associated with cancer prevention, with a particular emphasis on inflammatory indicators, oxidative stress, immunological modulation, and metabolic regulators.

Secondary objectives

To evaluate the effectiveness of a variety of exercise regimens (aerobic, resistance, yoga, and combination) in regulating biochemical markers that are associated with cancer.

To conduct an investigation on the differences in biochemical results between healthy adults who are at risk of developing cancer and cancer survivors.

To conduct a careful evaluation of the methodological integrity and potential biases that may be present in the studies that have been chosen.

To identify shortcomings in the current literature and to suggest different approaches for future interdisciplinary research that brings together the fields of physiotherapy, nutrition, and biochemistry.

6. METHODOLOGY:

Study Protocol:

In this research, the systematic review approach is implemented. In order to ensure that the study procedure is of the highest quality and can be applied universally, the PICO format and PRISMA protocol are closely adhered to.

Eligibility Criteria:

Inclusion Criteria:

Full text articles

English language only

Published, Peer reviewed studies

RCTs and Quasi experiments

Publication of last 25 years (2000- 2025)

Physiotherapy/ Structured Exercise based intervention

Bio-chemical markers related to cancer risk as outcome measure

Studies with participants above 18 years, with no gender variations

Healthy participants/ Cancer survivors who can actively participate in the structured exercise regime

Exclusion Criteria:

Any trials on Animals

Reviews, Case studies, Case Series.

Un-satisfactory mode of study or reporting

Participants with recurrent Cancer

Studies with other pathologies combined with cancer

Pharmaceutical and other interventions beyond exercise

Evidence Identification Methodology:

Databases: Embase, Cochrane Library, PubMed, Scopus, Google Scholar and Web of Science

Keywords and the Boolean strategy:

(Exercise OR Physical Activity OR Physiotherapy OR Physical Therapy OR Rehabilitation) AND (Cancer Prevention OR Neoplasm OR Oncology) AND (Biochemical Pathways OR Inflammatory Markers OR Cytokines OR Oxidative Stress OR Immune Response OR Hormonal Regulation)

Sources of grey literature: Google Scholar, clinical trial registries

In order to ensure the safety of the people, it is essential that the government take action to prevent such events from occurring in the future. We are going to examine the bibliographies of the research studies that were included in this analysis.

Selecting Courses of Study

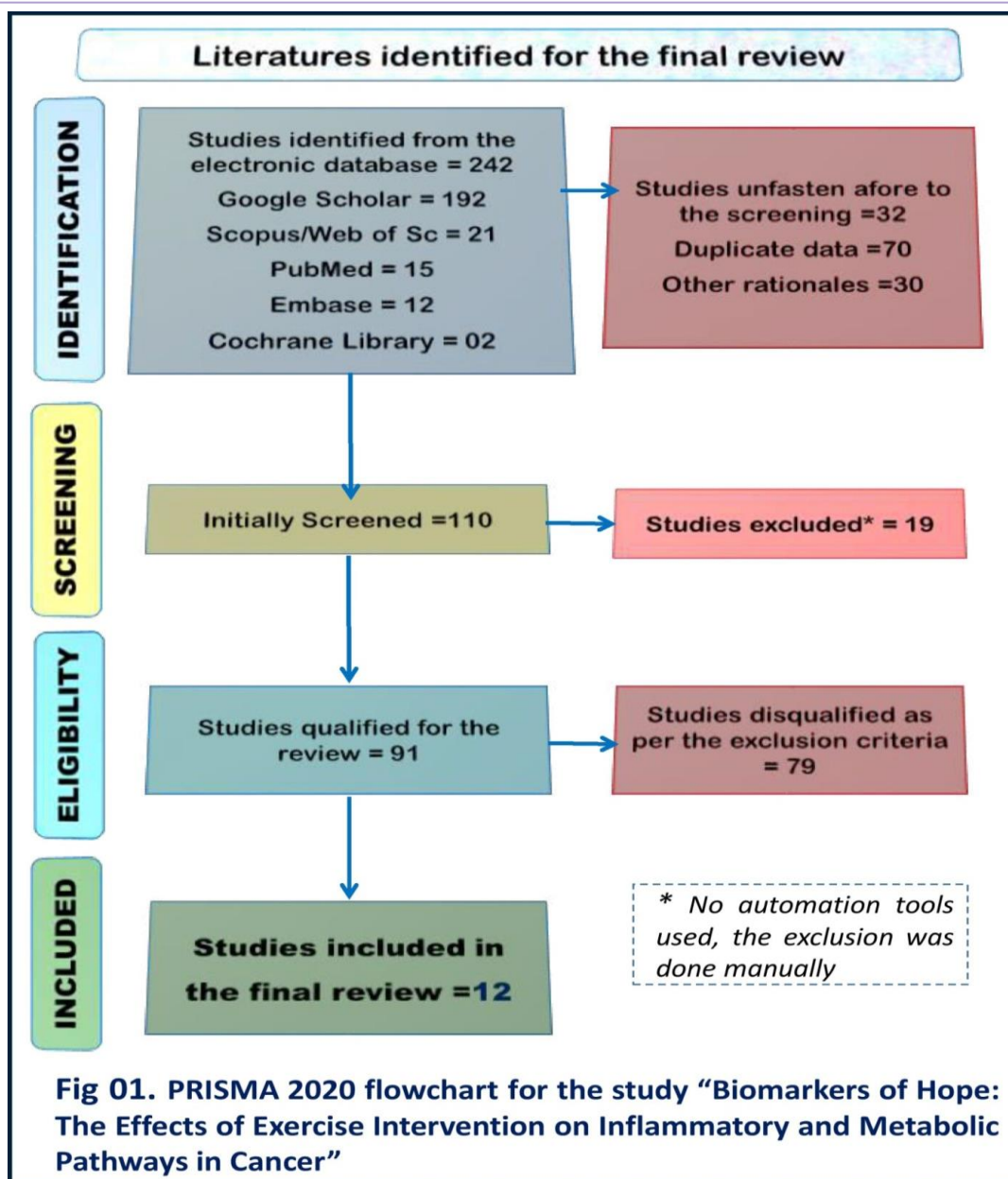
The titles, abstracts, full test, etc was examined by the four investigators.

Articles that fulfill all of the requirements were subjected to a comprehensive evaluation.

PICO format was applied (Population = Adults above 18 years old, Intervention = Physiotherapeutic based exercise approach, Comparison = Lack of Exercise/sedentary life style and outcome = variations in the biochemical markers related to cancer like Immunological Markers, Metabolic Hormones, Oxidative Stress Markers And Inflammatory Cytokines.)

In the event that a disagreement arose, it was resolved through discussion or with the involvement of a third reviewer.

The PRISMA flowchart will serve as a record of the methodology that was used to select the studies. (Fig 01, PRISMA flowchart).



Data Synthesis:

Narrative synthesis for biochemical pathways, which are sorted into four categories: inflammation, oxidative stress, hormonal pathways, and immune pathways.

If there is sufficient homogeneity among the biomarkers and therapies in question, a quantitative synthesis (also known as a meta-analysis) will be performed.

The standardized mean differences, along with their respective 95% confidence intervals, will be used to determine the effect sizes.

7. RESULTS:

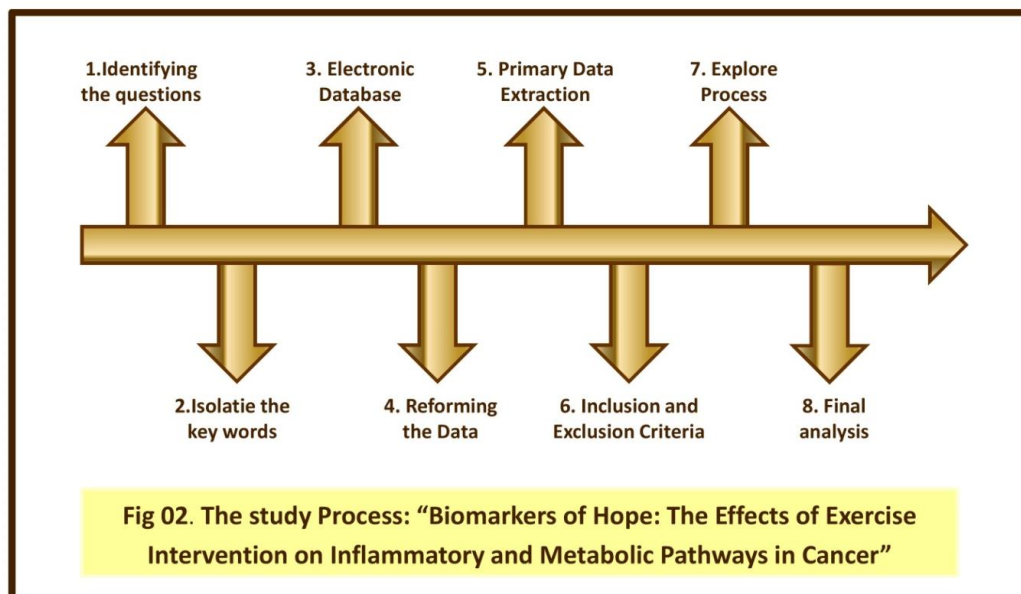
The PRISMA checklist is a component of the PRISMA 2020 recommendations, and the findings are reported in accordance with these standards.

A flowchart that illustrates the process by which studies were selected (Fig 02, The study Process flowchart)

The meaning of the sentence is not affected by the change in wording. A personalized data extraction table was developed in Microsoft Word format, and it included information about the researcher, the year of publication, the goals, the design

of the study, the number of cases in each of the experimental and control groups, the stage of the stroke, the physiotherapeutic approach that was utilized in both groups, the scales that were used for the pre-test and post-test, and the results.

An address that discusses the advantages and disadvantages of the situation, as well as the impact this has on policy and practice.



After framing the research question, the protocol for the study was designed. The steps involved in the study based on exercise effect on healthy or medically fit post cancer participants were 1. Framing the research question, 2. Designing the protocol, 3. Layout criteria, 4. Searching for databases, 5. Scrutinize the full test quality studies, 6. Extracting the data as per the eligibility criteria, 7. Synthesizing the extracted studies and 8. Final analysis.

Examination of qualitative research in this systematic review, the authors synthesizes non-numerical data from qualitative research papers to develop new or enhanced insights into the study topic, "Biomarkers of Hope: The Effects of Exercise Intervention on Inflammatory and Metabolic Pathways in Cancer." The process involved employing qualitative analytical methods, extracting conceptual information, and identifying themes through coding.

A customized data extraction table was constructed in Microsoft Word format, encompassing information pertinent to the researcher & publication year, study design, Participants/ population, interventions, Biomarkers assessed, and the outcomes.

Twelve published Randomized Controlled Trials, Mechanistic Laboratory Studies, and Quasi-Experimental Studies were selected for this review study after careful consideration of a number of criteria. The impact of physiotherapy or guided workouts on cancer prevention was documented through biochemical pathways in all 12 trials. These finalized studies were as per the PRISMA protocol and inclusion and exclusion criteria included, were high-quality observational intervention studies and randomized controlled trials. Populations consisted of healthy adults at elevated risk (e.g., overweight/obese or post-menopausal women), cancer survivors (breast, colorectal, head and neck in certain trials), and heterogeneous community samples. The interventions lasted anywhere from a few weeks (6–12) to a few months (6–12).

8. DISCUSSION:

Cancer is the leading cause of mortality and sickness around the world. The number of people who don't get enough exercise is gradually but steadily increasing to dangerously high levels. Several review articles have summarized the potential benefits of exercise on various aspects of cancer patients' lifestyles. However, just a few old review studies have investigated how exercise can assist fight cancer at the molecular level. Given the foregoing, the goal of this review study is to elucidate the molecular link between cancer and exercise by evaluating the most widely established molecular processes of exercise in relation to cancer formation and progression. This review study aims to provide persuasive evidence that exercise can be used as an addition to medical treatment for cancer patients, focusing on the key anti-cancer molecular processes that may aid in cancer prevention and treatment.

The research entitled "Biomarkers of Hope: The Effects of Exercise Intervention on Inflammatory and Metabolic Pathways

in Cancer” involved healthy participants aged over 18 years who are at risk for cancer. Only randomized controlled trials and quasi-experiments involving people are included; animal trials are excluded. Only publications with full text from the last 25 years (2000-2025) printed in English were considered for the review. Electronic databases constituted the primary sources of data.

The majority of the online data were obtained from Google Embase, Cochrane Library, PubMed, Scopus, Google Scholar, and Web of Science. The databases were examined based on the titles of the published articles and their abstracts. Keywords and the Boolean approach were utilized to investigate the pertinent articles. The Boolean method utilized was (Exercise OR Physical Activity OR Physiotherapy OR Physical Therapy OR Rehabilitation) AND (Cancer Prevention OR Neoplasm OR Oncology) AND (Biochemical Pathways OR Inflammatory Markers OR Cytokines OR Oxidative Stress OR Immune Response OR Hormonal Regulation).

This review study has adhered to the PRISMA 2020 criteria, which provided the framework for the methods of this systematic review. Figure 1 illustrates the processes undertaken to develop this review in compliance with PRISMA 2020. The investigation's route may be observed in figure 2.

The PICO format (Population = Adults over 18 years old - Healthy individuals or cancer survivors capable of actively engaging in the structured exercise programs, Intervention = Physiotherapeutic exercise approach, Comparison = Sedentary lifestyle, Outcome = Variations in biochemical markers associated with cancer, such as immunological markers, metabolic hormones, oxidative stress markers, and inflammatory cytokines) is applied to all studies reviewed to obtain the most robust evidence available.

The interventions that were investigated included aerobic training, resistance training, programs that combined both aerobic and resistance exercises, and physiotherapy or rehabilitation protocols that were carried out in an organized manner. The experimental group approaches demonstrated a considerable amount of heterogeneity when it came to the strength, frequency, and guidance that were shown. The comparison groups either engaged in a moderate degree of physical activity or followed a lifestyle that was primarily sedentary.

Following meticulous evaluation of many criteria, 12 published Randomized Controlled Trials, Mechanistic Laboratory Studies, and Quasi-Experimental Studies were selected for this review study. All 12 research involved physiotherapeutic or guided workouts, with their effects on cancer prevention documented via biochemical pathways, concentrating on inflammation, oxidative stress, controlling metabolism, and fixing DNA damage.

A data pulling up table that was custom-made and covered research-related information, such as the author, the year of publication, the design of the experiment, the number of participants in the experimental and control groups, the interventions, Biomarkers assessed, and the main results/ outcome; was mapped out in Microsoft Word format. Kindly refer the Summary chart/ Data pulling sheets, figure 03 (a) and figure 03 (b).

Biomarkers of Hope: The Effects of Exercise Intervention on Inflammatory and Metabolic Pathways in Cancer

Data pulling up table (Summary chart):

Characteristics of Included Studies (n = 12)

Author (Year)	Design	Population	Intervention	Biomarkers Assessed	Main Results
Schmitz et al. (2019)	RCT	Breast & colorectal cancer survivors (n ≈ 100)	Aerobic + resistance, 12 weeks	CRP, IL-6, TNF-α	↓ CRP and IL-6; improved inflammatory profile
Clifford et al. (2023)	Crossover trial	Cancer survivors, mixed types	Moderate vs high-intensity exercise, 2 weeks each	IL-6, TNF-α, oxidative stress markers	Moderate intensity lowered IL-6; high intensity transiently ↑ oxidative stress
Orange et al. (2022)	Mechanistic experimental	Healthy adults, post-exercise serum applied to colon cancer cells	Acute aerobic exercise	IL-6, DNA damage markers in vitro	Exercise-conditioned serum ↓ DNA damage, regulated IL-6
Kleckner et al. (2019)	Multicenter RCT	Patients receiving chemotherapy (breast, colorectal)	Supervised aerobic + resistance	CRP, IL-6, fatigue scores	↓ systemic inflammation; exercise attenuated chemo-induced fatigue
Steindorf et al. (2020)	RCT	Breast cancer patients on adjuvant therapy	12-week exercise program	IL-6, TNF-α, CRP	Reduced inflammation mediated lower fatigue
Kruk & Aboul-Enein (2007)	Review with mechanistic insights	General adult population	Observational evidence of regular physical activity	Oxidative stress markers, antioxidant enzymes	Moderate exercise ↑ SOD, GPx, ↓ ROS; protective against carcinogenesis

1 | Page

Fig 03 (a). Data pulling up table (Summary chart) for the study “Biomarkers of Hope: The Effects of Exercise Intervention on Inflammatory and Metabolic Pathways in Cancer”

Page 01 of 02

Biomarkers of Hope: The Effects of Exercise Intervention on Inflammatory and Metabolic Pathways in Cancer

AMC Head & Neck Study (2018)	Controlled trial	Head & neck cancer patients post-chemotherapy (n ≈ 40)	Aerobic + resistance, 8 weeks	SOD, GPx, catalase	↑ antioxidant enzymes, ↓ oxidative stress
BMC Women's Health Meta-analysis (2022)	Systematic review & meta-analysis	Breast cancer survivors	Exercise ± diet interventions	IGF-1, insulin, CRP	Exercise ↓ IGF-1 & insulin; improved inflammatory markers
ALPHA Trial (2010)	RCT	Postmenopausal overweight women (n ≈ 300)	Aerobic exercise, 12 months	F2-isoprostanes, antioxidant enzymes	↓ lipid peroxidation; improved antioxidant capacity
Exercise-Nutrition Trial (2015)	RCT	Breast cancer survivors	Exercise + diet modification, 6 months	IL-6, TNF-α, insulin	Combined program superior to diet alone for lowering inflammatory markers
Proteomic Mechanistic Study (2021)	Pilot mechanistic	Healthy adults	Resistance training, 8 weeks	Proteomic markers of oxidative stress	Exercise altered oxidative stress response proteins; improved cellular resilience
Systematic Review (2024)	Meta-analysis of RCTs	Cancer patients, mixed types	Aerobic & resistance	Antioxidant enzymes, ROS	Exercise improved antioxidant status; ↓ ROS across pool

Important findings from a number of studies

Some studies (Schmitz et al. 2019; Steindorf et al. 2020; Kleckner et al. 2019) on inflammatory pathways found that levels of CRP, IL-6, and TNF dropped greatly. This made the people in the study group less tired, which was good for them.

If you worked out moderately, your IL-6 levels dropped. But if you worked out hard, your reactive stress levels went up for a short time. There is a link between dose and reaction, as shown here.

Making reactive stress different: Antioxidant enzyme activity (SOD, GPx, and catalase) went up and oxidative damage (F2-isoprostanes and ROS) went down in studies with cancer patients (AMC 2018; ALPHA 2010) and healthy people (Proteomic Study 2021).

Certainty of Evidence:

Numerous well defined RCTs had proved strongly that properly structures exercise regime can bring down the systemic inflammation which is directly related to carcinogenesis.

Exploring in detail across the results of various studies, the evidence are significant that the guided exercise practice or physiotherapeutic procedures works in overcoming oxidative stress as well as inflammation assisting the participant to defend cancer.

Another noteworthy factor is that combination of proper physical activity with a healthy diet shall also contribute to cancer prevention and/ or recovery from medically stable tumors. Those studies had projected the positive effect of both to each other.

Study limitations:

The sample size of 12 studies is very small to explore the connections and to place the in sub-groups for much detailed examination.

Heterogeneity for the exercise interventions administrated for the experimental groups varied in the 12 studies. Where it is mode of approach like aerobic/ resisted combined, intensity, frequency or duration all varied making it complex during the analysis.

Finalized articles represent varied participants including healthy adults, recovered cancer cases, medically stable but had undergone chemotherapy recently limiting the applicability to certain groups.

Another variation among the finalized publication is inconsistency in the biomarkers. Different test used and the variations in the timings of the blood sample collection (Acute/ Chronic post exercise) makes it complicated to compare.

Some exercise protocol last a few days to a few months, such short duration post-test lead to an impractical situation to explore the risk of long term effect or future possibility of cancer.

The outcome of the Qualitative analysis:

This review study had provided an organized scientific picture of how the cancer risk shall be prevented or postponed by proper physiotherapeutic or guided exercise regimen. The findings were backed by the mechanistic pathways that cover biochemical markers of inflammation, oxidative stress, metabolism, and immunological regulation. The clarity of the study was based on the articles with the mixture of mechanist lab analysis with Randomized Control Trails.

9. CONCLUSION:

This systematic review study had synthesis the evidence from the properly scrutinized twelve published articles from the renowned journals, which displayed the modulation in the biochemical pathways through the guided exercise schedule, especially inflammation, oxidative stress, metabolism, and immunological regulation, the improvement of antioxidant and metabolic capacity.

However considering the Heterogeneity in the participants, mode of intervention, duration and the variety in the biomarkers, it is complex to have a final verdict. The results significantly favors the structured exercise or physiotherapeutic approach; the appropriate mode of intervention and best biochemical analytical approach and long term benefit on cancer prevention are yet to be explored.

Future study shall include a standardize biomarker panel, long term RCT studies, detailed comparison of various modes and parameters of the exercises, exploring other secondary/ associate factors like lifestyle and mindfulness, and the specific category of participants like age/ gender/ demographics class in study.

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