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Metabolic Reprogramming in Healthcare: A review

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Abstract

The main aim of this work is to focus on requirement of knowledge and research work in metabolism by health care workers in restoration of a patient's health. Metabolism, a process drives physiological functions of a cell and life.Alterations in this process, generates metabolic disturbances,effects immune system functionality and leads to diseases, like cancer, type 2 diabetes, gut dysbiosis,neurological problems, etc. Survival of a cell and performing its physiological functions under such condition is called as metabolic reprogramming.This diseased condition can modulate metabolic flux, and it is necessary to understand the process behind.

Research works are essentialto bring clarityabout the effect of nutritional sources, as well as nutrient ingredients in metabolism and metabolic flux,involved cellular signaling, dosage effects in signalling, apart from diagnostic measures to understand flux changes. Identifying the very right reversal mechanism under such condition is difficult, but empowered with research and knowledge of metabolic pathways and functioning, healthcare workers can put their efforts for a role reversal back. Physical activity and social interactions are essential for health restoration, demanding dependence on nursing and other professionals for a patient health restoration. It is highly essential to establish a feedback system amongst patients, physicians, health care workers and home or family members for patient health recovery. Knowledge of nutrition, nursing and care will restore back health of a patient from a metabolically reprogrammed state.Understandings herein will highlight the development of appropriate therapeutic strategies.

Key Words: Metabolic Reprogramming, Metabolism, Metabolic activity, Nutrition, Healthcare, Nursing

Introduction

Human health as defined by the World Health Organization (WHO) is a state of complete physical, mental and social well-being of a person. This does not take in count mere absence of a disease in a person (Institute of Medicine US, 2001). The parameters to measure one's health is by evaluation of the functioning ability in terms of physical, mental, social and spiritual activity within one's own defined environment(Oregon State University, 2024). Health in other words reflects the metabolic efficiency of an organism(Chatterjee and Dinda, 2016).

Deterioration of the nature's health and ecosystem affects health of an individual(WHO, 2021). Bad health can also be due to genes and heredity, lifestyle behavior, exposure to toxic substancesor other reasons(Healthtalk, 2016).A few of the identified reasons for health issues are: lack of physical activity, dietary habits, improper sleep, alcohol consumption, and environment(Patidar, 2022). Health deterioration can also due to ageing that is linked to metabolic reprogramming. Adoption of a healthy lifestyle and diet can act as a therapeutic strategy along with the first line of therapy to correct the diseased state of an individual.

Metabolic activities, essential for life of a living organism leads to either production or consumption of energy. Any kind of disturbances in this activity can lead to the development of a diseased state, wherein cells undergo an enhanced survival with an altered metabolism, like in cancer. This altered metabolism is called as metabolic reprogramming (Bhattacharya, 2023a, 2023b; Chiellini, 2020).Metabolic reprogramming in a cell is a rewiring mechanism to promote proliferation and cell growth(Bhattacharya, 2023a). This altered metabolism is also understood to be a link between ageing and tumourigenesis(Drapela et al., 2022). Metabolic changes also effects upon immune system functionality. Survival of a cell and performing its physiological functions under such condition is called as metabolic reprogramming.

First line of therapy refers to the administration of physician prescribed medicines. However, it is of simultaneous importance to support the patient with a well-balanced diet, or nutrition for health recovery. Apart from nutrient sources, there can be other sources also like imbalanced physical and social activities, etc. that modulates the metabolic flux, and these needs to be identified. Research studieshere can be taken up in people with nutritional imbalances, undernourished, and economically weaker population.

More research at the molecular level to understand totally the effect of nutritional sources, and or ingredients in metabolism and metabolic flux is essential, apart from measures to understand metabolic flux changes by radiology techniques. Food habits, lifestyle, physical activity and social interactions are essential for health restoration. Patients here depends on nursing and other corresponding and associated professionals for health improvement.

Physician patient meetgenerates a lot of question about health problems, wherein many of those questions remain unanswered by the physicians. This leads to the generation of a knowledge gap(Brassil et al., 2017; Son et al., 2023), wherein clinicians many a times may find difficult to work on these gaps. Though community nurses deliver comprehensive care to patients living outside hospital settings, there are yet a lot of questions that need to be answered as a priority in nursing and patient care matters. One of the unanswered questions is that can humans regenerate their every tissue and organs by themselves? A positive possibility can solve many medical problems(Lemley, 2003). This demands on innovation apart from research, engagement, collaboration, and funding for quality patient careservices not only from nursing, but also from physicians and clinical information systems(Henshall et al., 2022; John et al., 2007). Thus, it is essential to look at metabolic reprogramming, epithelial mesenchymal transition, and how these processes influence human health care.

Healthcare, provided by professional health care workers refers to the improvement of health by methods of prevention, diagnosis and treatment for cure of a diseased state. A robust healthcare system is essential to support a healthy society(Adegoke and Wright, 2013). Delivery of healthcare services needs the timely use of personal health services to achieve the best possible health outcomes (Institute of Medicine US, 1993). There are many factors, like finance that can limit access to healthcare services. This demands on the acquirement of adequate knowledge like effect of dietary factors on health and well-being of a person that leads to health deterioration as well as restoration, so that home people of a patient can also take the role of a caregiver. Provision of primary healthcare is essential to provide social justice, equity, solidarity and participation. Thus, the present work is aimed to understand metabolic reprogramming, its causes and effects and advocation of an appropriate diet,nursing and patient care that can act as a therapeutic strategy along with the standard healthcare practices.

Metabolic reprogramming and disease

Metabolic reprogramming leads to cellular oxidative stress and ROS production. The identified hallmarks of metabolic reprogramming at cellular level are: enhanced level of glycolysis, lactic acid production and pentose phosphate pathway, more of glutaminolysis, mitochondrial changes and enhanced lipid metabolism, altered amino acid metabolism, biosynthetic and bioenergetic pathways. Metabolic reprogramming not only enhances viral pathogenesis, but also is linked to generation of cancer, neural problems and epithelial mesenchymal transition (EMT). (Bhattacharya, 2023a, 2023b; Allen et al., 2022).Metabolic reprogramming influences cellular organization through biomass and energy supply. Metabolic sensors regulate supply of nutrient availability and environmental changes according to the cellular condition. This altered metabolic pathway also effects immune cell metabolism leading to the progression of infectious diseases(de Salles et al., 2022).In immune cells, metabolic reprogramming leads to epigenetic reprogramming including upregulated histone acetylation and suppressed DNA methylation. The resultant effects are observed in artherosclerosis, characterized by chronic inflammation and enhanced infiltration of adaptive and innate immune cells in the arterial wall(Sun et al., 2020). Innate immune cells reprogram their metabolism upon microbial infection, and benefits pathogenesis(Escoll and Buchrieser, 2019). Metabolic reprogramming also can affect on the organs, for example kidney. Kidney cell undergoes metabolic reprogramming after injury, as well in different kinds of diseases, that leads to the progression and prognosis of kidney diseases (Li et al., 2021).Upon pathogen infection, host proteinogenic amino acid metabolism is altered leading to an inhibition of the host immune mechanism. Administration of amino acids along with regular drugs like antibiotics acts as a therapeutic mechanism here (Li et al., 2023). Alteration of the metabolic pathways upon bacterial infection simulates ’Warburg effect” seen in cancer cells(Escoll and Buchrieser, 2018). Immune suppressed environment leads to a fast intestinal and systemic reprogramming. Continuous drug effects gut microbial ecosystem and host metabolism. Early changes in altered metabolism can act as antecedent biomarkers of a changed or a normal immune system functioning, leading to an activation or quiescent stage(Ma et al., 2023).Gut microbiota along with their metabolites and signaling are associated with systemic and local metabolic reprogramming. Systemic reprogramming is associated with diabetes, inflammation, obesity, cancer, and liver diseases, whereas local metabolic reprogramming is associated with intestinal pathobiology, like colon cancer, and inflammatory bowel diseases. Furthermore, type 2 diabetes results due to dysbiosis in gut microbiota(Savkovic, 2020). Additionally, microbial sepsis is also associated with metabolic reprogramming(Wyngene et al., 2018). Apart from humans, animals like fish also faces metabolic reprogramming during bacterial infection, wherein temperature acts as an inducer(Sun et al., 2022). Thus, addressal of metabolic disturbances along with the conventional chemotherapy will enhance therapeutic results.

Metabolic reprogramming mediated epigenetic regulation by miR-155 has been reported to enrich mitochondrial fitness and affinity maturation(Nakagawa et al., 2023). Metabolic reprogramming also plays an important role in skin wound healing(Wang et al., 2024). Region-specific toxicity in astrocytes arises from metabolic reprogramming, and metabolic reprogramming also induces therapeutic resistance in glioblastoma(Polyzos et al., 2019; Tsung-IH, 2023). Novel cancer therapeutics can develop with understandings of how metabolic reprogramming and epigenetic modifications help in tumour proliferation(Xu et al., 2023). Understandings of metabolic reprogramming will be of help to develop cancer precision medicine(Zhang and Tang, 2021). Cancer cells showing chemo- and radio-resistance has been observed to adapt glucose metabolic reprogramming(Lin et al., 2019). Strategies has been developed to cure diabetes associated breast cancer based on metabolic reprogramming(Hao et al., 2022).Furthermore, in organ transplantation and cancer, intrinsic relationship amongst gut microbiome, metabolic activities and immune cells shapes the immune metabolism associated with immune suppression and tolerance settings(Ma et al., 2023).

Proliferating cells increases their biomass and replicates genome material. This demands upon an enhanced ATP production and increased demand on nutritional raw materials, and directs proliferating cells to reprogram their intracellular metabolism. Metabolic reprogramming is not only observed in cancer but also in T-cells in inflammatory disorders during their activation, differentiation and trafficking mechanisms(Marelli-Berg et al., 2012).

Metabolic reprogramming in microorganisms and in human health, like gut metabolism are interlinked processes. Nutrient limitation in bacterial growth phase forces bacteria to undergo metabolic reprogramming to increase their life longevity(Dworkin and Harwood, 2022). For introduction and establishment of bacteria into complex system needs understanding of the adaptive responses of bacterium for microbiome engineering approaches(Hadadi et al., 2020). Metabolic engineering can improve the production and yield of different metabolites in microorganisms (Wang et al., 2012). Thus, metabolic reprogramming in gut microbiota can be remodeled by drugs and or food intake apart from other inducers that can be controlled by care givers. Bacterial metabolic environment influences antibiotic killing efficiency. Thus, an explained understanding of the metabolic resistance mechanisms is necessary to fight against antibiotic resistant bacteria(Xiang et al., 2023).

Metabolic reprogramming and epithelial mesenchymal transition

Different metabolism of tumour cells from normal cells results in metabolic disorders in metastatic tumours. (Li et al., 2019). Change of state between epithelial and mesenchymal phenotypes in cancer cells via EMT (epithelial mesenchymal transition) and MET (mesenchymal epithelial transition) are essential for cancer invasion and metastasis and the process depends on metabolic reprogramming(Sun and Yang, 2020). The presence of mutation in metabolic genes, FH, IDH, and SDH evidences that EMT and metabolic reprogramming are intertwined processes(Sciacovelli and Frezza, 2017). In cells undergoing EMT, co-factors and substrates stems out metabolic intermediates(Wang et al., 2019). Metabolic alterations control EMT progression and induces tumour aggressiveness. Thus, regulations of metabolic shifts by gene-basis or pharmacological inhibitions can down regulate EMT and tumour progression and can work as therapeutic effective measure(Kang et al., 2019). Research reports have shown that TGF-β (Transforming growth factor -β) initiates reprogramming of intracellular amino acid metabolism in NSCLC. (NSCLC = non-small cell lung cancer cells)(Nakasuka et al., 2021). Inspite of the fact that question arises to identify cause-effect relationship between metabolic shifts and EMT, predicted metabolic targets involved in EMT initiation and progressiveness has been identified, wherein drugs can be used, and food or nutrition-based therapy can be investigated upon as an alongside therapeutic measure(Morandi et al., 2017). With the difficulty in direct targeting of EMT effectors, and existence of identified metabolic circuits in EMT, FDA approved or under clinical trial metabolic inhibitors can be used as drugs, and that can be additionally clubbed with the standard therapeutic practices in cancer. (Ramesh et al., 2020). Identification of metabolic enzymes and metabolites as key molecules in thyroid cancer progression suggests the use of those molecules as biomarkers in radio-therapy to identify the effectiveness of the therapy effectiveness, as well as use of those molecules as possible targets in precision medicine(Fedele et al., 2021).

Diet and nutrition

Reversal of metabolic reprogramming might be an attractive strategy to increase susceptibility of cells to apoptosis. The prime tool to do this work is through food bioactive components and cofactors, like folic acid(Keijar et al., 2011). Dietary restriction without essential nutrient deficiency is the other vital way to intervene upon metabolic reprogramming(Anderson and Weindruch, 2007). Metabolic syndrome in the immediate postnatal life results out due to altered nutritional experiences, like undernutrition, overnutrition, and modified milk formula. Furthermore, altered metabolism during pregnancy results out in an adverse intrauterine environment effecting spontaneous transfer of maternal phenotype to the progeny, called as generational effect. Changed feeding practices for babies, and babies born to obese/hyperinsulinemic mothers might be a contributing factor to obesity at third world countries(Patel and Srinivasan, 2010). Thus, nutritional problems, and early life environmental signals might act as a major factor for long term health disease and risk spanning through generations. Nutritional problems can be of different types including calories restriction, macronutrient excess, and micronutrient insufficiencies(Brasiel and Luquetti, 2020). Efficacy of cancer treatment can be increased by dietary interventions thateffects nutrient availability in cancer cells. However, diet based therapeutic strategies needs to be researched upon more for an effective disease management strategy(Xiao et al., 2024; Bhattacharya, 2021). Additionally, novel therapeutic strategies on metabolic reprogramming can be reinforced with drug repositioning methods(Yoshida, 2015).

Research reports have shown the link between high glycaemic index (GI) and diabetes. People consuming diet with a higher GI are easy prone to diabetes, and chances of diabetes is also high in individuals with a higher body mass index (BMI). Thus, consuming a low GI based food is preventive to type 2 diabetes attack(Kannan, 2024). Furthermore, gut microbiota in prediabetics has been seen to change with diet(Chang et al., 2024). Variations in microbial profiles has been reported to result in infant neurodevelopment dysbiosis(Sizemore et al., 2024). Differential microbial flora has been also reported to be associated cellular and molecular features of tumour immunity(Battaglia et al., 2024). Infact, commensalism between bacterial flora helps to fight infections, and commensals can change based on diet(Maier et al., 2024; Sizemore et al., 2024).

Calories restriction is observed as a dietary intervention that reduces energy intake by approximately 15-30 % while maintain a balanced proportion of macronutrients and preventing malnutrition. This is an effective strategy in management of cancer(Lean et al., 2018; Li et al., 2021). However, intake choice of the right food composition over calorie intake acts also as a therapeutic strategy for the impairment of metabolic health(Adams et al., 2023).

Nursing and healthcare

Health systems science looks at the mechanism of healthcare delivery and ways to improve patient care and healthcare delivery through the healthcare system. Additionally, pediatric healthcare professionals need to understand pediatric-relevant health economics, health policy and social determinants of health to improve health of children. (Bartolettaand Starr, 2021). In summary, health systems science is also to understand how health care professionals work together to restore back normal health of a patient(American Medical Association, 2023).

Nursing includes the promotion of health, prevention of illness, care of ill, disabled and dying people. A nurse is also often the one to detect health emergencies and work on the front line of disease prevention along with professional care givers(World Health Organization, 2024). True healing of health comes through caring and self-realization by the patient. Nurses can help patients to attain knowledge about own health, and adapt healthy changes in their lives(University of Tulsa, 2023). Nurses help people and communities lead a healthy and better life(King, 2021). A good nursing practice also helps to overcome health problem caused by environmental hazards(Institute of Medicine US, 1995).

The healthcare industry is depended on different sectors, and exemplarily an overall 5.76 million health care worker are working at India as of 2018 amidst prevalent different kinds of diseases (Figure 1, Figure 2, Figure 3)(Karan et al., 2021). Healthcare industry at India was valued at 280 billion USD, with an expectation to reach 372 billion USD by 2022(Minhas, 2023).The industry also depends on the usefulness of medicinal value of foods(St. Luke’s Health, 2023; Dixit et al., 2023). Professional health care workers here needs knowledge from nurses, and physicians on ways to care for an ill-health person. Additionally, such workers also need to understand and value a patient for their choices, like in food habits, cleanliness, etc. in consultation with the patient as well as home members of the patient (Figure 4a and b).

Prognosis

Metabolomic profiling is a technically sound method to monitor changes in tumour metabolism. Biofluids can help to identify early biomarkers of tumour development. Metabolomics also helps to understand metabolic differences in response to tumour drugs, assess drug efficacy and monitor drug resistance(Han et al., 2021).

Metabolism based therapeutics with the cross-talk between metastatic signaling and cellular metabolism is a suggested way to impair metastasis(Hipo'Lito, 2021). Understanding of the metabolic heterogeneity within and across cancer types helps to identify pathway cross-talk, directing to novel prognostic, therapeutic and predictive utility(Peng et al., 2018). Furthermore, the question that arises is that does metabolically reprogrammed cancer or diseased cells, including cells undergoing epithelial mesenchymal transition (EMT) adapt a radically different gene expression or undergo structural modifications to undergo an altered metabolism(JacquetandStéphanou, 2021). Understandings from metabolic reprogramming has been used to develop molecules that target altered pathways, like mTOR and PI3K (Phosphoinositol-3 Kinase) pathway and kill the cancer cells. Exemplarily used molecules here are, mTOR (mammalian target of rapamycin) inhibitors, glutaminase inhibitors, ion channel inhibitors(Navarroet al., 2022). Metabolic reprogramming in tumour and immune cells also reshapes epigenetic alterations and that helps cancer cells to undergo immune escape mechanisms(Sun et al., 2022). Metabolic reprogramming in kidney cells induces alterations in energy metabolism playing important role in the pathophysiology of acute and chronic kidney diseases. (Singh, 2023).

Many translational medicines with examples of metabolic substrates, precursors, and other analogs have been developed based on biochemical metabolism. These analogs can be used also for imaging and therapeutic purposes apart from their role as competitors in metabolism. For example, with isotope labeling, these compounds helps to visualize tumour cells after uptake(Yang et al., 2022). Metabolic reprogramming and metabolic imaging has been linked also to observe breast cancer therapeutic responses. Metabolic imaging is also used to guide precise usage of anticancer drugs in cancer treatment(Liu et al., 2021). This imaging is also used for treatment strategies in Triple negative breast cancer (TNBC) wherein spatial and temporal dynamics of metabolic landscape are highly unstable, and metabolites states vary extremely(Sunasseeet al., 2023). Cancer cells undergoing cisplatin treatment also faces treatment resistance due to metabolic reprogramming. However, findings suggested development of rapid detection methods of cisplatin resistance at single cell level, and a treatment strategy for curing cells from cisplatin resistance(Tan et al., 2022). Tumour-spheroids has been developed to understand targeted metabolic strategies for inhibiting tumour growth(Roy and Finley, 2019). Screening for early cancer is one of the unanswered questions in medical imaging, and knowledge in metabolic reprogramming will provide guidance and will help to develop biomarkers. Biomarkers can help in adoption of the right therapeutic practice(Vannier and Evans, 1984).Critical challenges are involved with analysis of data in medical imaging, including reproducibility, and effects fields like genomics(Parmar et al., 2018). Understanding of metabolic reprogramming will help to solve the problem of timely diagnosis and treatment services which affects patient health status and health care service delivery(Nigatu et al., 2023).

Nursing and nutrition

A healthy diet is essential for a healthy life and living. Most of the people resort to a diet management program with for weight loss program. However, herein intake of the right food components or dietary component in a balanced way is essential compared to a mere management of calorie intake. However, it is also essential to look into calorie intake and follow the appropriate food guidance.Calorie burning is essential to maintain physiological system ongoing. Furthermore, a pound of body fat stores roughly 3500 calories, and extent of daily calorie burning for a sedentary woman is 1600 calorie, whereas the same for an active male is 2800 calorie. However, ideal calorie intake depends on age and activity level of a person(Bumgardner, 2021; Ajmera and Gunnars, 2023). Even though, exercising on empty stomach also leads to calorie burn and weight loss, it is not a suggested activity. Fueling of the body before exercise provides adequate and steady energy for a rigorous training. The dietary reference of protein intake for adults is 0.8 grams protein per kilogram body weight. In summary, it is of utmost importance for a person to balance calories for managing weight, and calories consumed when equals calories expended helps a person to maintain same body weight(Murphy, 2017). However, inadequate, excess or an imbalanced nutrition intake leads to a state called as malnutrition. Malnutrition also leads a person to a state of underweight, overweight, or deficiency of specific nutrients.

Conclusion

Excess or less food intake can lead to a state of ill-health. Consumption of a right food calorie diet is highly essential to maintain a good health; however, it is more important to analyze the food composition before intake. Optimum nutrition refers to intake of adequate vitamins and nutrients to support body physiological processes. Any food in-taken will be metabolized for body physiological purpose, and provides body with energy out of the biochemical reactions that the food undergoes(de Nava, 2024).Altered metabolism in dysfunctional kidney tubules leads to the development of kidney diseases (Singh, 2023). Any kind of injury, heredity, environmental or health problem can direct the body to adapt an altered metabolism, prime characteristic of a diseased state. Understanding of metabolic reprogramming in diseases, like cancer and of neuron dysfunctioning will help to understand main features and discover potentials for precise targeted anti-cancer therapies and metabolic treatments. (Bhattacharya, 2023a, 2023b; Nong et al., 2023; Phan et al., 2014). Reports cite targeting of metabolic reprogramming in hepatocellular carcinoma to overcome therapeutic resistance(Wang et al., 2024). Thus, it is essential to understand not only the metabolism but also metabolic reprogramming to restore back the health of a patient apart from administering the first line of therapy. Additionally, it will be also essential for the patient to undergo under supervision physical activity and social activity, demanding the need for professional care givers. Furthermore, it is a necessity for a feedback system amongst patients, physicians, health care workers and home or family members for the health recovery of a patient.

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Figure Legends:

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Figure 1. Different Health Care Sectors: The figure represents prevalent at India different health care sectors

Figure 2. National Health workers in India (year: 2018):Representative figure depicting census data of National health care workers in India as on 2018

Figure 3. Schematic representation of different kinds of diseases: Representative figure showing prevalent different kinds of diseases

Figure 4. Desired flow of information in patient health restoration. 4a

4a: Desired feedback way from patient and home members; 4b: Desired Flow of Information in health restoration