Impact of intermittent fasting on human health: an extended review of metabolic cascades

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ABSTRACT
In the present scenario, the literature is available regarding different challenging matters; however, some horizons still need to be elucidated and “Intermittent Fasting” is one of such examples. For millennia, several scientific interventions were carried out to probe the effect of fasting on human metabolic activities. There are three common strategies of fasting like caloric restriction (CR), dietary restriction (DR) and Intermittent fasting (IF) but IF has emerged as an avenue of potential benefit and wellbeing of the consumer. Intermittent fasting is the prehistoric surreptitious of human health as this powerful habit has been virtually forgotten. Nowadays, numerous researchers are reviving this dietary intervention. It carries enormous consequences such as increased energy, weight loss, and reversal of type-II diabetes. Moreover, it encloses the important evidence validating the health claims of IF with special reference to cancer, coronary heart diseases, biomarkers of oxidative stress and insulin sensitivity. Furthermore, the impact of intermittent fasting on human health based upon metabolic case studies are the limelight of the current manuscript. Conclusively, Intermittent fasting (IF) is the most appropriate tactic for its capability to ameliorate different lifestyle related disorders for instance; diabetes, cardiovascular disorder, cancer, antioxidant stress, and renal diseases.

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Introduction
Fasting is partial or total refrain from all foods or avoiding prohibited foods. Fasting has remained a centre point owing to the potential non-pharmacological strategy to improve health and increasing longevity in various scientific interventions.[1] Generally, there are three most commonly studied fasting strategies; they are a caloric restriction (CR), dietary restriction (DR) and intermittent fasting (IF).[2] The research outcomes of these strategies in different in vivo and vitro studies are given below.

In calorie restriction approach reduction in kilocalorie intake to about 20–40% of ad libitum consumption is practised.[3] This approach has been extensively investigated in many experimental models including the dog, fruit fly, rodents and non-human primates. CR has a potential to reduce the initiation of certain disease like atherosclerosis, cardiomyopathies, cancer, diabetes, renal diseases, neurodegenerative diseases and respiratory diseases.[4] In case of cardiovascular health, CR is known to reduce resting heart rate (HR) and blood pressure (BP), elevation in heart rate variability, enhancing the left ventricular function and improving flow-mediated vasodilation.[5]
Calorie restricted strategy also reduces the blood glucose level thereby decreasing the plasma insulin level and thus favouring the process of lipolysis.\[6\] In the calorie-restricted mode, the body uses its stored reserves thereby decreasing the body fat percentage and decreases the incidence of diabetes. However, extreme long-term practising CR regimen for a period of 6 months result in excessive fat and muscle loss that may cause a variety of physiological abnormalities.\[7\]

In dietary restriction approach, one or more food components (macronutrients) are reduced with nominal or no decrease in total caloric intake. The outcomes of extensive scientific research in different experimental subjects have proved that both carbohydrates and fats have no effect on lifespan, however, protein restriction increases maximum lifespan up to 20% and this may be due to a decrease in amino acid methionine.\[8\] Reduced methionine intake reduces the generation of mitochondrial reactive oxygen species that damage the mitochondrial DNA and ultimately affecting the functioning of mitochondria. Before approaching any solid decision about the outcomes of DR for humans it is necessary to carry out intensive human trials as the previously provided data has been generated through animal studies.\[9,10\]

The IF is another emerging avenue of research with superior outcomes than other fasting regimens, it comprises calorie restriction for several hours a day, alternating days or several days a week including feast period in which fasters are allowed to consume food ad libitum while during the fast period the faster refrains from food consumption, however faster is allowed to take water ad libitum all the time.\[11\] Many scientific studies were carried out to assess the impact of IF on possible health outcomes and it was found that IF resulted in prolonging lifespan and prevention of an array of discrepancies including CVDs, renal diseases, different forms of cancers and diabetes.\[12\] IF was observed to provoke the beneficial outcomes in cardiovascular health including lower heart rate and blood pressure, increased post-exercise heart rate variability.\[13\] Moreover, gender-specific effects were observed for glucoregulatory health, IF was observed to mend insulin sensitivity in male subjects but no such effect was noticed in females, however glucose tolerance was observed to be impaired in female subjects while no change was observed in male subjects.\[14\] IF is not a recommended approach for children and teenager on account of rapid growth and development phase and having elevated nutritional and caloric requirements.\[15\] However, this methodology has proved to be effective in adults with BMI 25 and above with negligible side effects. IF has varied effect in different age groups owing to transitions in metabolic status.\[16\] IF results in ketone bodies (acetoacetate, β-hydroxybutyrate and acetone) generation, recent studies have shown that ketone bodies enhanced the expression of gene encoded for mitochondrial enzyme and energy metabolism in hippocampus (learning and memory part of brain). Among the ketone bodies β-hydroxybutyrate behaves as even more efficient energy source than glucose by delivering more energy per unit oxygen used. Ketone bodies in contrast to glucose do not release any reactive oxygen species (ROS) but directly inhibit the production of these violent molecules and momentously increase the destruction of these vicious molecules by enhancing the functioning of glutathione peroxidase thus safeguarding body against brain degenerative malady like Parkinson’s disease.\[17\] The review article is a limelight of health benefits of IF and is an inspiration for future studies on this avenue of pronounced potential.

**Anticancer perspective**

Cancer cells are glucose loving as they have more insulin trans-membrane receptor sites to increase the uptake of glucose; however normal body cells are flexible to use other available energy sources like fat and proteins during fasting when glucose is not available.\[18\] During the fasting phase hepatocytes are capable to carry out a process called ketogenesis that produces ketone bodies (acetoacetate, β-hydroxybutyrate and acetone) that are delivered to peripheral tissues for energy production.\[19\] In this way cancer cells being inflexible to use an energy source other than glucose result in their death.\[20,21\] Another approach to initiate ketogenesis is by introducing a ketogenic diet highly recommended for cancer patients, it comprises of a negligible amount of carbohydrates and high-fat content (> 50% of energy intake) (Figure 1).\[22\]
Cancer cells have reduced activity of succinyl-CoA: 3-ketoacid CoA transferase, the rate-controlling step for utilizing β-hydroxybutyrate as a respiratory fuel.[23] Therefore, tumour cells experience high metabolic stress following the gradual replacement of glucose with ketone bodies.[24] The stressed tumour cells being weakly unable to adopt a phenomenon called differential stress sensitization (DSS) that is established on the fact that mutation in cancer cells promote growth under normal conditions but make them unable to harmonize with transitional energy source.[25] In this way cancer in its initial phase can be treated only by fasting, therefore Food and Drug Administration (FDA) recommends IF as necessary therapy to mitigate the atrocious risks of cancer (Figure 2).[26]

TCA cycle metabolites can also be produced through glutamine in addition to glucose in tumour cells. Glutamine after converting to α-ketoglutarate can provide energy through substrate-level phosphorylation within the Krebs cycle.[27] Substrate level phosphorylation during glycolysis and Krebs cycle can provide sufficient energy for tumour cells having defective oxidative phosphorylation mechanism. Here ketone bodies further reduce the substrate level phosphorylation under hypoxia by reducing the activity of succinyl-CoA synthetase (SCS).[17,28] In this way ketone bodies indirectly play their role in tumour cell death by targeting the ATP production from glutamine metabolism.[29]

Another reason for cancer cell death is due to mitochondrial DNA mutation that results in defective inner mitochondrial membrane altering the proton motive gradient and ATP production even during oxidative metabolism. Moreover, β-hydroxybutyrate dehydrogenase that is involved in the first step of β hydroxyl butyrate to acetoacetate interacts with cardiolipin and other phospholipids in the inner mitochondrial membrane.[30] In a nutshell, the mitochondria of tumour cells are dysfunctional resulting in electrons transfer ineffectively coupled to oxidative energy production thereby generating an insufficient number of ATP through oxidative phosphorylation.[31]
Recently outcomes of rodent modelling experiments on cancer cell lines delineate that leptin has oncogenic, mitogenic, pro-inflammatory, and pro-angiogenic role in cell proliferation and anti-apoptosis in a variety of cells and inducer of cancer stem cells.\footnote{32} IF sharply reduces serum insulin-like growth factor – I (IGF-I) and leptin levels, and increases adiponectin that safeguards cell proliferation. IGF-I is a nutrient-responsive growth factor that initiates two main signalling pathways; Ras/MAPK and PI3K/AKT.\footnote{33,34} These two cascades are involved in proliferation and cellular growth by favouring the action of transcription factors and succeeding gene expressions. Activation of PI3K/AKT route favours reduced apoptosis by interfering with Bcl-2-associated death promoter complex, enhances the protein production through mTOR initiation, and elevates glucose metabolism by suppressing GSK-3 β supporting the tumour proliferation.

Working antagonistically to IGF-I mediated activation of mTOR, AMP-activated protein kinase (AMPK) under IF regimen behaves as a molecular sensor that enhances catabolism and suppresses anabolism thereby initiating apoptosis in cranial cancer cells lines and safeguarding the normal cells from strain.\footnote{35} AMPK triggers SIRT1 metabolism regulator gene expression that results in augmented fatty acid oxidation and glutaminolysis and delivering intermediary substrates for energy production when glucose is unavailable.\footnote{36}

Some scientific studies have reported AMPK/mTOR possess autophagy regulatory ability that results in the packing of macronutrients and organelles in doubled- membrane structures and

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\caption{Overview of ketone synthesis and metabolism.}
\end{figure}
degraded into micro-components that may be utilized in a variety of metabolic cascades.\textsuperscript{[37]} The autophagy is believed to be a tumour oppressive due to abnormalities in autophagy drive oxidation stress, defective mitochondria, damaged DNA, genomic instability and tumour growth.\textsuperscript{[38]} Alternatively, it is thought to be involved in tumour proliferation as tumours can exploit autophagy to decrease oxidative stress and enhance mitochondrial functionality to promote cell survival and overcome stress in low nutrient conditions.\textsuperscript{[39]} Owing to the dual nature of autophagy it has become the subject of mutual interest in cancer controlling therapies.\textsuperscript{[40]}

In a variety of preclinical and human efficacy trials, IF is suggested to suppress the inflammatory response cascades. Under IF regimen amount of adipose tissue the main endocrine organ is reduced that produces pro-inflammatory factors like leptin, adiponectin, monocyte chemoattractant protein-1, tumour necrosis factors, and interleukin-6. These human studies have associated IF with decreased adiposity and low inflammatory adipose secretome together the with reduced systemic pro-inflammatory adipokines levels.\textsuperscript{[41]} Moreover, IF is known to steadily decrease the pro-angiogenic factors vascular endothelial factor expression and plasminogen activator inhibitor-1, these two provide oxygen and glucose to the growing cancer cyst by inducing growth of new blood vessels.\textsuperscript{[42]} IF is also responsible for reducing inflammatory gene expression in cancer cells, including nuclear factor kappa B and peroxisome proliferator-activated receptors mostly expressed in tumour cells playing their role in inflammation regulation, proliferation and glucose and lipid homeostasis.\textsuperscript{[43,44]}

**Antihypertensive perspective**

In different in vitro studies IF has proved to mitigate the risk factors involved in cardiovascular diseases and stroke. Cardiovascular diseases and stroke have been associated with impaired glucose hemostasis (insulin resistance) resulting in elevated blood glucose level and insulin. In different in vitro studies on rodent modelling IF improved insulin sensitivity. Elevated low-density lipoprotein and low level of high-density lipoprotein cholesterol also increase the risk of atherosclerosis and stroke.\textsuperscript{[45]} Recently fasting studies conducted in human subjects have shown to decrease LDL and the increase HDL levels, as indicated by reduced oxidative modification of proteins and DNA and decreased the level of lipid peroxidation in the heart.\textsuperscript{[46]} Fasting is known to reduce oxidative stress in the cardiovascular system. It also minimizes the inflammatory process that contributes to atherosclerosis, indicated by reduced levels of leukocytes and circulating levels of tumour necrosis factor and other inflammatory cytokines.\textsuperscript{[47]}

Hypertension is another major contributor to coronary heart diseases. Fasting reduces the resting heart rate and blood pressure (both systolic and diastolic) in experimental rodents.\textsuperscript{[48]} It also improves the cardiovascular stress-bearing capacity in the rodents, due to the activation of the stress-responsive hypothalamic pituitary adrenal neuroendocrine system as indicated by an increase in plasma adrenocorticotropic (ACTH) and corticosterone levels.\textsuperscript{[49]} The scientists have discovered two main effects of IF in promoting cardiovascular stability that is a decreased oxidative radical production and increased cellular stress resistance.\textsuperscript{[50]} In a recent study oxidative damage to protein, lipids and DNA was observed to be reduced in rodents maintained on IF than rodents fed on an ad libitum diet.\textsuperscript{[51]} Oxidative stress is responsible for the ischemic injury to cardiac myocytes that results in atherosclerosis.\textsuperscript{[42]} IF initiates the release of protein chaperones heat-shock protein 70 and glucose-regulated protein 78 these proteins are produced in response to the stress during the IF and involve in the repair of cells by performing chaperone function and stabilizing new proteins to ensure correct folding or by helping to refolding proteins that were damaged by the cell stress.\textsuperscript{[52]} IF imparts antihypertensive effect by autonomic modulation of vascular smooth muscles and cardiac myocytes.\textsuperscript{[53]}

IF decreases the blood pressure by reducing the activity of the sympathetic nervous system. The blood pressure and heart rate are also affected by the decreased production of catecholamines (norepinephrine and epinephrine) as IF decrease the level of dopamine beta-hydroxylase (the enzyme required for the production of catecholamines).\textsuperscript{[54]} Blood pressure may also be modulated
by the effect of IF on hypothalamic-pituitary neuroendocrine pathways. The ACTH and corticosterone levels are increased by the stress during IF and improve the cardiovascular system.\cite{55}

In a recent study IF has shown to be effective against cardiac hypertrophy by recovering the biomarkers like cardiac sarcomeric α-actin, β-MHC and elevated brain natriuretic peptide (BNP) responsible for cardiac adenomegaly.\cite{56} Furthermore, the age-linked increase in left ventricle weight and cross-sectional area of individual cardiomyocytes are improved by IF. The ameliorative role of IF is achieved by restoring over activated ERK1/2 and PI3K γ signalling, these two are responsible for pathological cardiac hypertrophy.\cite{57} Moreover, the oxidative stress, fibrosis and inflammation in the ageing heart are reported to be attenuated by IF.

It has been validated through rodent modelling experiments that IF has the capacity to mitigate the risk factors for coronary heart disease like blood pressure abnormalities, variation in heart rate and reduction in insulin levels. The beneficial role of IF against coronary heart diseases is attributed to modulations of adipokines. In many animal studies IF has successfully modified many prominent risk factors associated with CVD and stroke. The experimental subjects with the compromised glucose controlling mechanism, that is solely associated with increased plasma glucose and insulin are more prone to CVDS and stroke.\cite{58} In all the experimental trials IF decreased the threat of diabetes and CVDs by enhancing the insulin sensitivity. The occurrence of CVD and stroke are directly linked with the elevated level of low-density lipoprotein (LDL) cholesterol and decreased levels of high-density lipoprotein (HDL) cholesterol. Some studies on human subjects elucidated that IF can significantly lower down LDL cholesterol, whilst elevating the HDL cholesterol levels.\cite{59} These studies also showed a decrease in plasma reactive oxygen species (ROS) levels during IF regime, as depicted by reduced oxidative modification of proteins and DNA and reduced lipid peroxidation in heart tissues.\cite{60} IF decreases the level of leukocytes and circulating tumour necrosis factor and other inflammatory cytokines resulting in promoting inflammatory responses that probably contribute to atherosclerosis.\cite{61} IF by reducing the progression of atherosclerosis IF plays a major role in reducing the risk of CVD and stroke. Hypertension is the major contributor in CVDs and stroke.\cite{62} IF momentously decreases the resting blood pressure (BP) (both systolic and diastolic) and resting heart rate (HR). It recovers cardiovascular stress adaptation. IF dietary regime elevates the plasma ACTH and corticosterone levels by activating stress responsive hypothalamic-pituitary neuroendocrine system during immobilization stress.\cite{63}

**Biomarkers of oxidative stress**

The human body is equipped with a natural defence mechanism against the hurtful effects of ROS, the disparities between ROS and antioxidant production is known as oxidative stress. It is a major culprit in a wide range of human maladies like cancer, CVDs, neurological disorders, hepatic necrosis and even the physiological ageing process.\cite{64}

ROS are produced as byproducts during energy generation within the mitochondria through electron transport chain (ETC). The free electrons escape from complex I or II of the ETC reduces oxygen (O$_2$) to superoxide (O$_2^-$).\cite{65} Normally it is converted by copper-zinc superoxide dismutase localized in cytosol and manganese superoxide dismutase found in mitochondria to hydrogen peroxide (H$_2$O$_2$). This H$_2$O$_2$ produced may follow two paths depending upon the cellular environment firstly being cytotoxic it is rapidly changed into water through catalase and glutathione peroxidase secondly it can be converted to highly reactive OH through iron-catalyzed Fenton reaction.\cite{66} This highly reactive OH produces 4-hydroxynonenal (HNE) by the lipid peroxidation of unsaturated fatty acids that binds with the membrane proteins and impairing the cellular function (Figure 3).\cite{67}

The production of ROS in mitochondria is directly linked with mitochondrial potential ($\Delta$$\psi$), hyperpolarization facilitates the ROS synthesis. The background cascade of this phenomenon is the changed redox potential of ETC carriers (reduced) and an enhanced semiquinone anion half-life.\cite{68} Alternatively, ETC is unable to shift protons out of the mitochondrial matrix (against the proton
concentration gradient) when the mitochondrion is hyperpolarized (high $\Delta \psi$), this results in intermediates remain reduced longer and enhancing the probability that the electrons outflow from these intermediates, reducing oxygen and increasing ROS.\textsuperscript{[69]} As the amount of ROS generation primarily depends upon mitochondrial polarization, therefore even a slight decrease through proton permeability across the mitochondrial inner membrane (uncoupling) can reduce ROS.\textsuperscript{[70]} This proton permeability can be increased by endogenous mitochondrial uncoupling mediated by uncoupling proteins (UCPs). UCPs are sensitive to ROS and ATP levels as they are inhibited by purine nucleotides and activated by FFAs and O$_2^-$. Recent scientific outcomes have justified that functions and expressions of UCPs are upregulated by fasting during which fatty acids are produced via beta-oxidation within the mitochondrial matrix (Figure 4).\textsuperscript{[71]}

There are two possible pathways for uncoupling the ETC from ATP production through UCP assisted proton translocation. The first suggested pathways elucidate that protonated free fatty acids
flip-flop across the inner membrane (left side of Figure 5) by using UCPs as a platform. The second possible mechanisms state that free fatty acids activate UCPs that form pore through which protons can then flow (right side of Figure 5). Both of these ROS dependent pathways serve as an endogenous anti-ROS mechanism.

In a recent animal study, it has been proposed that ROS generation is facilitated by elevated blood glucose levels as increased plasma glucose level contribute in glycation of proteins and lipids peroxidation, resulting in the formation of advanced glycation end products (AGEs). Different tissues and cell types including endothelial cells, vascular smooth muscle cells and macrophages contain receptors for AGEs (RAGE). AGEs on binding with RAGE result in ROS production that is further involved in complex cytotoxic cascades.

IF results in a momentous increase in the superoxide dismutase (SOD) levels and malondialdehyde (MDA) levels in hyperglycemic subjects. Recently silent information regulator 2 (Sir2)-family proteins (sirtuins) are reported to affect the apoptosis in response to DNA damage and oxidative stress. Sirtuins are Class III protein deacetylases conserved from prokaryotes to mammals. In vitro and in vivo studies sirtuins have shown to bind and deacetylate p53, and they target many proteins that are not histones. P53 activation results in cell cycle arrest, and the initiation of apoptosis and autophagy. In response to DNA damage and oxidative stress, sirtuins are overexpressed and have shown to inhibit p53 dependent apoptosis. In a recent study conducted in diabetic subjects overexpression of p53gene resulted in apoptosis. However, the expression of p53 was momentously decreased in the diabetic subject on IF retro. It is assumed that the activation, as well as expression of the p53 gene, is mediated by Sir2 dependent deacetylation. Under IF regime the Sir2 expression is reduced and at the same time, p53 is up-regulated. Alterations in p53 expression in diabetic subjects kept on IF regimen elucidates the contribution of anti-apoptotic pathways. Caspases are a family of protease enzymes playing essential roles in programmed cell death and inflammation, caspases when activated initiate a chain reaction of events resulting in cleavage of PARP and self-autolysis producing 20 kDa fragment indicating apoptosis. The cleavage of 20 kDa fragment is distinctively decreased in diabetic subjects following IF regime. It is still unclear that how IF exerts anti-apoptotic effect but a decrease in caspase-3 cleavage and suppression and activation of p53 and Sir2 respectively propose a cross-link between Sir2, p53 and caspase-3. Another stress-activated protein kinase p38 was also identified in diabetic subjects; it is also known to up-regulate the apoptotic cell death. Interestingly, IF decreases the expression of p38 in diabetic subjects with elevated p38 expression. P38 Mitogen-activated protein kinase (MAPK) cascade induces phosphorylation of histone H3. The diabetic subjects on IF regime showed decreased in phosphorylation of histone H3.
Insulin sensitivity

A great deal of available scientific data on animal studies proposes that IF improves the insulin sensitivity. The extended duration of fasting or exercise shifts liver, cardiac tissues and skeletal muscles to fat oxidation and amino acid catabolism, while well-fed state facilitates the metabolic pathways of glucose uptake and oxidation.\textsuperscript{[78]} The two hormones glucagon and insulin along with transitions in cytological levels of metabolites like fatty acids, pyruvate, citrate and malonyl CoA (regulates mitochondrial enzymes) regulate the mutual fat and glucose oxidation systematically this systematic fat and glucose switching is commonly known as metabolic flexibility.\textsuperscript{[79]} During the period of physiological stress and nutrient availability if the body successfully shifts between fat and glucose oxidation, then the body energy metabolism is considered to be optimum.\textsuperscript{[80]} This switching in energy metabolism is responsible for sustaining metabolic well-being and ideal cellular activities.\textsuperscript{[81]} Overfed individuals cannot easily switch between fat and glucose oxidation and therefore experience metabolic inflexibility.\textsuperscript{[82]} The mitochondrial functioning is disturbed by the production of ROS, ceramides, diacylglycerols and acylation of mitochondrial proteins due to simultaneous oxidation of fat, glucose and amino acids. The irregularities in metabolic flexibilities are thought to be the main reason for insulin resistance.\textsuperscript{[83]} IF up-regulates the genes responsible both for lipid storage (PPAR\textsubscript{γ}\textsubscript{2} and Fsp27) and fat oxidation (MCPT1) elucidating optimal metabolic flexibility with enhanced fat oxidation during fasting period and lipogenesis on non-restricted retro of IF.\textsuperscript{[84]} The adipocyte variation and expression of adipocyte regulatory genes is controlled by a transcription factor peroxisome proliferator-activated receptor- γ (PPAR\textgamma).\textsuperscript{[85]} This transcription factor has two isoforms i.e PPAR\textgamma\textsubscript{1} and \textgamma\textsubscript{2} resulting from alternate merging and having ligand-dependent and independent initiation sites.\textsuperscript{[86]} PPAR\textgamma\textsubscript{2} contains ligand-independent activation domain owing to the presence of additional 28 amino acids at its amino end making it more effectively foldable than that of PPAR\textgamma\textsubscript{1}.\textsuperscript{[87]} The ligand-independent activation of PPAR\textgamma\textsubscript{1} and \textgamma\textsubscript{2} is stimulated by insulin, conversely, obesity and nutritional factors only influence the PPAR\textgamma\textsubscript{2} expression in human adipocytes.\textsuperscript{[88,89]} Martinez et al.\textsuperscript{[90]} reported that a common Pro12Ala replacement in PPAR\textgamma\textsubscript{2} is associated with lower body mass index (BMI) and improved insulin sensitivity among middle-aged and elderly subjects.

Insulin resistance and type 2 diabetes may be initiated due to irregularities in adipose tissue metabolism.\textsuperscript{[91]} Fatty acids and eicosanoids may initiate the stimulation of target genes responsible for adipocyte differentiation and glucose homeostasis by binding to PPAR\textgamma.\textsuperscript{[92]} PPAR\textgamma gene is responsible for encoding PPAR\textgamma it is 100 kb long and is composed of 9 exons. A C→G variant (creating an Hgal site) envisages the exchange of Ala for Pro at location 12 in the PPAR\textgamma specific exon B, and a synonymous C→T replacement in exon 6. Previously an association between the synonymous polymorphism and leptin levels was observed among the obese individuals.\textsuperscript{[93]}

Conclusion

Intermittent fasting is a promising strategy among different approaches of fasting such as caloric restriction, dietary restriction and intermittent fasting. Intermittent fasting has proved the most fruitful approach for its ability to cope up with different diseases such as cancer, diabetes, antioxidant stress, cardiovascular diseases, renal diseases and blood pressure through various in-vivo and in-vitro studies. Moreover, intermittent fasting resulted in prolong lifespan. However, further research is needed with respect to health claims of intermittent fasting in humans and animals.

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