

## A SYSTEMATICAL REVIEW OF THE EFFECT OF KETOGENIC DIET ON BCL-2 EXPRESSION AS AN APOPTOSIS MARKER IN CANCER TREATMENT

### ABSTRACT

**Summary :** Currently, a lot of people are interested in consuming ketogenic diet, and it also exhibited several beneficial effects, including as cancer prevention. However, there is still unclear detail mechanism of it yet. Therefore, this systematical review is conducted. 25 articles were identified from PubMed, 18 of these articles were excluded according to inclusion and exclusion criterias. Remaining 7 articles were proceeded to data extraction. As the result, Bcl-2 expressions in high-fat diet mostly found lower compare to the control group. This result indicates that the possible mechanism of how ketogenic diet affects cancer is through inducing apoptosis process. Hence, ketogenic diet can be helpful as cancer prevention or treatment.

**Background :** Currently, a lot of people are interested in consuming ketogenic diet. It is also found that ketogenic diet shows several beneficial effects, one of them is to be used as cancer prevention. However, the detail mechanism is still remain unknown.

**Objectives :** To find out the effect of ketogenic diet on Bcl-2 expression in cancer.

**Method :** Literatures from PubMed that published in 2011-2020 were searched using specific keywords. Then these literatures were filtered according to inclusion and exclusion criterias. Animal model, total sample size, underlying condition/inflammatory process occurred, details of the intervention/diet including diet contents in control group and high-fat group, and the duration of the intervention, Bcl-2 results, and p-value were extracted.

**Results :** 7 studies were included in this systematic review. Bcl-2 expression shows a decrease in 5 out of 6 studies. Similar result is also obtained in Bcl-2 protein level, which measured by western blot. Bcl-2 protein level shows a decrease in 2 out of 3 studies.

**Conclusion :** This study shows that high-fat diet that is contained in ketogenic diet most likely to decrease Bcl-2 expression. Thus, ketogenic diet will affect cancer progression by inducing apoptosis process.

**Keywords :** *ketogenic diet, cancer, Bcl-2, systematic review*

### List of Abbreviations

3'-UTR binding : Three Prime Untranslated Region  
Apaf-1 : Apoptotic Protease Activating Factor-1  
ASP : Associated Speck-like Protein  
BAD : Bcl-2 associated death promoter  
BAFF : B-cell activating Factor receptor  
BAK : Bcl-2 homologous antagonist/killer  
BAX : Bcl-2 Associated X protein  
Bcl-2 : B-cell lymphoma-2  
Bcl-xL : B-cell lymphoma-extra large  
BH-3 only protein : Bcl-2 Homology-3 only protein  
BID : BH-3 interacting domain death agonist  
BIK : Bcl-2 Interacting Killer  
BIM : Bcl-2-interacting mediator of cell death  
BMF : Bcl-2 Modifying Factor  
BOK : Bcl-2 related Ovarian Killer  
CBP : CREB Binding Protein  
CREB : cAMP Response Element Binding Protein  
DNA-PK : DNA-dependent Protein Kinase  
FADD : Fas associate protein with Death Domain  
GLUT-1 : Glucose Transporter-1  
GLUT-3 : Glucose Transporter-3  
GTP : Guanosine Triphosphate  
HIV : Human Immunodeficiency Virus  
HPV : Human Papilloma Virus  
HRK : Harakiri/Bcl-2 Interacting Protein  
IKK : I $\kappa$ B Kinase  
IL-1 : Interleukin-1  
I $\kappa$ B : Inhibitor of  $\kappa$ B  
LGIT : Low Glycemic Index Treatment  
MAD : Modified Atkins Diet

Mcl-1 : Myeloid-cell lymphoma-1  
MCT : Medium Chain Triglyceride  
Mdm-2 : Murine Double Minute-2  
miR-429 : micro RNA-429  
MPT : Mitochondrial Permeability Transition  
mTORC2 : Mammalian Target of Rapamycin Complex 2  
NADPH : Nicotinamide Adenosine Dinucleotide Phosphate  
NF- $\kappa$ B : Nuclear Factor kappa B  
PARP : Poly ADP-Ribose Polymerase  
PDK-1 : 3-phosphoinositide-dependent protein kinase-1  
PI3K : Phosphatidylinositol 3-Kinase  
PIP-2 : Phosphatidylinositol-4,5-bisphosphate  
PIP-3 : Phosphatidylinositol-3,4,5-bisphosphate  
PMAIP-1 : Phorbol-12-myristate-13-acetate inducing protein-1  
PUMA : p53 Upregulated Modulator of Apoptosis  
RANKL : Receptor Activator of NF- $\kappa$ B ligand  
ROS : Reactive Oxygen Species  
RTK : Receptor Tyrosine Kinase  
TNF : Tumor Necrotic Factor  
TNF-R1 : Tumor Necrotic Factor Receptor type 1  
TRADD : TNF-R1 associated Death Domain Protein  
TRAIL : TNF-related apoptosis-inducing ligand  
VLCKD : Very Low Carbohydrate Ketogenic Diet