

LOW GLYCEMIC INDEX FOOD AND FOOD PRODUCTS- FANTASY OR REALITY?

Manvi Patni^{1*}, Dr. Monika ²

¹Research Scholar, Tantia University, Sriganganagar, Rajasthan, India

²Associate Professor, Tantia University, Sriganganagar, Rajasthan, India

*Corresponding author: dt.manvipatni13@gmail.com

ABSTRACT

Glycemic index (GI) is the ranking of food based on the post prandial blood glucose after consuming a carbohydrate rich diet whereas glycemic load (GL) or glycemic stack of sustenance is a number that evaluates how much the food would raise a person's blood glucose level after consumption. Very little is known about the effects of carbohydrates, specifically any association between glycemic index/glycemic load and diseases. The Carbohydrates which are slowly digested, absorbed and metabolized in the human body are classified as low GI foods (55 or less) leading to slow rise in the blood glucose and therefore insulin whereas carbohydrates with a high GI (>70) value leads to hyperglycemia. The constructive and destructive health effects of dietary carbohydrates are of concern to both scholars as well as shoppers. Many supportive evidences have been discussed which highlights the significant link between GI/GL and risk for diabetes mellitus, cardiovascular disease, retinal disorders and the recent being acute macular degeneration. The intent of this review is to critically analyze the scientific evidence on the role of GI in human body and how is it interconnected to several metabolic diseases such as CVD's, cancer, diabetes mellitus, retinal disorders. GI may serve as a practical criterion to assist people in order to opt healthy choices.

Key words: Glycemic index; glycemic load; hyperglycemia.

INTRODUCTION

In the modern era, people are very much dependent upon fast food, processed food and packaged material. Fast food are not only easy to make but are also –fast to our body's digestive system and can directly or indirectly disturb our metabolism leading to decrement in the chances of weight loss and ultimately damages overall health ^(1,2). A balanced diet comprises of many nutritious elements such as carbohydrates, proteins, fats and fibers. Each component performs different functions which are directly or indirectly involved in the growth and maintenance of the body ⁽³⁾.

The consumption of carbohydrate based diet is a widely accepted practice. Carbohydrate consumption has increased in the last few years in western countries following to the advice of consuming minimal fats especially the saturated one ⁽⁴⁾. Carbohydrates serve as energy sources (starch and glycogen), they are the components of coenzymes and the part of nucleic acids ⁽⁵⁾. It is a form of glucose which acts as a fuel for the body and provides energy leading to smooth functioning of all the metabolic activities taking place in the body. It is a major macronutrient contributing to 65-70% of the total energy ⁽³⁾. It is not only used for satisfying hunger but also to

fulfill the nutritional requirements of the individual and to optimize the performance ⁽⁶⁾.

Dietary starches have been subjected to negative exposure after the growing popularity and huge demand of high protein diets for weight reduction; the recent findings suggest that starches might be more terrible than immersed fats for cardiovascular disease (CVD) hazard ⁽⁷⁾. People who desire to experience permanent, healthy weight loss or those affected with diabetes mellitus can get benefit from consuming food stuffs according to a system of ranking called glycemic index ⁽⁸⁾. Foods with high glycemic index are known as fast carbohydrates as they break down in the body quickly, leading to sudden hike in blood sugar levels. Some foods have high carbohydrate content (pasta, pizza etc.) whereas other food stuffs (maize, red gram, peas etc.) have low level of carbohydrates ⁽⁹⁾.

These carbohydrates release glucose after the complete absorption. The released glucose is used up for the metabolic processes and the remaining glucose is stored in the form of glycogen in the liver. Excessive consumption of carbohydrates leads to hyperglycemia i.e. increased glucose level in the blood and blood insulin depending upon the type of carbohydrate consumed i.e. complex or simple, amount, processing method and presence of other nutrients ⁽¹⁰⁾. The concept of glycemic index (GI) was evolved by Jenkins and his colleagues in 1981 for management of glycemic control in patients with Diabetes Mellitus type 2 (DM2). Glycemic index is a ranking of foods based on the postprandial blood glucose response compared with the reference food ⁽¹¹⁾. It is a method of classifying and arranging the carbohydrate content of the individual food according to their postprandial glycemic effects and their after effects on blood insulin levels ^(10, 12, 13, 14). GI has proved to be applicable nutritional notion, providing new cognizance into the relationship between the food consumed and its after effect. GI would also develop the interrelation between food and chronic diseases ^(10, 15, 16, 17, 18,19). GI is calculated by area covered by blood glucose within 2 hours of post consumption of 50g available carbohydrate divided by the amount of control food (white bread), multiplied by 100 ^(20, 21). GI is a property of the sustenance itself. Sustenances having sugar that is processed, retained and utilized rapidly are viewed as high GI sustenances ($GI \geq 70$ on the glucose scale) while those that are utilized, ingested and processed gradually are viewed as low GI sustenances ($GI \leq 55$ on the glucose scale).

$$GI = \frac{\text{area covered by blood glucose (2 hours of consumption)}}{\text{amount of control food}} \times 100$$

According to Ray *et al.*, (2011) Glycemic Load is a result of GI and the aggregate accessible sugar

$$\text{Glycemic load} = \text{glycemic record} \times \text{total sugars accessible} \div 100$$

content in a given measure of sustenance (GL = GI x accessible starch/given measure of sustenance). ⁽²²⁾

Glycemic record and glycemic stack changes from nourishment to sustenance. For instance watermelon has a high GI and low GL esteem ⁽¹⁴⁾. **Table 1** indicates the classification of GI and GL on the basis of their post prandial glucose release. A similarity has been noted between the lifestyle risk factors for insulin resistance like obesity, lack of physical activity, high intakes of refined carbohydrates and the major chronic diseases, signifying the hypothesis that hyperinsulinemia may be one of the encouraging factors for conditions such as cancer, diabetes etc. ⁽²³⁾. Epidemiological evidence suggests direct associations between GI and risk of diabetes ⁽²⁴⁾, CHD ⁽¹⁷⁾ as well as obesity and CVD ⁽²⁵⁾. Evidences also highlighted the possible link with cancers of the colon ⁽²⁶⁾, breast ⁽²⁷⁾ and pancreas ⁽²⁸⁾. The blood glucose may also be affected by other physiological and nutritional factors, which include the digestibility of the starch, interactions of the starch with protein, the amounts and kinds of fat, sugar and fiber, the presence of other constituents, such as molecules that bind starch, and the level and type of the food processing ⁽²⁹⁾. A wide range of food processing methods and cooking methods is being used for different food materials. These methods influence the food structure and nutritional properties of food including starch digestibility, resistance starch, glycemic load and glycemic index ^(30, 31). The intent of this review is to critically analyze the scientific evidence on the role of glycemic index (GI) in human body and how is it interconnected to several metabolic diseases such as CVD's, cancer, diabetes mellitus etc.

Starch digestibility and starch composition

Starch which is a major contributor in normal diet contributes approximately 70-80% of the total carbohydrates in the diet regardless of therapeutic diets ^(32, 33). Starch is structurally composed of 2 major units (amylose and amylopectin). Amylose consists of 15-20% of starch whereas amylopectin consists of 75-80%. Amylose is a linear polymer of α -D glucose units possessing α -1, 4 glycosidic bonds whereas amylopectin is a branch chain polymer of α -D glucose units linked by α -1, 4 and α -1, 6 glycosidic linkages ⁽³⁴⁾. Processing condition (explosion, puffing, extrusion and instantiation) along with the state of starch strongly influence the nutritional quality of the same. Instantisation increases digestibility even in high amylose starches whereas puffing increases digestibility due to gelatinization, weakened and porous structure ⁽³⁵⁾. The capacity of the starch to release glucose and the time required for its digestion are the major physiological properties of starch ⁽²⁹⁾. Amylose (linear starch): amylopectin (complex starch) ratio significantly affects the starch digestibility ⁽³⁶⁾. On the basis of their rate and degree of digestion, starch can be classified into 3 categories namely rapidly digestible starch (RDS), slowly digestible (SDS) and resistant starch (RS) ^(29, 37, 38, 39). Hypothetical mechanism of RDS, SDS and RS has been explained in **Figure 1**.

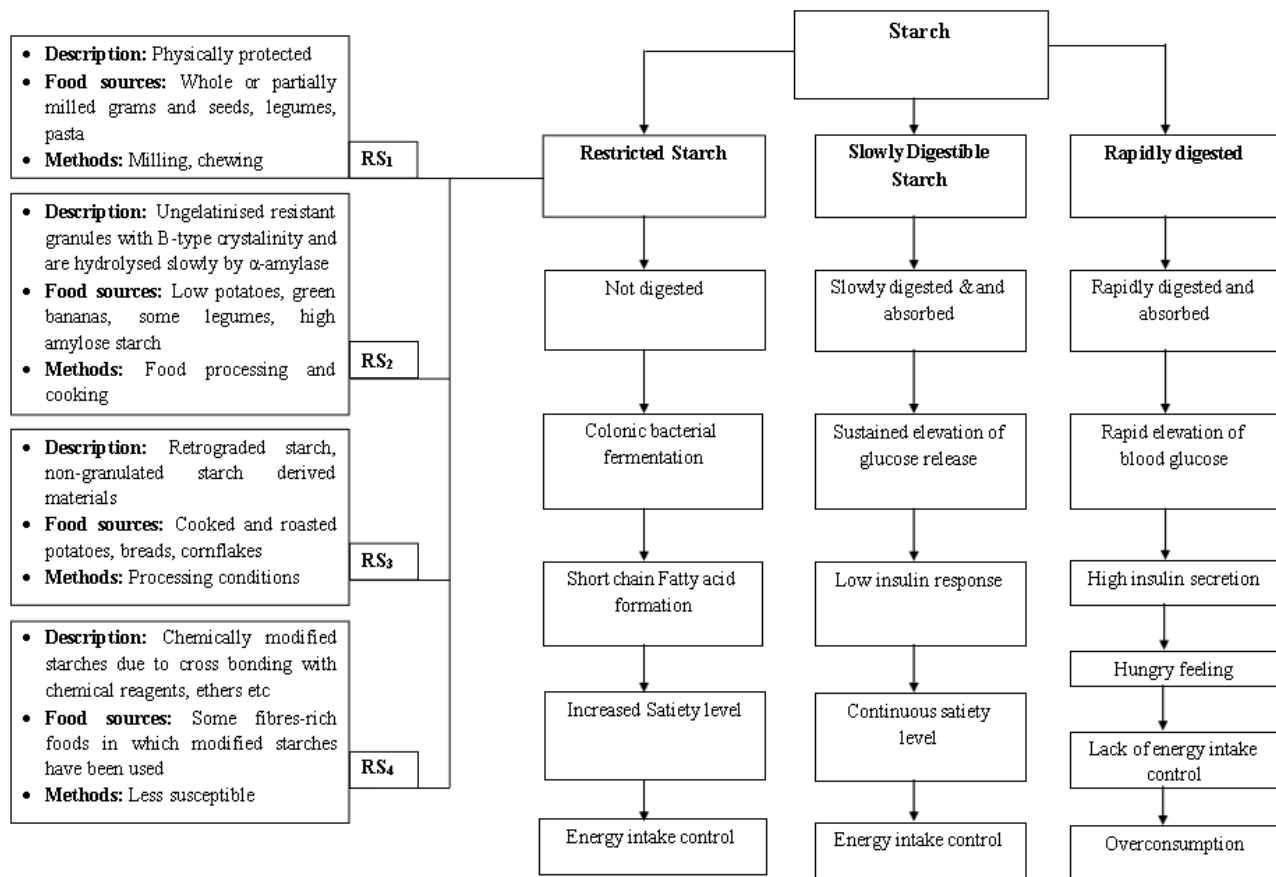


Figure 1- Hypothetical mechanism of slowly digestible starch (SDS), rapidly digestible starch (RDS), resistant starch (RS) along with resistant starch 1,2,3,4 and the methods affecting their resistance.

RDS is the measure of glucose discharged during hydrolysis after 20 min in mouth and small digestive tract. The structure of this starch is formless, fast wellspring of vitality and thus is the most quickly absorbed ⁽³⁴⁾.

SDS is the measure of glucose discharged during the process of hydrolysis in the vicinity of 20 to 120 min in small digestive system. Structure of this starch is undefined and it gives moderate and sustained vitality and also controls the measure of glucose. Examples of this starch are local maize starch, millet, vegetables and so forth as these gradually increase the blood glucose level. Thus it is also known as gradually absorbable starch ^(34, 40).

RS is acquired from the hydrolyzed starch subtracted from the aggregate starch within 120 minutes of consumption in the digestive tract. Due to its crystalline structure it has a solid impact on gut along with its anti-carcinogenic functions. Examples are crude potato, staled bread and so on ⁽⁴⁰⁾.

$$RS = TS - (RDS + SDS)$$

Resistance of starch

Resistant starch refers to the sum of starch and product of its degradation undigested in the small intestine of human beings. Ungelatinized granules from potatoes, high amylose maize and green bananas are ineffectively processed. Starch made impervious to amylase because of new covalent ties, shaped at warm treatment or present in starch subsidiaries utilized as nourishment added substances, may likewise be pretty much indigestible⁽⁴¹⁾. Amylose-lipid complexes appear to be totally caught up notwithstanding their imperviousness to amylase debasement in vitro. There are 4 types of resistant starches⁽⁴²⁾ such as Type 1, 2, 3 and 4 resistant starches. Type 1 resistant starch is the one which is at the point when the amylolytic chemicals have no entranceto starch aggregation in the undamaged plant cells prompting physically inaccessible starch. It is because of the fact that the GI tract needs compounds which are equipped for debasing the parts of plant cell dividers but human gut lacks these enzymes. Type 2 resistant starch is the crude starch of some plant species (potato). Type 3 resistant starch is retrograded starch which is framed by the procedure of amylose substance of starch increments while Type 4 resistant starch is essentially a changed type of starch. It can be framed through the methods for compound or on the other manual physical change⁽⁴¹⁾. There are various factors which affects the starch digestibility, GI and GL of the food commodity. Major being particle size, fiber content-soluble and insoluble, nature of monosaccharide components (fructose, sucrose etc.), β glucan content, amylose content, cooking methods and ripeness⁽⁴³⁾. Various factors affecting rate of glucose reabsorption from starchy foods in blood has been discussed in **Table 2** along with the approach in which they could increase or decrease their release rate.

Table 2: recent studies on the incidents of Diabetes mellitus

Sample size (n)	Sex	Age (years)	Place of survey	Diagnosis method	Observations	References
9529	Both	45-64	America	Self-examination	1447 incidents of DM 2 were diagnosed in 9 years of study.	Steven <i>et al.</i> ⁽⁷⁷⁾
36787	Both	40-69	Australia	Self-examination	365 cases of DM2 were reported in the time duration of 4 years.	Hodge <i>et al.</i> ⁽⁷⁸⁾
91249	Female	24-44	America	Biochemical test	741 incidents of DM2 were diagnosed in 8 years of cohort study.	Schulze <i>et al.</i> ⁽⁷⁹⁾
13110	Female	24-44	America	Self-examination	1428 women with gestational diabetes were diagnosed in 10 years study process.	Zhang <i>et al.</i> ⁽⁸⁰⁾
75512	Both	45-75	Hawaii	Biochemical test	8587 cases of diabetes were detected in 14 years long study with regular follow ups.	Hopping <i>et al.</i> ⁽⁸¹⁾
64227	Female	40-70	China	Biochemical test	1608 cases of diabetes were diagnosed in 5 years of follow up cohort study. Dietary CHO was solely related with the chances of developing DM2.	Villegas <i>et al.</i> ⁽⁸²⁾
40078	Female	21-69	America	Biochemical test	1938 cases of DM2 were detected in average 8 years follow up study. GI was directly related with the incidence of developing DM2.	Krishnan <i>et al.</i> ⁽⁸³⁾

DIET-DISEASE RELATIONSHIP

GI and Weight loss

Weight reduction is known to be associated with broad changes in blood lipids and other fiery biomarkers such as Triglyceride's levels, elevated Renal Function Tests (RFT's) etc. ^(44, 45).

Gogebakan *et al.*, (2011) carried out a DiOgenes (Diet, Obesity and Genes) ponder configuration isolate impacts from weight reduction from those because of various dietary admissions in weight upkeep period. The connection among GI, GL and body weight is an important factor. Weight gain and weight loss may require distinctive dietary methodologies as some weight reduction regimes have low or no starch as basic eating regimen column while others permit carbohydrates only if carbs are low GI/GL ⁽⁴⁵⁾. Many studies confirm that the more prominent weight reduction happens for the time being when calorie counters utilize a low GI and GL technique contrasted with other eating regimen methodologies ^(11, 46). Insulin affectability and weight reduction go hand in hand and thus these are independent of diet composition. In short, bringing down the glycemic stack and glycemic list of weight lessening diets does not give any additional advantage to vitality confinement in advancing weight reduction in overweight subjects. But when calories are entirely controlled, the GI or GL of the acting routine has no effect ⁽⁴⁷⁾. Low GI nourishments are possibly helpful for weight control. They incorporate the capacity to advance satiety and defer hunger, lessen changes in glycaemia, insulinaemia, advances the rates of fat oxidation(increases)and limit decreases in metabolic rate amid vitality limitation ^(48, 49).

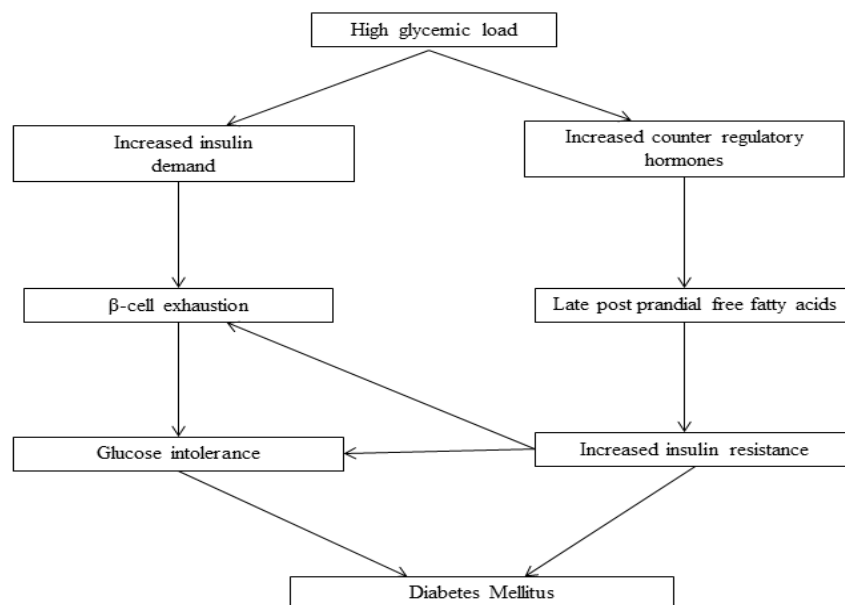
GI and Diabetes

In sedentary middle-aged men with one or more traditional cardiac risk factors, a high-GI, high carbohydrate diet was associated with the least favorable postprandial profile, whereas the low GI, high-carbohydrate diet had the most favorable profile ⁽⁵⁰⁾. In another study conducted by Steven *et al.*, (2002) for over a time span of 9 years 1447 incidents of diabetes were observed and after low-GI diet, improvement in glycemic control, glucose use, some lipid profiles, and the capacity for fibrinolysis in type 2 diabetes were observed. Results of a 2004 meta-analysis support the use of the GI as a scientifically based tool to enable selection of carbohydrate- containing foods to reduce total cholesterol levels in order to improve overall metabolic control of diabetes ⁽⁵¹⁾. In summary, a low GI diet has been found to help with weight management, to improve insulin sensitivity and glycated hemoglobin level, and to reduce the overall risk of type2 diabetes. According to Chiasson *et al.*, (2002) use of acarbose also reduces diabetes risk. Both here and now and in long haul considerations indisputably show that low GI diets enhance glycemic control in individuals with diabetes ^(50, 52, 53). Thus, Low-GI foods tend to delay glucoseabsorption by increasing the transit time thereby resulting in reduced peak insulin concentrations and overall insulin demand by the human body ⁽²⁷⁾. Recent studies based on GI diets and incidents of the same have been discussed in **Table 3**.

Table 3: recent studies showing the prevalence of CVD around the world on the basis of self-examination, biochemical test and medical history.

Sample size (n)	Sex	Age range (Years)	Place of survey	Sample used	Diagnosis method	Observations	References
646	Male	64-84	Netherland	wheat bread, cooked potatoes, fruit, milk, sugar	Medical history	Population based study, a high dietary glycemic index was not associated with an increased risk of coronary heart disease	Vandam <i>et al.</i> ⁽⁸⁴⁾
1209	Both	40-65	8 European countries	Low GI versus High GI protein	Self-examination and biochemical test	Consumption of low GI and energy restricted diet with high protein lead to decrease in initial weight and CRP	Gogebakan <i>et al.</i> ⁽⁸⁵⁾
18137	Female	45-56	America	Low GI and High GI foods	Biochemical test	GL and GI had direct link with the concentrations of lipids in blood such as HDL, LDL, VLDL and CRP (C reactive protein).	Levitane <i>et al.</i> ⁽⁸⁶⁾
82802	Female	30-55	America	Low GI versus High GI foods	Medical history	This study mainly suggested that with the intake of high fiber diet the chances of CVD can be reduced.	Halton <i>et al.</i> ⁽⁸⁷⁾
47749	Both	35-74	Italy	High GI foods- bread, sugar and jam, rice, pizza and low GI foods- pasta, fruit	Medical history	The risk of cardiovascular diseases was more prominent in women having high carbohydrate diet as that of Men	Sieri <i>et al.</i> ⁽¹⁰⁾
3959	Both	30-70	Denmark	Rye bread, potatoes, pastry, beer, soft drink, white bread	Medical history	GI had inverse relation heart problems in men. However, in women there was no significant relation between GI and heart diseases	Graue <i>et al.</i> ⁽⁸⁸⁾
121700	Female	30-55	America	Low and High GI foods	Medical history	1020 women had incident stroke, 515 had ischemic attack and 279 were identified with hemorrhagic stroke.	Oh <i>et al.</i> ⁽⁸⁹⁾
17357	Female	49-70	Netherlands	Low GI and High GI foods	Medical history	High GI foods lead to a total of 556 medical cases CHD and 243 cases of CVA.	Beulens <i>et al.</i> ⁽⁹⁰⁾

Hypothetical mechanism of high sugar levels and diabetes has been discussed in **Figure 2**.

**Figure 2-** Glycemic Index in relation to Diabetes Mellitus (Srilaxmi, 2012)

Hyperglycemia decreases the insulin efficiency by downcasting the insulin receptors resulting to insulin resistance. This condition acts as fatal by increasing the glucose concentrations in blood leading to more insulin secretions ⁽¹⁸⁾.

GI and CVD

In cardiovascular disease, dietary fats and lipids tend to receive the majority of attention. Carbohydrates having high GI, however, may not be the ideal alternative when fats are restricted ⁽⁵⁴⁾. Effects of a low-GI, low-GL diet on cholesterol appear to be most dramatic on triglycerides because there is less need for the liver to make this cholesterol to bind excessive glucose in the blood to be stored as fat ⁽⁵⁵⁾. Mixed meals containing slowly digestible carbohydrate that induce low glycemic and insulin responses reduce the postprandial accumulation of both hepatically and intestinally derived triacylglycerol rich lipoproteins in obese subjects with insulin resistance. In a study comparing a low-GI diet with legumes and fiber to a healthy American diet with no legumes and less fiber, the GI diet was associated with lower fasting total cholesterol and low density lipoprotein levels ⁽⁵⁶⁾. Postprandial hyperglycemia tends to elevate the risk of CVD by leading to oxidative stress ⁽⁵⁷⁾. GL appears to be an important independent predictor of high-density lipoprotein cholesterol in youth. Findings suggest that high intake of refined carbohydrates is associated with risk for hemorrhagic stroke, particularly among overweight or obese women. In addition, high consumption of cereal fiber was associated with lower risk of total and hemorrhagic stroke ⁽²¹⁾. An ad libitum low-GL diet may be more efficacious than a conventional, energy restricted, low-fat diet in reducing cardiovascular disease risk ⁽⁵⁸⁾. When saturated fats were replaced with carbohydrates with a low GI, there was a lower risk of myocardial infarction, but if saturated fat was replaced with carbohydrates possessing high GI, the risk was increased. A retrospective analysis of cardiovascular deaths in Denmark found that men who ate a high-GI diet were more likely to die of heart disease. In an Italian cohort (The EPICOR study), a high-GL diet increased the overall risk of cardiovascular disease in women but not in men.

Gogebakan *et al.*, (2011) examined the effect of low GI and protein diet in reduction the risk of cardiovascular disease. It is found in the study that low GI diet has effect on lowering the low density lipoproteins and triglycerides and low level of hsCRP (C reactive protein). He related the high level of C reactive protein as a mark of cardiovascular disorders and low grade inflammation. Study was designed for 26 weeks in 932 overweight adults with high protein and low glycemic index diet ⁽⁴⁴⁾. Various epidemiological proofs have been discussed in **Table 4** which kept high v/s low GI diet as the baseline.

Table 4: Studies based on low and high GI diet in context to various types of Cancer.

Sample size (N)	Sex	Age range (years)	Place of survey	Sample used	Type of cancer	Diagnosis method	Observations	References
10786	Female	34-70	Italy	Low GI and High GI foods	Breast cancer	Biochemical test	5 years of prospective study which resulted that high GI diet is linked with breast cancer in women having BMI <25 and 289 were diagnosed with breast cancer.	Sieni <i>et al.</i> ⁽⁹¹⁾
11576	Female	34-66	Denmark	Low GI and High GI foods	Breast cancer	Anthropometry & biochemical test	This study indicated that the high GL and GI diet has relation with increased in the risk of producing estrogen receptor in postmenstrual women.	Romieu <i>et al.</i> ⁽⁹²⁾
63307	Female	40-87	America	Low GI and High GI foods	Breast cancer	Medical history	According to this study glycemic index and load were not related with elevated the risk of postmenopausal breast cancer rate.	Jonas <i>et al.</i> ⁽⁹³⁾
12270	Female	40-69	Australia	Low GI and High GI foods	Breast cancer	Medical history	This study suggested the association of fiber, CHO and low grade estrogen receptor tumors.	Giles <i>et al.</i> ⁽⁹⁴⁾
49613	Female	40-59	Canada	Low GI and High GI foods	Breast cancer	Medical history	Overall glycemic index is not related with the breast cancer, high GI is directly proportional to breast cancer risk.	Silveira <i>et al.</i> ⁽⁹⁵⁾
2569	Female	23-73	Italy	Bread, cakes sweets fruits vegetables	Breast cancer	Medical record	This study showed the intermediate relation of GI and GL with breast cancer and role of high level of insulin in blood in breast cancer.	Augustin <i>et al.</i> ⁽⁹⁶⁾
62739	Female	40-74	America	Low GI and High GI foods	Breast cancer	Medical history	This study documented 1812 cases of breast carcinogens in 9 years of follow up study.	Lajouet <i>et al.</i> ⁽⁹⁷⁾
39227	Female	50-60	Sweden	Low GI and High GI foods	Breast cancer	Medical history	2952 cases of breast cancer were ascertained in this study.	Larsson <i>et al.</i> ⁽⁹⁸⁾
1166	Female	35-79	America	Salty and refined products	Breast cancer	Medical history	Women having BMI >25 are more prone to development of risk of breast cancer.	McCannet <i>et al.</i> ⁽⁹⁹⁾
4154	Both	19-74	Italy	Low GI and High GI foods	Colon-rectum cancer	Medical history	According to this study GI and GL of refined CHO were directly associated with the risk of colorectal cancer.	Franceschi <i>et al.</i> ⁽¹⁰⁰⁾
49124	Female	40-59	Canada	Low GI and High GI foods	Colon-rectum cancer	Medical history	In this 16.5 years of data study 616 cases of colorectal cancer were diagnosed which included 436 colon cancer and 180 rectal cancer.	Terry <i>et al.</i> ⁽¹⁰¹⁾
152536	Female	50-79	America	Low GI and High GI foods	Colon-rectum cancer	Self-examination	According to average of 11.3 years of study 1920 cases of colorectal cancer were diagnosed which composed of 1559 colon cancer and 361 rectum cancer cases.	Tabunget <i>et al.</i> ⁽¹⁰²⁾
131349	Both	Male 40-75 Female 30-55	America	Low GI versus High GI foods	Colon-rectum cancer	Medical history	1809 cases were detected with colorectal cancer.	Michaud <i>et al.</i> ⁽¹⁰³⁾
35197	Female	55-69	America	Low GI and High GI foods	Colon-rectum cancer	Medical history	An average 15 years of follow up 954 cases were diagnosed with colorectal cancer included 757 cases of colon and 209 cases of rectum cancer.	McCarlet <i>et al.</i> ⁽¹⁰⁴⁾
45561	Female		America	Low GI and High GI foods	Colon-rectum cancer	Medical history	490 cases were diagnosed with colorectal cancer.	Staryer <i>et al.</i> ⁽¹⁰⁵⁾
61433	Female	40-76	Sweden	Salty products refined grains	Colon-rectum cancer	Medical history	In this study 870 cases of colorectal cancer were identified.	Larsson <i>et al.</i> ⁽¹⁰⁶⁾
124907	Female	50-74	America	Low GI and High GI foods	Pancreatic cancer	Medical history	In 9 years of follow up study 401 cases were identified with pancreatic cancer.	Patelet <i>et al.</i> ⁽¹⁰⁷⁾
162150	Both	45-75	America	Low GI and High GI foods	Pancreatic cancer	Medical history	An average 8 years of follow up 434 cases of patients were detected with pancreatic cancer.	Nothings <i>et al.</i> ⁽¹⁰⁸⁾

23335	Female	55-69	Sweden	Low GI and High GI foods	Endometrial cancer	Medical history	415 cases of this type of cancer were identified through 15 years of cohort study.	Folsom <i>et al.</i> (109)
288428	Female	42-55	Europe	Low GI and High GI foods	Endometrial cancer	Medical history	710 incidents were diagnosed as endometrial carcinoma.	Cust <i>et al.</i> (110)
36369	Female	34-54	Sweden	Low GI and High GI foods	Endometrial cancer	Medical history	608 cases of endometrial cancer were detected according to this study in 15.4 years of cohort study.	Larsson <i>et al.</i> (111)
2411	Female	18-79	Italy	Low GI and High GI foods	Ovarian cancer	Medical history	1031 cases of ovarian cancer were detected in 7 years of case control study.	Augustin <i>et al.</i> (112)
49613	Female	40-59	Canada	Low and High GI	Ovarian cancer	Medical history	In 16.4 years of study 264 cases were diagnosed with ovarian cancer.	Silvera <i>et al.</i> (113)

GI and Cancer

In this strenuous way of life, individuals experience the ill effects of different various ailments because of unbalanced dietary patterns and absence of physical activity. High dietary GI is related with expanded danger of colorectal tumor, and that high dietary GL is related with increased risk of bosom and endometrial disease, leading to direct or little hazard increment ⁽¹⁰⁾. High GI is observed to be associated with expanded danger of different tumors among men then ladies, while high GL was related with diminished danger of malignancy in both men and ladies. Subgroup examinations found that the expanded all malignancy chance related with high GI was restricted to men and ladies with high body mass file; and the lessened all-tumor hazard related with high GL was kept to men and ladies with low body mass file ⁽⁵⁹⁾. Sieri and Krogh revealed that the dangers of creating different diseases don't seem, by all accounts, to be affected by dietary GI or GL ⁽¹⁰⁾. However, low GI diets have a few other wellbeing points of interest and have a tendency to be rich in dietary fiber, micronutrients and phytochemicals (e.g. plant sterols) that are vital components in a solid eating regimen and way of life ⁽¹⁰⁾. Silvera *et al.*, (2004) reported that elevated plasma insulin levels and postprandial glucose maybe related with the risk of pancreatic cancer. Researcher adjusted the quartiles value of energy to glycemic load and observed the results from the BMI, eating habits, lifestyle, total fiber, glycemic index and glycemic load ⁽⁶⁰⁾. In a study conducted by Nothlings *et al.*, (2017) no significant result was found related to pancreatic cancer but she suggested that high glycemic index diet has possibility in relation to the risk of pancreatic cancer ⁽²⁸⁾. Lajous *et al.*, (2005) researched the danger of bosom growth among postmenopausal ladies is more in contrast with premenopausal ladies with admission of high starches and high glycemic file abstain from food. Quickly retained starches raise the level of insulin and glycemic reaction. Plasma insulin manages the IGF restricting proteins (globulins) which additionally influence IGF-1 (controls cell multiplication and apoptosis) availability. The individual with troubled glucose digestion has higher danger of bosom malignant ⁽⁶¹⁾. Different studies in **Table 5** have explained that two third causes of cancer are due to the life style and eating patterns of population.

GI and Retinal disorders

The retina is the most metabolically dynamic tissue in the human body, with double blood supplies and fast utilization of glucose and oxygen ⁽⁶²⁾. It is not astonishing that glucose homeostasis in retina assumes a vital part in retinal wellbeing and sickness. People suffering from diabetes undergoes through biochemical changes in cells and tissues. In severe cases it may also lead to Necrosis of the tissues. Necrosis refers to the death of tissue. According to Fong *et al.*, (2004) Diabetic retinopathy (DR) is most common micro vascular complication ⁽⁶³⁾. High sugar glucose levels can deteriorate and harm the blood vessels of the retina. Hyperglycemia acts as the base cause for DR ^(64, 65). It may also lead to hemorrhages, exudates or even swelling of the retina. Due to the differences in the duration of hyperglycemic exposure and the related metabolic abnormalities such as blindness, early staged lesions (abnormal damage or change) and advanced lesions, the range of pathologic retinal lesions differ between diabetic and non-diabetic age related lesions ⁽⁶⁶⁾.

GI and Age Related Macular Degeneration (AMD)

Naturally, one may expect an epidemiological relationship between two illnesses which share a typical hazard factor. Specifically one may expect a relationship between chance for diabetes and AMD since they both offer expending high GI and consuming fewer calories as a typical hazard factor. Data showing association between diabetes and AMD have been unreliable. Some major studies show a positive association between these two hazardous diseases ^(67, 68, 69, 70) whereas others deny these associations ^(71, 72, 73, 74). There are 5 well-developed hyperglycemic pathways out of which four are glycolysis associated and one is mitochondria associated pathway ⁽⁶⁶⁾. All these pathways could prompt a typical intracellular or extracellular affront i.e. oxidative stress. Hypoxia inducible factors (HIF) which is necessary for maintaining functional homeostasis seems to get elevated under hyperglycemic conditions leading to enhanced expressions of HIF-inducible genes ⁽⁷⁵⁾. Thus, it is also known as –Hyperglycemia Induced Factor as it can affect the oxidative stress responses, inflammations and various mechanisms which are directly or indirectly involved in the pathogenesis of AMD. The stage of oxidative stress occurs in human figure when the body is unable to balance free radical production and anti-oxidant capacity thus making the organ more prone towards damage ⁽¹⁹⁾. **Figure 3** depicts series of events leading to diabetic retinopathy due to various factors such as oxidative stress, weakening of muscles etc.

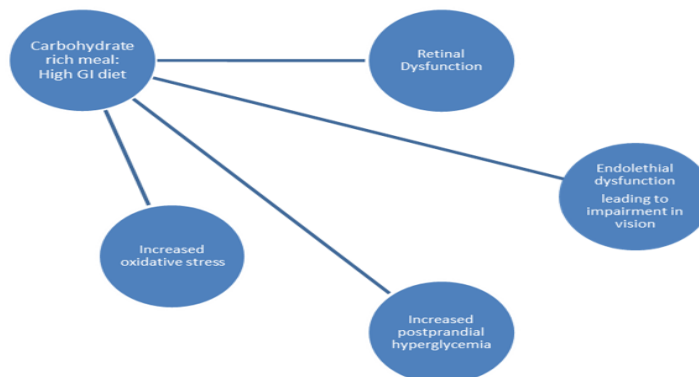


Figure 3- series of events leading to diabetic retinopathy which may cause permanent impairment in vision (blindness).

Conclusion and Future Prospects

It can be concluded that the present studies provide evidence for inter-relationship between GI and chronic diseases such as AMD, DM, CVD's, cancer as well as weight loss. In almost all the conditions hyperglycemia acts as the base factor leading to these metabolic disorders. Similar to other dietary factors, GI should not be the sole factor upon which food choices should be made. Rather, the concept of GI should be applied wisely and low GI alternatives should be provided so as to reduce the incidence of chronic diseases. Also, these low GI diets are convenient to opt in our daily lives as these do not demand any kind of peculiar restrictions in the diet either in the fat content or in the protein. But on the other hand, the research on GI is yet to gain importance in India. It is mandatory that the deep relationships between GI and various chronic and acute diseases should be highlighted. More studies are needed to validate the mechanisms of GI/GL with other body organs and its long term effects. Various starches and its correlation with heat, temperature, pressure, kinetics is yet to be done. Several puzzling questions are unanswered such as biomarkers for the indication of hyperglycemia etc. Further research on the cheap sources of low GI foods to make handy snacks could be done so as to increase commercialization and thereby, making a contribution in the economic sector.

References:

1. Barclay AW, Brand-Miller JC & Wolever TM (2005) Glycemic index, glycemic load, and glycemic response are not the same. *Diabetes Care* **28**, 1839-40.
2. Gangwisch JE, Hale L, Garcia L, *et al.* (2015) High glycemic index diet as a risk factor for depression: analyses from the Women's Health Initiative. *The Am J Clin Nutr*, ajcn103846.
3. Srilakshmi B, (2007) *Dietetics*. New Age International.
4. Lemlioglu-Austin, Dilek, Nancy D. Turner, *et al.* (2012) Effects of sorghum [*Sorghum bicolor* (L.) Moench] crude extracts on starch digestibility, estimated glycemic index (EGI), and resistant starch (RS) contents of porridges, *Molecules* **17**, no. 9, 11124-11138.

5. Safina & Gulnara (2012) Application of surface plasmon resonance for the detection of carbohydrates, glycoconjugates, and measurement of the carbohydrate-specific interactions: A comparison with conventional analytical techniques. A critical review. *Analytica chimica acta* **712**, 9-29.
6. Rodriguez, Nancy R., Nancy M, *et al.* (2009) Nutrition and athletic performance, *Med and sci in sports and exerc* **41**, 709-731.
7. Augustin, Livia SA *et al.* (2015) Glycemic index, glycemic load and glycemic response: An international scientific consensus summit from the international carbohydrate quality consortium (ICQC), *Nutr, metab and Cardiovascular Disease* **25**, 795-815.
8. Liu, Simin, Hyon K, *et al.* (2006) A prospective study of dairy intake and the risk of type 2 diabetes in women, *Diabs Care* **29**, no. 7, 1579-1584.
9. Gopalan C, Sastri BVR, & Balasubramanian (1980) *Nutr value of Indian foods*.
10. Sieri S, Krogh V, Berrino F, *et al.* (2010) Dietary glycemic load and index and risk of coronary heart disease in a large italian cohort: the EPICOR study. *Arch of Intr Med* **170**, 640-7.
11. Jenkins DJ, Wolever TM, Taylor RH, *et al.* (1981) Glycemic index of foods: a physiological basis for carbohydrate exchange. *Am J clin nutr* **34**, 362-6.
12. Jenkins DJ, Kendall CW, McKeown-Eyssen G, *et al.* (2008) Effect of a low-glycemic index or a high-cereal fiber diet on type 2 diabetes: A randomized trial. *Jama* **300**, 2742-53.
13. Brand-Miller J, Hayne S, Petocz P, *et al.* (2003) Low-glycemic index diets in the management of diabetes. *Diab care* **26**, 2261-7.
14. Foster-Powell K, Holt SH & Brand-Miller JC (2002) International table of glycemic index and glycemic load values. *Am J clin nutr*, **76**, 5-6.
15. Salmeron J, Manson JE, Stampfer MJ, *et al.* (1997) Dietary fiber, glycemic load, and risk of non—insulin-dependent diabetes mellitus in women. *Jama* **277**, 472-7.
16. Meyer KA, Kushi LH, Jacobs DR, *et al.* (2000) Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. *Am J clin nutr*, **71**, 921-30.
17. Liu S, Willett WC, Stampfer MJ, *et al.* (2000) A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J clin nutr* **71**, 1455-61.
18. Augustin LS, Polesel J, Bosetti C, *et al.* (2003) Dietary glycemic index, glycemic load and ovarian cancer risk: a case-control study in Italy. *Annals Onco* **14**, 78-84.
19. Fraser-Bell S, Kaines A & Hykin PG (2008) Update on treatments for diabetic macular edema. *Current opinion in ophtho* **19**, 185-9.
20. Ludwig DS (2002) The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *Jama* **287**, 2414-23.
21. Yadav D, Mishra M, Jadaun P, *et al.* (2016) Glycemic index and glycemic load in cardiovascular disease risk. *Prog in Nutr* **18**, 95-101.
22. Preiss D, Seshasai SR, Welsh P, *et al.* (2011) Risk of incident diabetes with intensive- dose compared with moderate-dose statin therapy: a meta-analysis. *Jama* **305**, 2556-64.

23. Giovannucci E (1995) Insulin and colon cancer. *Cancer Causes & Control* **6**, 164-79.
24. Salmerón J, Ascherio A, Rimm, *et al.* (1997). Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabs care* **20**, 545-50.
25. Gögebakan Ö, Kohl A, Osterhoff MA, *et al.* (2011) Effects of weight loss and long-term weight maintenance with diets varying in protein and glycemic index on cardiovascular risk factors. *Circulation* **111**.
26. Franceschi S, Masco LD, Augustin L, *et al.* (2001) Dietary glycemic load and colorectal cancer risk. *Annals of Onco* **12**, 173-8.
27. Augustin LS, Franceschi S, Jenkins DJ, *et al.* (2002). Glycemic index in chronic disease: a review. *Eur J clin nutr* **56**, 1049-72.
28. Nöthlings U, Murphy SP, Wilkens LR, *et al.* (2007) Dietary glycemic load, added sugars, and carbohydrates as risk factors for pancreatic cancer: the Multiethnic Cohort Study. *Am j clin nutr* **86**, 1495-501.
29. Englyst HN, Veenstra J & Hudson GJ. (1996) Measurement of rapidly available glucose (RAG) in plant foods: a potential in vitro predictor of the glycaemic response. *Br J Nutr* **75**, 327-37.
30. Chung HJ, Liu Q & Hoover R. (2009) Impact of annealing and heat-moisture treatment on rapidly digestible, slowly digestible and resistant starch levels in native and gelatinized corn, pea and lentil starches. *Carb Poly* **75**, 436-47.
31. Kim EH, Petrie JR, Motoi L, *et al.* (2008) Effect of structural and physicochemical characteristics of the protein matrix in pasta on in vitro starch digestibility. *Food Biophysics* **3**, 229-34.
32. Urooj A, Puttraj SH. (1999) Digestibility index and factors affecting rate of starch digestion in vitro in conventional food preparation. *Mol Nutr & Food Res* **43**, 42-7.
33. Dona AC, Pages G, Gilbert RG, *et al.* (2010) Digestion of starch: In vivo and in vitro kinetic models used to characterize oligosaccharide or glucose release. *Carb Polymers* **80**, 599-617.
34. Singh J, Dartois A & Kaur L. (2010) Starch digestibility in food matrix: a review. *Trends in Food Sci & Tech* **21**, 168-80.
35. Holt SH, Brand Miller JC, Petocz P, *et al.* (1995) A satiety index of common foods. *Eur J clin nutr* **49**, 675-90.
36. Behall KM, Scholfield DJ & Canary J (1988) Effect of starch structure on glucose and insulin responses in adults. *Am J clin nutr* **47**, 428-32.
37. Goni I, Garcia-Diz L, Maetañás E, *et al.* (1996) Analysis of resistant starch: a method for foods and food products. *Food chem* **56**, 445-9.
38. Sajilata MG, Singhal RS & Kulkarni PR (2006) Resistant starch—a review. *Compreviews in food sci and food safety* **5**, 1-7.
39. Fuentes-Zaragoza E, Riquelme-Navarrete MJ, Sánchez-Zapata E *et al.* (2010) Resistant starch as functional ingredient: A review. *Food Res Int.* **43** 931-42.
40. Lehmann U & Robin F (2007) Slowly digestible starch—its structure and health implications: a review. *Trends in Food Sci & Tech* **18**, 346-55.

41. Leszczyński W (2004) Resistant starch—classification, structure, production. *Polish J Food and Nutr Sci.* **13**, 37-50.
42. Haralampu SG (2000) Resistant starch—a review of the physical properties and biological impact of RS 3. *Carbs poly* **41**, 285-92.
43. Kaur B, Ranawana V & Henry J (2016) The glycemic index of rice and rice products: a review, and table of GI values. *Crit Rev Food Sci Nutr* **56(2)**, 215-36.
44. Gogebakan O, Kohl A, Osterhoff MA, *et al.* (2011) Effects of weight loss and long-term weight maintenance with diets varying in protein and glycemic index on cardiovascular risk factors. *Circulation*. CIRCULATIONAHA-111.
45. Astrup A, Ryan L, Grunwald GK, *et al.* (2000) The role of dietary fat in body fatness: evidence from a preliminary meta-analysis of ad libitum low-fat dietary intervention studies. *Br J Nutr* **83**, S25-32.
46. Schwingshackl L & Hoffmann G (2013) Long-term effects of low glycemic index/load vs. high glycemic index/load diets on parameters of obesity and obesity-associated risks: a systematic review and meta-analysis. *Nutr Metab Cardiovasc Dis* **23**, 699-706.
47. Raatz SK, Torkelson CJ, Redmon JB, *et al.* (2005) Reduced glycemic index and glycemic load diets do not increase the effects of energy restriction on weight loss and insulin sensitivity in obese men and women. *J Nutr* **135**, 2387-91.
48. Stevenson EJ, Williams C, Mash LE, *et al.* (2006) Influence of high-carbohydrate mixed meals with different glycemic indexes on substrate utilization during subsequent exercise in women. *Am J Clin Nutr* **84**, 354-60.
49. Brand-Miller JC, Holt SH, Pawlak DB *et al.* (2002) Glycemic index and obesity. *Am J Clin Nutr* **76**, 281S-5S.
50. Chandalia M, Garg A, Lutjohann D, *et al.* (2000) Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. *New Engl J of Med* **342**, 1392-8.
51. Hodge AM, English DR, O'Dea K *et al.* (2004) Glycemic index and dietary fiber and the risk of type 2 diabetes. *Diabetes care* **27**, 2701-6.
52. Chiasson JL, Josse RG, Gomis R, *et al.* (2002) STOP-NIDDM Trial Research Group. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. *The Lancet* **359**, 2072-7.
53. Thomas D & Elliott EJ (2009) Low glycaemic index, or low glycaemic load, diets for diabetes mellitus. *The cochrane library*.
54. Garg A, Bantle JP, Henry RR, Coulston AM, Griver KA, Raatz SK, Brinkley L, Chen YI, Grundy SM, Huet BA & Reaven GM (1994) Effects of varying carbohydrate content of diet in patients with non—insulin-dependent diabetes mellitus. *Jama* **271(18)**, 1421-8.
55. Levitan EB, Cook NR, Stampfer MJ, *et al.* (2008) Dietary glycemic index, dietary glycemic load, blood lipids, and C-reactive protein. *Metabolism* **57**, 437-43.
56. Halton TL, Willett WC, Liu S, *et al.* (2006) Low-carbohydrate-diet score and the risk of coronary

heart disease in women. *N Engl J Med* **355**, 1991-2002.

57. Ceriello A (2000) Oxidative stress and glycemic regulation. *Metabolism* **49**, 27-9.
58. Sloth B, Krog-Mikkelsen I, Flint A, *et al.* (2004) No difference in body weight decrease between a low-glycemic-index and a high-glycemic-index diet but reduced LDL cholesterol after 10-wk ad libitum intake of the low-glycemic-index diet. *Am J Clin Nutr* **80**(2), 337-47.
59. Harriss DJ, Atkinson G, Batterham A, *et al.* (2009) Lifestyle factors and colorectal cancer risk (2): a systematic review and meta-analysis of associations with leisure-time physical activity. *Colorectal Disease* **11**(7), 689-701.
60. Silvera SA, Jain M, Howe GR, *et al.* (2005) Dietary carbohydrates and breast cancer risk: a prospective study of the roles of overall glycemic index and glycemic load. *Int. J. Cancer* **114**, 653-8.
61. Lajous M, Willett W, Lazcano-Ponce E, *et al.* (2005) Glycemic load, glycemic index, and the risk of breast cancer among Mexican women. *Cancer Causes & Control* **16**(10), 1165-9.
62. Cohen LH, Noell WK (1965) Relationships between visual function and metabolism. *Biochemistry of the Retina* 36-50.
63. Fong DS, Girach A & Boney A (2007) Visual side effects of successful scatter laser photocoagulation surgery for proliferative diabetic retinopathy: a literature review. *Retina* **27**(7), 816-24.
64. UK Prospective Diabetes Study (UKPDS) Group (1998) Effect of intensive blood- glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *The Lancet* **352**, 854-65.
65. Diabetes Control and Complications Trial Research Group (1993) The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* **(329)**, 977-86.
66. Chiu CJ & Taylor A (2011) Dietary hyperglycemia, glycemic index and metabolic retinal diseases. *Prog Retin Eye Res* **30**(1), 18-53.
67. Klein R, Klein BE & Linton KL (1992) Prevalence of age-related maculopathy: the Beaver Dam Eye Study. *Ophthalmology* **99**(6), 933-43.
68. Age-Related Eye Disease Study Research Group (2005) Risk factors for the incidence of advanced age-related macular degeneration in the Age-Related Eye Disease Study (AREDS): AREDS report no. 19. *Ophthalmology* **112**(4), 533-9.
69. Leske MC, Wu SY, Hennis A, *et al.* (2006) Barbados Eye Studies Group. Nine-year incidence of age-related macular degeneration in the Barbados Eye Studies. *Ophthalmology* **113**(1), 29-35.
70. Topouzis F, Anastasopoulos E, Augood C, *et al.* (2009) Association of diabetes with age-related macular degeneration in the EUREYE study. *Br J Ophthalmol* **93**(8), 1037- 41.
71. Age-Related Eye Disease Study Research Group (2000) Risk factors associated with age-related macular degeneration: a case-control study in the age-related eye disease study: age-related eye disease study report number 3. *Ophthalmology* **107**(12), 2224-32.

72. Delcourt C, Michel F, Colvez A, *et al.* (2001) Associations of cardiovascular disease and its risk factors with age-related macular degeneration: the POLA study. *Ophthalmic epidemiology* **8**(4), 237-49.
73. Tomany SC, Wang JJ, van Leeuwen R, Klein R, Mitchell P, Vingerling JR, Klein BE, Smith W & De Jong PT (2004) Risk factors for incident age-related macular degeneration: pooled findings from 3 continents. *Ophthalmology* **111**(7), 1280-7.
74. Fraser-Bell S, Wu J, Klein R, Azen SP, Hooper C, Foong AW & Varma R (2008) Los Angeles Latino Eye Study Group. Cardiovascular risk factors and age-related macular degeneration: the Los Angeles Latino Eye Study. *Am J Ophthalmol* **145**(2), 308-16.
75. Bonello S, Zähringer C, BelAiba RS, Djordjevic T, Hess J, Michiels C, Kietzmann T & Gorlach A (2007) Reactive oxygen species activate the HIF-1 α promoter via a functional NFB site. *Arterioscler Thromb Vasc Biol* **27**(4), 755-61.
76. Bigdon J (2005) Glycemic index and glycemic load. Linus Pauling Institute, *Corvallis*.
77. Bhupathiraju SN, Tobias DK, Malik VS, *et al.* (2014) Glycemic index, glycemic load, and risk of type 2 diabetes: results from 3 large US cohorts and an updated meta- analysis. *Am J clin nutri* **079**533.
78. Hodge AM, English DR, O'Dea K, *et al.* (2004) Glycemic index and dietary fiber and the risk of type 2 diabetes. *Diabs care* **27**, 2701-6.
79. Schulze MB, Liu S, Rimm EB, *et al.* (2004) Glycemic index, glycemic load, and dietary fiber intake and incidence of type 2 diabetes in younger and middle-aged women. *Am J clin nutr* **80**, 348-56.
80. Zhang BB, Zhou G & Li C (2009) AMPK: an emerging drug target for diabetes and the metabolic syndrome. *Cell metab* **9**, 407-16.
81. BN, Erber E, Grandinetti A, *et al.* (2009) Dietary fiber, magnesium, and glycemic load alter risk of type 2 diabetes in a multiethnic cohort in Hawaii. *J nutr* **109**.
82. Villegas R, Liu S, Gao YT, *et al.* (2007) Prospective study of dietary carbohydrates, glycemic index, glycemic load, and incidence of type 2 diabetes mellitus in middle-aged Chinese women. *Archives of Internal Med* **167**, 2310-6.
83. Krishnan S, Rosenberg L, Singer M, *et al.* (2007) Glycemic index, glycemic load, and cereal fiber intake and risk of type 2 diabetes in US black women. *Archives of Internal Med* **167**, 2304-9.
84. Van Dam RM, Visscher AW, Feskens EJ, *et al.* (2000) Dietary glycemic index in relation to metabolic risk factors and incidence of coronary heart disease: the Zutphen Elderly Study. *Eur J Clin Nutr.* **54**, 726.
85. Gögebakan Ö, Kohl A, Osterhoff MA, *et al.* (2011) Effects of weight loss and long-term weight maintenance with diets varying in protein and glycemic index on cardiovascular risk factors. *Circulation* **111**.
86. Levitan EB, Cook NR, Stampfer MJ, *et al.* (2008) Dietary glycemic index, dietary glycemic load, blood lipids, and C-reactive protein. *Metabolism* **57**, 437-43.

87. Halton TL, Willett WC, Liu S, et al (2006) Low-carbohydrate-diet score and the risk of coronary heart disease in women. *N Engl J Med.* **355**, 1991-2002
88. Grau K, Tetens I, Bjørnsbo KS, et al. (2011) Overall glycaemic index and glycaemic load of habitual diet and risk of heart disease. *Public health nutr* **14**, 109-18.
89. Oh K, Hu FB, Cho E, et al. (2005) Carbohydrate intake, glycemic index, glycemic load, and dietary fiber in relation to risk of stroke in women. *Am J Epidemiology* **161**, 161-9.
90. Beulens JW, de Bruijne LM, Stolk RP, et al. (2007). High dietary glycemic load and glycemic index increase risk of cardiovascular disease among middle-aged women: a population-based follow-up study. *J Am Coll Cardiology* **50**, 14-21.
91. Sieri S, Pala V, Brighenti F, et al. (2007) Dietary glycemic index, glycemic load, and the risk of breast cancer in an Italian prospective cohort study. *Am j clin nutr* **86**, 1160-6.
92. Romieu I, Ferrari P, Rinaldi S, et al. (2012) Dietary glycemic index and glycemic load and breast cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Am J clin nutr* **96**, 345-55.
93. Jonas CR, McCullough ML, Teras LR, et al. (2003) Dietary glycemic index, glycemic load, and risk of incident breast cancer in postmenopausal women. *Cancer Epidemiology and Prevention Biomarkers.* **12**, 573-7.
94. Giles GG, Simpson JA, English DR, et al. (2006) Dietary carbohydrate, fibre, glycaemic index, glycaemic load and the risk of postmenopausal breast cancer. *Int j cancer* **118**, 1843-7.
95. Silvera SA, Jain M, Howe GR, et al. (2005) Dietary carbohydrates and breast cancer risk: a prospective study of the roles of overall glycemic index and glycemic load. *Int J cancer.* **114**, 653-8.
96. Augustin LS, Maso LD, Vecchia CL, et al. (2001) Dietary glycemic index and glycemic load, and breast cancer risk: a case-control study. *Annals of Oncology* **12**, 1533-8.
97. Lajous M, Boutron-Ruault MC, Fabre A, et al. (2008). Carbohydrate intake, glycemic index, glycemic load, and risk of postmenopausal breast cancer in a prospective study of French women. *Am J Clin Nutr* **87**, 1384-91.
98. Larsson SC, Bergkvist L & Wolk A. (2009) Glycemic load, glycemic index and breast cancer risk in a prospective cohort of Swedish women. *Int J cancer.* **125(1)**, 153-7.
99. McCann SE, McCann WE, Hong CC, et al. (2007) Dietary patterns related to glycemic index and load and risk of premenopausal and postmenopausal breast cancer in the Western New York Exposure and Breast Cancer Study. *Am J clin nutr* **86**, 465-71.
100. Franceschi S, Masco LD, Augustin L, et al. (2001) Dietary glycemic load and colorectal cancer risk. *Annals of Oncology* **12**, 173-8.
101. Terry PD, Jain M, Miller AB, et al. (2003) Glycemic load, carbohydrate intake, and risk of colorectal cancer in women: a prospective cohort study. *J Nat Cancer Inst* **95**, 914-6.
102. Tabung FK, Steck SE, Ma Y, et al. (2015) The association between dietary inflammatory index and risk of colorectal cancer among postmenopausal women: results from the Women's Health

Initiative. *Cancer causes & control* **26**, 399-408.

103. Michaud DS, Fuchs CS, Liu S, *et al.* (2005) Dietary glycemic load, carbohydrate, sugar, and colorectal cancer risk in men and women. *Cancer Epidemiology and Prevention Biomarkers* **14**, 138-47.
104. McCarl M, Harnack L, Limburg PJ, *et al.* (2006) Incidence of colorectal cancer in relation to glycemic index and load in a cohort of women. *Cancer Epidemiology and Prevention Biomarkers* **15**, 892-6.
105. Strayer L, Jacobs DR, Schairer C, *et al.* (2007) Dietary carbohydrate, glycemic index, and glycemic load and the risk of colorectal cancer in the BCDDP cohort. *Cancer Causes & Control* **18**, 853-63.
106. Larsson SC, Bergkvist L & Wolk A. (2006) Consumption of sugar and sugar-sweetened foods and the risk of pancreatic cancer in a prospective study. *Am j clin nutr* **84**, 1171-6.
107. Patel AV, McCullough ML, Pavluck AL, *et al.* (2007) Glycemic load, glycemic index, and carbohydrate intake in relation to pancreatic cancer risk in a large US cohort. *Cancer Causes & Control* **18**, 287.
108. Nöthlings U, Murphy SP, Wilkens LR, *et al.* (2008) A food pattern that is predictive of flavonol intake and risk of pancreatic cancer. *Am J clin nutr* **88**, 1653-62.
109. Folsom AR, Demissie Z & Harnack L. Glycemic index, glycemic load, and incidence of endometrial cancer: the Iowa women's health study. *Nutr and cancer* **46**, 119-24.
110. Cust AE, Kaaks R, Friedenreich C, *et al.* (2007) Metabolic syndrome, plasma lipid, lipoprotein and glucose levels, and endometrial cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Endocrine-Related Cancer* **14**, 755-67.
111. Larsson SC, Orsini N & Wolk A. Body mass index and pancreatic cancer risk: A meta-analysis of prospective studies. *Int J cancer* **120**, 1993-8.
112. Augustin LS, Polesel J, Bosetti C, *et al.* (2003) Dietary glycemic index, glycemic load and ovarian cancer risk: a case-control study in Italy. *Annals of Oncology* **14**, 78-84.
113. Silvera SA, Jain M, Howe GR, *et al.* (2007) Glycaemic index, glycaemic load and ovarian cancer risk: a prospective cohort study. *Public health nutr* **10**, 1076-81.

Figure caption:

Figure 1: flow chart depicts the hypothetical mechanism of RDS, SDS and RS. Also the food sources along with various cooking methods affecting RS 1, 2, 3 and 4 have also been discussed

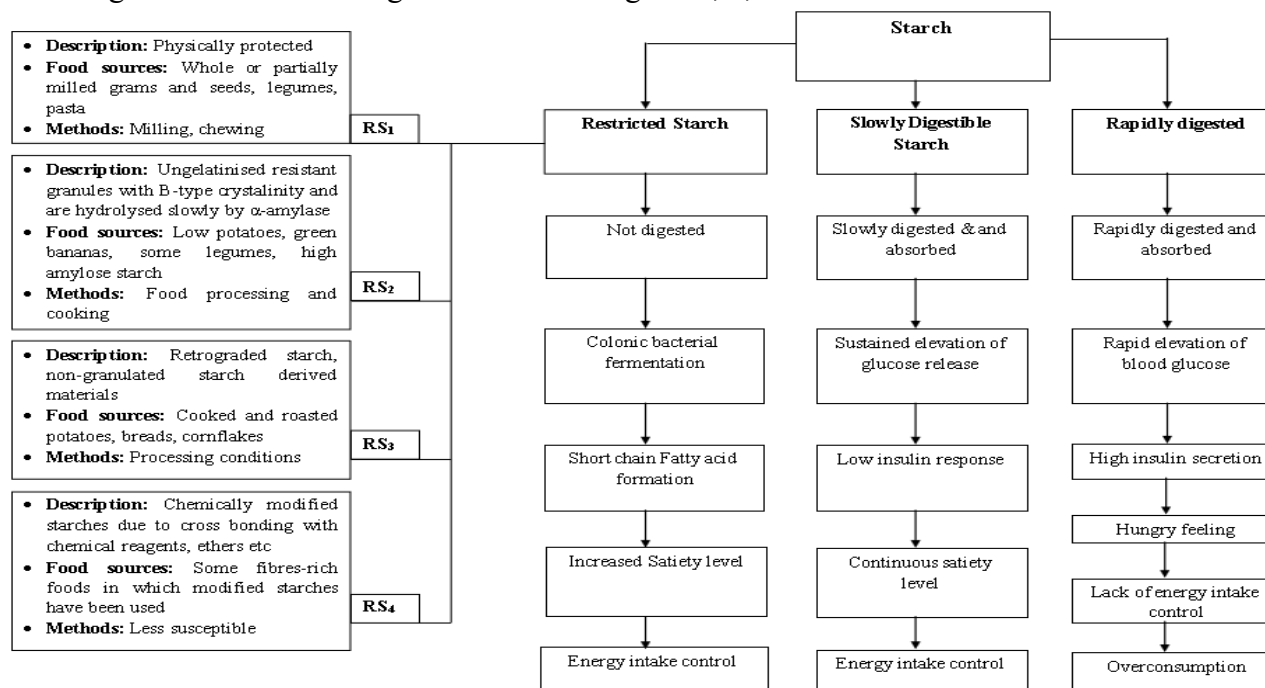


Figure 2: Hypothetical mechanism of high glycemic load and diabetes. When high glycemic index diet is consumed then the production of free fatty acid increases leading to increased insulin resistance which either would increase insulin demand or would increase glucose tolerance leading to diabetes.

Table 2: recent studies on the incidents of Diabetes mellitus

Sample size (n)	Sex	Age (years)	Place of survey	Diagnosis method	Observations	References
9529	Both	45-64	America	Self-examination	1447 incidents of DM 2 were diagnosed in 9 years of study.	Steven <i>et al.</i> ⁽⁷⁷⁾
36787	Both	40-69	Australia	Self-examination	365 cases of DM2 were reported in the time duration of 4 years.	Hodge <i>et al.</i> ⁽⁷⁸⁾
91249	Female	24-44	America	Biochemical test	741 incidents of DM2 were diagnosed in 8 years of cohort study.	Schulze <i>et al.</i> ⁽⁷⁹⁾
13110	Female	24-44	America	Self-examination	1428 women with gestational diabetes were diagnosed in 10 years study process.	Zhang <i>et al.</i> ⁽⁸⁰⁾
75512	Both	45-75	Hawaii	Biochemical test	8587 cases of diabetes were detected in 14 years long study with regular follow ups.	Hopping <i>et al.</i> ⁽⁸¹⁾
64227	Female	40-70	China	Biochemical test	1608 cases of diabetes were diagnosed in 5 years of follow up cohort study. Dietary CHO was solely related with the chances of developing DM2.	Villegas <i>et al.</i> ⁽⁸²⁾
40078	Female	21-69	America	Biochemical test	1938 cases of DM2 were detected in average 8 years follow up study. GI was directly related with the incidence of developing DM2.	Krishnan <i>et al.</i> ⁽⁸³⁾

Figure 3: complications due to high GI diet. Uncontrolled glucose level acts as an underlying cause for ocular complications which in turn increases the oxidative stress. In the initial phase the protective layer (endometrial) is damaged which when uncontrolled may lead to retinal dysfunction, complete blindness.

Table 3: recent studies showing the prevalence of CVD around the world on the basis of self-examination, biochemical test and medical history.

Sample size (n)	Sex	Age range (Years)	Place of survey	Sample used	Diagnosis method	Observations	References
646	Male	64-84	Netherland	wheat bread, cooked potatoes, fruit, milk, sugar	Medical history	Population based study, a high dietary glycemic index was not associated with an increased risk of coronary heart disease	Van dam <i>et al.</i> ⁽⁸⁴⁾
1209	Both	40-65	8 European countries	Low GI versus High GI protein	Self-examination and biochemical test	Consumption of low GI and energy restricted diet with high protein lead to decrease in initial weight and CRP	Gogebakan <i>et al.</i> ⁽⁸⁵⁾
18137	Female	45-56	America	Low GI and High GI foods	Biochemical test	GL and GI had direct link with the concentrations of lipids in blood such as HDL, LDL, VLDL and CRP (C reactive protein).	Levitane <i>et al.</i> ⁽⁸⁶⁾
82802	Female	30-55	America	Low GI versus High GI foods	Medical history	This study mainly suggested that with the intake of high fiber diet the chances of CVD can be reduced.	Halton <i>et al.</i> ⁽⁸⁷⁾
47749	Both	35-74	Italy	High GI foods- bread, sugar and jam, rice, pizza and low GI foods- pasta, fruit	Medical history	The risk of cardiovascular diseases was more prominent in women having high carbohydrate diet as that of Men	Sieri <i>et al.</i> ⁽¹⁰⁾
3959	Both	30-70	Denmark	Rye bread, potatoes, pastry, beer, soft drink, white bread	Medical history	GI had inverse relation heart problems in men. However, in women there was no significant relation between GI and heart diseases	Grau <i>et al.</i> ⁽⁸⁸⁾
121700	Female	30-55	America	Low and High GI foods	Medical history	1020 women had incident stroke, 515 had ischemic attack and 279 were identified with hemorrhagic stroke.	Oh <i>et al.</i> ⁽⁸⁹⁾
17357	Female	49-70	Netherlands	Low GI and High GI foods	Medical history	High GI foods lead to a total of 556 medical cases CHD and 243 cases of CVA.	Beulens <i>et al.</i> ⁽⁹⁰⁾