The role of postprandial hyperglycemia in contributing to the risk of macrovascular complications in patients with diabetes mellitus is being increasingly recognized. In type 2 diabetes, there is a progressive shift in the relative contributions of postprandial fasting glycemia to the overall glycemic control as the disease progresses. For patients with fairly good glycemic control (glycosylated hemoglobin [HbA1c] > 8.5%), postprandial hyperglycemia makes a relatively greater contribution to the overall glycemic load than fasting hyperglycemia, but in patients with poorer control the relative contributions of the two states to the overall glycemic load is reversed. This finding coupled with epidemiological evidence that elevated postprandial glucose concentration is an independent risk factor for cardiovascular disease (CVD), and is associated with a greater CVD risk than elevated fasting glucose, points to the need to monitor and target postprandial glucose, as well as fasting glucose and HbA1C levels, when optimizing insulin therapy for patients with type 2 diabetes. HbA1C and glycated albumin (GA) can be satisfactorily predicted by fasting blood glucose (FBG) and postprandial glucose (PPG). HbA1C reflects FBG more than PPG, whereas GA better reflects PPG. Thus depending on the characteristics of the glycated protein, a different glycemic status is reflected. Postprandial glycaemia is a phenomenon often neglected by patients as well as doctors. It is however undeniable that the postprandial glycemic excursion plays an important role in total hyperglycaemia reflected in glycated hemoglobin. The postprandial glycaemia measurement or more appropriately the postprandial glycemic excursion (the difference between postprandial and pre-prandial glycaemia, also called the post prandial delta glycaemia), is important to measure, and there are specific tools to correct it when abnormal. Post prandial delta glycaemia should lie between 30 and 50 mg/dl. It is thus suggested to measure it not necessarily on a daily basis, but when it is expected that the glyemic couple, or the pre-postprandial couple is high. The specific tools for treatment of postprandial hyperglycemia can be dietetic (carbohydrate quantity reduction or ingestion of fiber rich and/or low glycemic index foods) or medicinal. Among the specific medicinal treatments are the alpha-glycosidase-inhibitors (which can be used for both type 1 and type 2 diabetic patients), glinides and fast acting insulins. Rather than first treating fasting and interprandial hyperglycemia, as has been commonly done by physicians, the authors recommend the simultaneous treatment of pre, inter and postprandial hyperglycemia. The optimal time at which to evaluate postprandial glycaemia is approximately 1h and 15 minutes for type 1 and type 2 diabetic patients. The measurement of HbA1c concentrations is considered the gold standard for assessing long term glycemic control at present & is regarded as key therapeutic target for the prevention of diabetes-related complication. The HbA1c concentration, although a useful measure of metabolic control and the efficacy of diabetes therapeutic interventions, is an integrated summary of circadian blood glucose concentrations during the preceding 6-8 weeks. It therefor does not reverse any information on the extent or frequency of blood glucose excursions but provide an overall mean value only. This being the case, one can argue that the HbA1c concentration is not necessarily the best or the most clinical useful glycemic indicator of risk of complications, particularly at the lower end of elevated HbA1c concentrations. For instance in patients, in whom glucose concentration fluctuate markedly, the
HbA1c may indicate adequate metabolic control; however, such patients are exposed to the risks of hypoglycemia and the possibly harmful effects of excessive postprandial hyperglycemic excursion. HbA1c is an easily measured biochemical marker that strongly correlates with the level of ambient glycemia during a 2-3 mo period. Tests for HbA1c are also expensive and can be done at any time of the day. The concentration of HbA1c predicts the risk of incident eye, kidney, and nerve disease in persons with type 1 and type 2 diabetes mellitus. Epidemiologic evidence also indicates that HbA1c is a progressive risk factor for cardiovascular disease in both persons with diabetes and those without diabetes. Glycated Albumin has been reported as a rapid and useful indicator of glycemic control since the turnover of serum albumin is much shorter (half life of 17 days) than that of HbA1c. Circulating albumin is strongly glycated at 4 sites of lysine residues and the glycation reaction occurs ten times more than in HbA1c. Human Serum Albumin is very sensitive to glycation, the slow, non-enzymatic (Maillard reaction) initially involves the attachment of glucose or other carbohydrate compounds such as galactose and fructose, to the free amine groups of albumin.

Introduction:-
Diabetes mellitus (DM) comprises a group of common metabolic disorders that share phenotype of hyperglycemia, and is often accompanied by presence of glucose in urine, from which the name of condition is derived (Gowenlock, 2002). It is found that a 14 to 16% decrease in macro vascular complication occurs for every 1% absolute reductions in glycated Hb (Stratton et al., 2000). However, HbA1c is not used for diagnosis as it is not sufficiently sensitive (Haslett et al., 2002). The measurement of glycated albumin (GA), which is considered to be a marker of glycemic control over the preceding 2–3 weeks, is convenient and accurate regardless of diet (Kouzuma et al., 2004). A recent study showed that GAcould be a better marker for glycemic control than HbA1c in diabetic patients, especially for evaluating glycemic excursion (Yoshiuchi et al., 2008).

The aim:-
It was to evaluate the relative contribution of fasting and postprandial plasma glucose to both glycated hemoglobin (HbA1C) and glycated albumin(GA) in type 2 diabetic patients.

Subjects and methods:-
This cross-sectional study was conducted on 50 non acarbose non insulin receiving type 2 diabetic subjects attending the out patient endocrinology clinic at Benha University Hospitals during the period from July 2014 to July 2015 after approval of BenhaUniversity ethical committee. All the patients were subjected to full history taking with special stress on age,sex,type and duration of diabetes ,medications and complications. Complete physical examination ,fasting , postprandial and prelaunch blood glucose measurement ,serum GA and HbA1C measurement. Serum GA concentration was quantitatively measured using an Enzyme–Linked Immuno–Sorbant Assay (ELISA) kit (Quantikinehuman GA Immunoassay; R&D Systems, Minneapolis, MN, USA) according to manufacturers’ instructions. Patients were classified into 3 groups according to HbA1C: Group 1 patients where HbA1C > 7.3% and it comprises 20 patients ,Group 2 patients where HbA1C ranges from 7.3% to 8.0% and it comprises 10 patients and Group3 patients where HbA1C <8.0% and it comprises 20 patients.

Statistical analysis:-
The collected data were tabulated and analyzed using SPSS version 16 software (SpssInc, Chicago, ILL Company). Categorical data were presented as number and percentages while quantitative data were expressed as mean ± standard deviation, an and range. Fisher's exact test (FET), was used to analyze categorical variables. Quantitative data were tested for normality using Kolmogorov Smirnoff test, using Student "t", if normally distributed, or Man Whitney U test, Krauskal Wallis test and Spearman’s correlation coefficient ( rho ) if not normally distributed. Statistical significance was accepted at P value <0.05 (S). A P value <0.001 was considered highly significant (HS) while a P value >0.05 was considered non-significant.
Results:
Among the 50 studied patients 12 were males (24%) and 38 were females (76%) with their age ranged from 43-75 year with the mean age being 57.4±8.6 (Table1).

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (N=50)</th>
<th>% (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean ±SD</td>
<td>57.4±8.6</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>43-75</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>38</td>
</tr>
</tbody>
</table>

In our study 20 patients belonged to group 1 with the mean of HbA1C being 6.27±0.42 and 10 patients belonged to group 2 with the mean of HbA1C being 7.84 ±0.08 and 20 of them belonged to group 3 with the mean of HbA1C being 9.11±0.47 (Table 2).

Table 1: characters of the studied sample.

Table 2: Distribution of the studied patients according to the level of glycated hemoglobin.

The study revealed that the mean value of FBG was significantly higher in group 3 patients compared to group 1 patients (185.6 ±43.01 and 130.8±31.75 respectively). On the other hand, the mean value of PPG was significantly higher in group 1 patients compared to group 3 patients (210.6±39.06 and 157.0±24.61 respectively) (Table 3).

Table 3: Mean values of Fasting and Post Prandial and prelaunch plasma glucose in the different groups.

The study revealed that the relative contribution of the postprandial plasma glucose to HbA1C (rho =0.710 and p<0.001) was higher than that of fasting plasma glucose (rho=.574 and p=0.021) in group 1 patients, the relative contribution of the postprandial plasma glucose to HbA1C (rho=0.707 and p= 0.022) was equal to that of fasting plasma glucose (rho=0.707 and p=0.022) in group 2 patients and the relative contribution of the fasting plasma glucose to HbA1C (rho=0.679 and p=.001) was higher than that of the postprandial plasma glucose (rho =0.659 and p= 0.002) in group 3 patients (Table 4).
Table 4: Correlation between HbA1c and both means of Fasting and PostPrandial plasma glucose levels in the different groups.

<table>
<thead>
<tr>
<th>With</th>
<th>FBG</th>
<th>Mean PP</th>
<th>FBG</th>
<th>Mean PP</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c Group I (&lt;7.3%) (N=20)</td>
<td>0.574</td>
<td>0.710</td>
<td>0.707</td>
<td>0.679</td>
</tr>
<tr>
<td>HbA1c Group II (7.3-8.0) (N=10)</td>
<td>0.021 (S)</td>
<td>&lt;0.001 (HS)</td>
<td>0.022 (S)</td>
<td>0.001 (HS)</td>
</tr>
<tr>
<td>HbA1c Group III (&gt; 8%) (N=20)</td>
<td>0.707</td>
<td>0.659</td>
<td>0.002</td>
<td></td>
</tr>
</tbody>
</table>

\( \rho = \) Spearman’s correlation coefficient

The study revealed that the relative contribution of the postprandial plasma glucose to glycated albumin (\( \rho = 0.515 \) and \( p < 0.001 \)) was higher than that of fasting plasma glucose (\( \rho = 0.338 \) and \( p = 0.016 \)) (Table 5).

Table 5: Correlation between glycated albumin and Fasting and PostPrandial plasma glucose levels.

<table>
<thead>
<tr>
<th>With</th>
<th>GA</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBG</td>
<td>0.338</td>
</tr>
<tr>
<td>Mean PP</td>
<td>0.515</td>
</tr>
</tbody>
</table>

Discussion:-

Day time suppression of post-meal excursion is lost first, followed by nocturnal deterioration of fasting sugars with worsening diabetes (Leahy, 2005). As HbA1c levels increases with duration of type 2 diabetes in patients not treated with insulin, diurnal glycaemic control is lost in progressive steps – first during post-prandial periods then in the morning period (during the ‘dawn phenomenon’ of rising blood glucose), and then in the nocturnal fasting period (Monnier et al., 2007). As glycaemic control improves with basal-insulin treatment, PPBG coverage is needed to achieve or to keep HbA1C at < 7%. In addition to being a marker for the onset of type 2 diabetes, elevated PPBG is an independent risk factor for the development of micro- and macrovascular complications and affects the morbidity and mortality associated with long-term hyperglycaemia (Torfjørt, 2003). The current study revealed that the relative contribution of the postprandial plasma glucose to HbA1C was higher than that of fasting plasma glucose in fairly controlled patients (HbA1C < 7.3%) whereas the contribution of fasting hyperglycemia increases gradually with diabetes worsening (HbA1C > 8%). This was in agreement with Monnier et al., (2003) who conducted a study on 290 non-insulin- and non acarbose using patients with type 2 diabetes, plasma glucose (PG) concentrations were determined at fasting (8:00 A.M.) and during postprandial and post-absorptive periods (at 11:00 A.M., 2:00 P.M., and 5:00 P.M.). They evaluated the relative contributions of postprandial and fasting PG increments to the overall diurnal hyperglycaemia. The data were compared over quintiles of HbA1c. They found that the relative contribution of postprandial glucose excursions is predominant in fairly controlled patients whereas the contribution of fasting hyperglycemia increases gradually with diabetes worsening. Similar results were reached by Woerle et al., (2004) who found that in response to an OGTT the change in 2-h postprandial glucose concentrations was much greater than that in FPG levels for every unit increase in HbA1c, in individuals with HbA1c < 7.0% indicating that postprandial glucose contributes more than fasting glucose to HbA1c in this cohort of diabetic subjects. Regarding the role of fasting hyperglycaemia was major as soon as the HbA1c level was above 8%. This finding result was in agreement with the result of Peter et al., (2006) who conducted a study on T2DM subjects (n= 262) consumed a standard MTT in the morning after a 10-h overnight fast. Frequent samples for plasma glucose (PG) were collected over the 4-h test period. The relationship between HbA1c and other glycaemic indices derived from the MTT were explored. The participants were divided into three subgroups according to HbA1c (Group 1 equal or < 7.0%:

Group 2 7.1–9.0%; Group 3 9.0%) and the relative contribution calculated of the postprandial glucose and fasting hyperglycaemia were calculated. They found that the contribution of fasting hyperglycaemia to excess hyperglycaemia increases as glycaemic control deteriorates. The level of GA is approximately three times higher than that of HbA1c. Since the half-life of albumin is shorter than that of RBC, GA reflects a shorter duration, two to three weeks, of glycomic control, than that of HbA1c (Koga et al., 2011), when compared with HbA1c values, GA values have more correlation with postprandial glucose levels and glucose excursions (Hirsch and Brownlee, 2010). Our study revealed that the relative contribution of the postprandial plasma glucose to glycated albumin was higher than that of fasting plasma glucose. This was in agreement with Sumitani et al., (2014)
who conducted a study by starting Metformin and lifestyle interventions in 18 patients with newly diagnosed type 2 diabetes. Metformin was titrated to 1500 mg/day or maximum-tolerated dose. HbA1c and GA were measured every four weeks up to 24 weeks. They concluded that Metformin decreased the GA/HbA1c ratio in patients with newly diagnosed type 2 diabetes. This suggests that metformin improves postprandial hyper-glycaemia in patients with newly diagnosed type 2 diabetes. This is indirect proof that GA correlates better with PPG.

In conclusion, both fasting blood glucose and postprandial blood glucose correlated significantly with HbA1c and GA. The relative contribution of postprandial plasma glucose was high in patients with fairly good control of diabetes (HbA1C > 7.3%) and decreased progressively with worsening diabetes (HbA1c < 8%). In contrast the contribution of fasting plasma glucose showed a gradual increase with increasing level of HbA1c. For patients with A1c between 7.4 percent and 8 percent, postprandial & fasting make equal contributions to overall hyperglycemia.

References: