RESEARCH ARTICLE

ESTIMATED AVERAGE GLUCOSE, EAG – A MORE INTUITIVE UNDERSTANDING OF GLYCEMIC CONTROL

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Manuscript Info	Abstract
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Objective: Glycosylated hemoglobin (HbA1c) is considered as an index of glycemic status over the preceding 2-3 months. Because the HbA1c level is a marker of blood glucose for the previous 60–90 days, average blood glucose levels can be estimated using HbA1c levels. Our aim in the present study was to investigate the relationship between estimated average glucose (eAG) levels, as calculated by HbA1c levels, and fasting plasma glucose (FPG) levels.
Methods: Retrospective analysis of 1000 patients in the Department of Biochemistry for FPG and HbA1c was done. The eAG levels were calculated using the following formula: $(28.7 \times HbA1c) – 46.7$. FPG and HbA1c levels were determined using glucose oxidase-peroxidase method and turbidimetric inhibition immunoassay (TINIA), respectively. According to FPG levels, the patients were divided into Group A (FPG<126mg/dl), Group B (FPG 126-200 mg/dl) and Group C (FPG>200 mg/dl).
Results: A strong positive correlation between FPG levels and eAG levels ($r=0.83$, $p<0.0001$) was observed. The difference was statistically significant.
Conclusion: The discrepancy between HbA_{1c} and blood glucose level units is problematic and confusing among patients. So we suggest, eAG which shows strong correlation with FPG, to be reported along with HbA1c. This will help promote positive patient outcomes, as well as enhance each individual's understanding and ability to manage his or her diabetes more effectively. |

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Introduction:-

Diabetes mellitus is a chronic metabolic disorder characterized by rise in blood glucose level and derangement in protein and fat metabolism.[1] Its management requires an accurate evaluation of blood glucose control to assess the efficiency of a particular therapy.[2] HbA1c is the gold standard for assessment of glycaemic control in patients with diabetes.[3] Because the HbA1c level is a marker of blood glucose for the previous 60–90 days, average blood glucose levels can be estimated using HbA1c levels.[2]

Despite its wide international use, there is a substantial lack of standardization among HbA1c determination methods. The desire to standardize the HbA1c results obtained from different techniques led to the development of a

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reference method.[4] However, the new method results in lower values expressed in different units (millimoles per mole of unglycated hemoglobin), which may cause confusion for patients and health care providers.[5]

The relationship between the mean blood glucose level and the level of HbA1c has been investigated in different studies, and various equations have been obtained.[6,7,8]

Using Nathan's regression equation, which has been recommended by the American Diabetes Association (ADA) , the estimated average glucose (eAG) level calculation and its relationship to the fasting plasma glucose (FPG) level were investigated in the present study.

Materials and Methods:-
Retrospective analysis of 1000 patients in the Department of Biochemistry for FPG and HbA1c was done. FPG and HbA1c levels were determined on fully automated analyzer ROCHE MODULAR P 800 using glucose oxidase - peroxidase method and turbidimetric inhibition immunoassay (TINIA), respectively. The eAG levels were calculated using Nathan's regression equation, $(28.7 \times HbA1c) - 46.7$ recommended by American Diabetes Association. According to FPG levels, the patients were divided into Group A (FPG<126mg/dl), Group B (FPG 126-200 mg/dl) and Group C (FPG>200 mg/dl).

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, version 11.0 for Windows). Data were expressed as the means ± standard deviation of the mean (SD). A p-value <0.05 was accepted as significant. The Pearson correlation coefficient was used to test the correlation between FPG, eAG and HbA1c levels, and independent t-test was used to find the difference between male and female.

Results:-
The mean FPG, eAG, and HbA1c levels in the whole group are presented in Table1. A positive significant correlation was found between FPG and eAG levels for the entire study group (r = 0.8364 , p< 0.0001).

The mean FPG, eAG and HbA1c levels in groups A, B and C are shown in Table1. When the data was split based on FPG it was observed that the three groups showed significant positive correlation with eAG. The eAG levels were higher compared to FPG levels in the three groups.
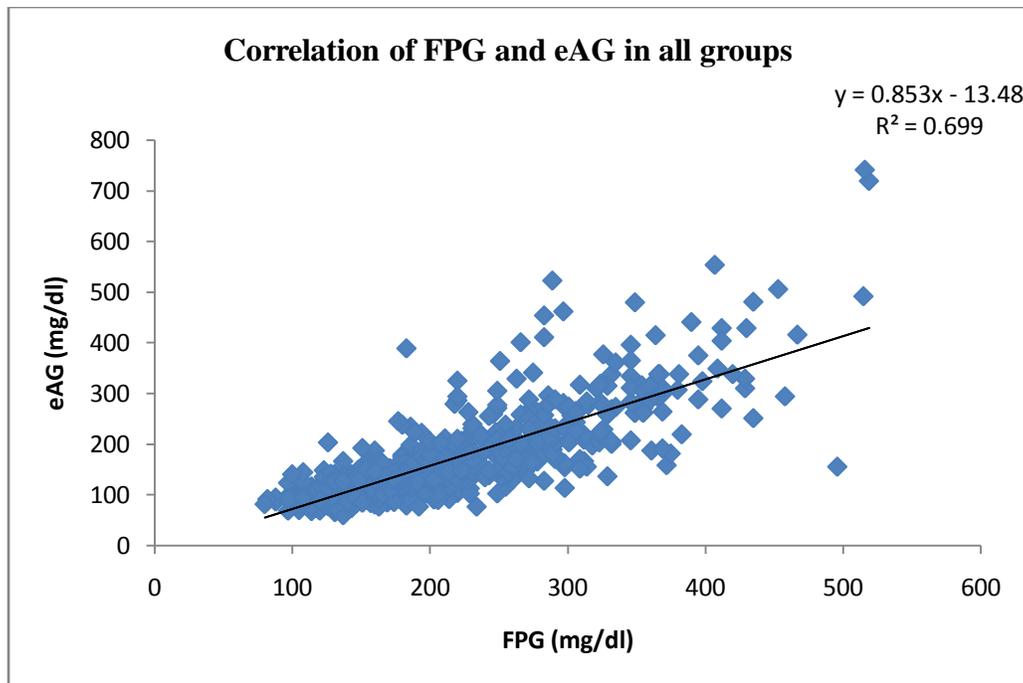
The mean levels of FPG, eAG and HbA1c were higher in males than in females .However, there was no significant gender difference for the following variables (Table2).

Table 1:- The levels of the glycemic parameters and the correlation coefficients for all groups (mean ± SD)

	Entire Group (n=1000)	Group A (FPG<126mg/dl) (n=558)	Group B (FPG:126-200 mg/dl) (n=272)	Group C (FPG>200mg/dl) (n=170)
FPG (mg/dl)	146.00±77.99	99.80±13.34	153.40±21.08	285.82±88.67
eAG (mg/dl)	186.80±76.41	140.38±26.76	206.22±54.52	308.11±69.69
HbA1c (%)	8.14±2.66	6.52±0.93	8.82±1.898	12.36±2.42
FPG vs eAG	r= 0.8364	r= 0.4103	r= 0.4743	r= 0.6039
FPG vs HbA1c	r= 0.8360	r = 0.4118	r = 0.4733	r = 0.6015

Table 2:- A comparison of glycemic parameter levels in males and females (mean±SD)

	Male (n=569)	Female (n=431)	p-value
FPG (mg/dl)	149.46±77.50	141.92±79.83	0.1329
eAG (mg/dl)	190.58±76.03	181.82±76.69	0.0725
HbA1c (%)	8.27±2.65	7.96±2.66	0.0677

Correlation of FPG and eAG in all groups

$y = 0.853x - 13.48$
$R^2 = 0.699$

(Scatter plot: x-axis "FPG (mg/dl)" ranging 0 to 600, y-axis "eAG (mg/dl)" ranging 0 to 800)

Discussion:-

Monitoring of glycemic status has been considered the cornerstone of diabetes care. The results of monitoring are used to assess efficacy of therapy and to guide adjustments in lifestyle to achieve best possible glucose control. The most common tests used today for this purpose are blood glucose and glycated hemoglobin (HbA1c).[9]

HbA1c results are expressed as the percentage of hemoglobin that is glycated and reflects the average blood glucose control over a period of approximately three months. In contrast, blood glucose levels are expressed in mg/dl and are used for daily monitoring by the patient and healthcare professionals. The discrepancy between HbA1c and blood glucose level units has always been problematic and has created confusion among patients. To eliminate this confusion , a mathematical relationship has been established translating HbA1c results into estimated average glucose (eAG). In using eAG, HbA1c results can be reported to patients in units they are already familiar with from their experience in self-monitoring. Similar to HbA1c, eAG evaluates a patient's overall success at controlling glucose levels and helps patients understand the monitoring of their long-term treatment.[5]

Using the Nathan's regression equation, we calculated the eAG levels of our study group and investigated their relationship with the FPG levels. The eAG levels were positively correlated with the FPG levels. In addition, the decrease in the significant strong correlation coefficient showed that the association depended on the patients' levels of glucose control. As glucose control worsened, the association became stronger. Similar findings were reported by Bozkaya et al.[2]

Most patients who come to the clinic for plasma glucose determination pay more attention to fasting and diet rules. The eAG levels in the study group were higher than the FPG levels (93.3%) not only because patients come to the lab in a fasting state but also because the eAG level is reflective of all plasma glucose levels over the previous three months, including the postprandial glucose levels. Our results were in harmony with the previous studies that showed eAG levels being higher than FPG levels, concluding that the eAG and FPG values cannot be used interchangeably.[2,10]

The effect of gender on eAG, FPG and HbA1c levels was also studied. Our results revealed lower eAG, FPG and HbA1c levels in females than those of males (Table 2), otherwise this decrease was non-significant. In concordance to our results, a previous study has observed that these variables did not differ significantly between males & females.[10] However, a study reported a significant gender difference with respect to eAG and HbA1c levels.[2] The

above reported variation can be explained by the difference in the population studies and possibly, the different laboratory methodologies used.

In concordance to the results reported by other studies[2], the eAG levels of males and females were found to be higher than the FPG levels in most cases (92.6% and 94.2% , respectively), similar to the results found for the group as a whole (93.3%).

It is thought that diabetic patients require better strategies to improve self-management.[11] One of these strategies is the use of eAG levels together with HbA1c values.[12,13]Although the clinical usefulness of eAG is not clear, it is believed that every patient's eAG level should be calculated and provided in addition to the HbA1c level. This will help patients better understand the importance of keeping their blood glucose levels within acceptable limits and may rescue them from invasive approaches for glucose homeostasis.[14]

Conclusion:-
According to our data, patients with good to moderate blood glucose control are not entirely successful at managing their blood glucose, as reflected by their eAG levels, and the association between FPG and eAG levels depends on the extent of glycemic control. The study concludes that there is a positive correlation between eAG and FPG, hence it seems intuitive that the reporting of eAG together with the HbA1c level will assist patients and doctors determine the effectiveness of blood glucose control measures.

References:-
1. Aaron & Vinik. Diabetes and macrovascular disease. Journal of diabetes and its Complications 2001;16:235-245
2. Bozkaya G, Ozgu E, Karaca B. The association between estimated average glucose levels and fasting plasma glucose levels. Clinics 2010;65(11):1077-1080
3. Lai Leslie C. Global standardisation of HbA1c.Malaysian J Pathol 2008;30(2):67–71
4. Makris K, Spanou L, Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem 2002;48:436-72
5. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ. A1c Derived Average Glucose Study Group. Translating the A1C assay into estimated average glucose values. Diabetes Care 2008;31:1473-8
6. Nathan DM, Turgeon H, Regan S. Relationship between glycated hemoglobin and mean glucose levels over time. Diabetologica 2007;50:2239-44
7. K, Spanou L, Sacks DB, Bruns DE, Goldstein DE, Maclaren NK. Et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Cli Chem 2002;48:436-72
8. Rohlfing CL, Wiedmeyer HM, Little RR, England JD, Tennilll A, Goldstein DE. Defining the relationship between plasma glucose and HbA(1c): analysis of glucose profiles and HbA(1c) in the Diabetes Control and Complications Trial. Diabetes Care 2002;25:275-8
9. Nathan DM. Long-term complications of diabetes mellitus. N Engl J Med 1993;328(23):1676–85
10. Reddy Raja P,Reethesh RP, Mahesh V. The association between estimated average glucose levels and fasting plasma glucose levels in a rural tertiary care centre. Global Journal of Medicine and Public Health 2013;2(1):1-5
11. Karahan E, Ozkara E, Oner FK, Saatci AO. HbA1c awareness in Turkish diabetic population at a tertiary setting. Turkiye Klinikleri Med Sci 2009;29:927-31
12. Leslie RD, Kilpatrick ES. Translating the A1c assay into estimated average glucose values: response to Nathan et al. Diabetes Care 2009;32:e11
13. Rodriguez-Segade S, Rodriguez J, Paz JM, Camina F. Translating the A1c assay into estimated average glucose values: response to Nathan et al. Diabetes Care 2009;32:e10
14. Miguel GP, Azevedo JL, Gicovate Neto C, Moreira CL, Viana EC, et al. Glucose homeostasis and weight loss in morbidly obese patients undergoing banded sleeve gastrectomy: a prospective clinical study. Clinics 2009;64:1093-8