Statistical Analysis of Diabetic Mellitus on Dynamic Human Blood Flow by Noninvasive Laser Doppler Technique in Real Time

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Summary
This paper presents a statistical analysis chart suitable for continuous processes like the human blood flow in the real time. Noninvasive measurement of blood glucose concentration based on reflected laser beam from the index finger has been reported in this paper. This method depends on Helium-Neon gas (He-Ne) laser operating at 632.8nm wavelength. During measurement the index finger is placed under the laser beam transceiver unit, the reflected optical signal is converted in to a electrical signal, compared with the reference electrical control limit signal, and the obtain difference signal is processed by the six-sigma concept which presents the results in the form of blood glucose concentration chart with respect to blood flow particles, Red Blood Carpusels (RBC). This method would enable the monitoring of blood glucose level of the diabetic patient continuously, safely and noninvasive. Certain aspects that are unique to this kind of process make conventional charts inadequate and misleading, causing false information and search of non-existent problems.

Key words:
Control Charts, Diabetic Mellitus, Hematocrit, Red Blood Cells, Viscosity

1. Introduction

Several attempts to introduce statistical analysis in the medical field have been unsuccessful. Various are the reasons alleged for this fact, but the main one is the non -acquaintance with certain control charts, referred to as special, destined to control diabetic mellitus, as is the case of the human body.
These charts are exceptions with regard to the conventional control charts in managing the diabetic mellitus. Therefore it is important to understand for which reasons they should be adopted and how to analyze them out.
This paper tries to introduce the control chart of diabetic mellitus, as it monitors simultaneously three parameters from the blood flow process viz. RBCs, HbA1c and Hematocrit. In the end, a comparative example of this one and a traditional table is presented.

2. Conventional Control Charts

The control charts, developed by Shewhart (1931) [1], admit that a given observation of a quality characteristic X (x_t) obtained from (1) a statistically stable process [4] [5] (with constant average μ and standard deviation σ) can be adequately represented through the mathematical model:

$$x_t = \mu + \varepsilon_t \qquad (1)$$

where ε_t is the assumed sample related error, normally and independently distributed, with average 0 and constant standard deviation.
Shewhart adopted the criterion that given any statistics (W) calculated based on these observations, independently of its sample related probability distribution, will have as control limits are given in (2).

$$\begin{aligned} UCL_W &= \mu(W) + 3.\sigma(W) \\ CL_W &= \mu(W) \\ LCL_W &= \mu(W) - 3.\sigma(W) \end{aligned} \qquad (2)$$

Due to the fact that the sample related means tend to have a normal distribution, by virtue of the Central Limit Theorem, as well as because the variance of the means is lower than the blood flow variance, it is usual to adopt mean (x-bar) and range (R) type charts. The latter are those most frequently used in every kind of diagnostic analysis of blood glucose is no exception.

Manuscript received January 5, 2010
Manuscript revised January 20, 2010

The control limits for the mean chart are given in (3) as follows,

$$UCL_{\bar{X}} = \bar{\bar{x}} + A_2 \bar{R}$$
$$CL_{\bar{X}} = \bar{\bar{x}} \quad (3)$$
$$LCL_{\bar{X}} = \bar{\bar{x}} - A_2 \bar{R}$$

where x-two bars ($\bar{\bar{x}}$) is the grand mean of the k number of samples obtained, A_2 being defined in (4).

$$A_2 = \frac{3}{d_2 \sqrt{n}} \quad (4)$$

The value of constants A_2 and d2 are in Annexure: A

Some important comments follow:

The control charts are robust as to deviations from normality in the data, as it was demonstrated by Burr (1967)[2] and Schilling; Nelson (1976)[3], i.e. even when a blood flow generates data with a distribution that cannot be admitted to be normal, even so the control charts will work satisfactorily.

When there is no statistical independence between the data (presence of serial correlation or autocorrelation), the model proposed by Shewhart[1] is unsuitable and may lead to mistakes in the interpretation of the statistical diagnosis stability of the blood flow. In other words, there is an excessive generation of false information's, i.e. several points will fall outside the control limits, indicating the presence of a special cause of variation, while in fact this one does not exist.

The control chart, which monitors the process centering, make use of the variation inside the sample to establish the of its control limits with regards to the grand mean. Intrinsically it is admitted that the variation represented by R-bar in the formula (4) is suitable to define the amount of variation permitted for the sample related means. It is noted that the control limits to the mean line in the x-bar chart is a function of R-bar, as well as of factor A_2, which on the other hand depends on the number of sample n.

3. HbA1c: Impact on Diabetic Mellitus

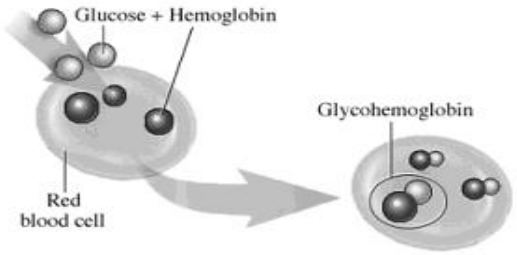

Fig.1. Glycosylated hemoglobin A1c

The HbA1c test (haemoglobin A1c test or glycosylated hemoglobin A1c test, or glycohemoglobin A1c test, or A1c test) is a laboratory test which reveals average blood glucose over a period of the previous two to three months as long-term control test. It helps in assessing (a) if the patient has optimal glycemic control and (b) the control status between checkups. The glycosylated hemoglobin A1c shown in Figure 1. Therefore, provide a reliable reflection of long-term blood glucose control since its value is not affected by brief or infrequent fluctuations in blood glucose.Region of Interest (ROI) Identification It is a 'quality control' test. The result is used with regular blood glucose testing (usually self-monitoring of blood glucose) to determine the success of diabetes management and whether chanes to treatment are required [6]. The following linear regression is used to estimate mean blood glucose from the HbA1c value are calculated using (5).

Mean blood glucose estimate = 33.3 (%HbA1c) – 86 (5)

More simply stated, a 1% change in HbA1c corresponds to a 30 mg/dl change in mean blood glucose are tabulated in Table 1.

Table 1: Relationship between HbA1c and mean blood glucose

HbA1c Test Score (%)	Mean blood glucose
14.0	380
13.0	350
12.0	315
11.0	280
10.0	250
9.0	215
8.0	180
7.0	150
6.0	115
5.0	80
4.0	50
< 7% : Excellent control 7-8% : Good control > 8% : Poor control	

4. Viscosity of blood

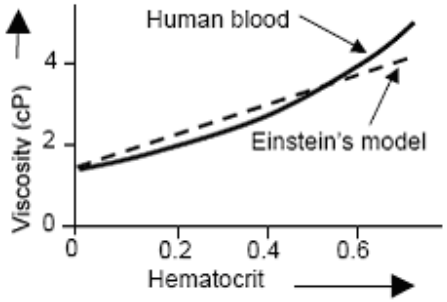

Fig.2. Viscosity as function of hematocrit

Blood consists of plasma and particles, such as the red blood cells. The viscosity of blood thus depends on the viscosity of the plasma, in combination with the hematocrit (Ht) are shown in Figure 2. Higher hematocrit implies higher viscosity [7]. The relation between hematocrit and viscosity (η) is complex and many formulas exist. One of the simplest is given by Einstein (6).

$$\eta = \eta plasma(1 + 2.5H_t) \qquad (6)$$

The viscosity of plasma is about 0.015 Poise (1.5 cP) and the viscosity of whole blood at a physiological hematocrit of 45 is about 3.2 centipoise (cP) , or 3.2 10-3 Pa.s.

4.1 Anomalous viscosity or non-Newtonian behavior of blood

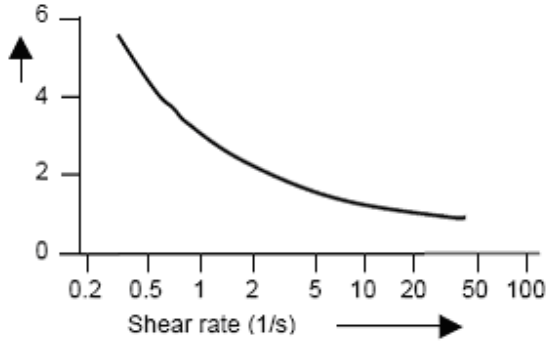

Fig.3. VISCOSITY as function of shear rate for hematocrit of 48

The viscosity of blood depends on its velocity of the blood. More exactly formulated, when velocity (shear rate) increases viscosity decreases. At higher velocity the disc-shaped Red Blood cells (RBC's, erythrocytes) orient in the direction of the flow and viscosity is lower are clearly shown in Figure 3. For extremely low shear rates formation of RBC aggregates may occur, thereby increasing viscosity to very high values.

5. Result and Discussion

On a dynamic human blood flow mechanism, the continuous data are taken in transverse palmar section of the index finger of sampled subject. These ones are sent to the laboratory, which determines their basis weight. The results of consecutive sampled are shown in Table 1.

Considering the way the data are presented and taking into account the habitual use of charts for the mean and range (x-bar and R), the natural tendency would be to call every sample and consequently one would go over to calculating the mean (x-bar) and the range (R) per sampled subject.

As grand mean (x-two bars) and mean range (R-bar), the following values are obtained from (7) and (8).

$$\overline{\overline{x}} = \frac{\sum_{i=1}^{25} \overline{x}_i}{25} = 39.31 \qquad \overline{R} = \frac{\sum_{i=1}^{25} R_i}{25} = 5.88 \qquad (7)$$

$$\overline{\overline{x}} = \frac{\sum_{i=1}^{25} \overline{x}_i}{25} = 39.7 \qquad \overline{R} = \frac{\sum_{i=1}^{25} R_i}{25} = 6.46 \qquad (8)$$

Applying these results to the formulas (7) and (8) and remembering that in this case n = 5, the control charts of subject 1 and 2 mean and Range are shown in Figure 4,5,6 and 7 respectively, are obtained.

The control chart of the mean indicates the presence of a special cause of variation and stratification. In other words, the chart points to an apparently curious problem, which is the lack of variation in the blood flow. When stratification appears, its cause is usually either in the way the samples have been collected or else, how they have been applied to the control limit calculation. In the particular case, the charts have been set up without analyzing which kind of variation in sampled data of the dynamic human blood flow is being pointed to on each of them are given in Table 2 and 3.

The range (R) chart always presents a variation called within sample, i.e. in the present situation the basis weight variation in palmar transverse section of the index finger of sampled subject, since all samples are thus obtained. On the other hand, the mean chart (x-bar) shows another type of variation, called between samples.

Table 2: Sampled data of the dynamic human blood flow of Subject 1

S.No.	Sampled Data					Mean	Range
1	37.4	35.6	36.5	36.6	39.9	37.2	4.3
2	38.1	37.3	37.9	36.6	37.9	37.5	1.5
3	37.6	37.2	37.1	37.1	37.7	37.4	0.6
4	37.3	38.1	38.5	42.1	42.9	39.8	5.6
5	38.1	45.8	43.8	36.7	37.4	40.3	9.1
6	38.8	36.8	37.6	35.9	36.7	37.2	2.9
7	37.3	36.1	35.5	37.7	36.0	36.5	2.1
8	42.5	42.9	43.9	37.8	44.5	42.3	6.7
9	44.8	35.8	37.7	37.9	37.6	38.8	9.0
10	38.1	35.9	36.8	45.4	45.9	40.4	10.0
11	37.4	42.1	38.6	38.5	38.4	39.0	4.7
12	36.6	36.7	37.5	37.5	36.4	36.9	1.1
13	37.7	36.9	37.2	47.3	40.4	39.9	10.5
14	39.8	43.5	44.8	36.3	37.3	40.3	8.5
15	36.9	37.8	35.3	36.5	36.3	36.6	2.5
16	36.9	37.9	37.3	37.1	39.2	37.7	2.3
17	37.0	45.1	47.3	41.1	44.9	43.1	10.3
18	38.4	45.0	39.1	37.8	39.8	40.0	7.2
19	37.3	36.6	36.6	36.7	43.9	38.2	7.3
20	46.1	46.6	40.2	45.4	38.9	43.4	7.7
21	40.5	38.1	43.5	36.4	37.5	39.2	7.1
22	37.0	37.4	44.6	45.7	39.3	40.8	8.7
23	43.6	37.9	44.9	45.4	38.0	41.9	7.5
24	38.3	37.7	38.2	36.9	35.8	37.4	2.5
25	45.0	45.3	38.1	37.9	38.4	40.9	7.4

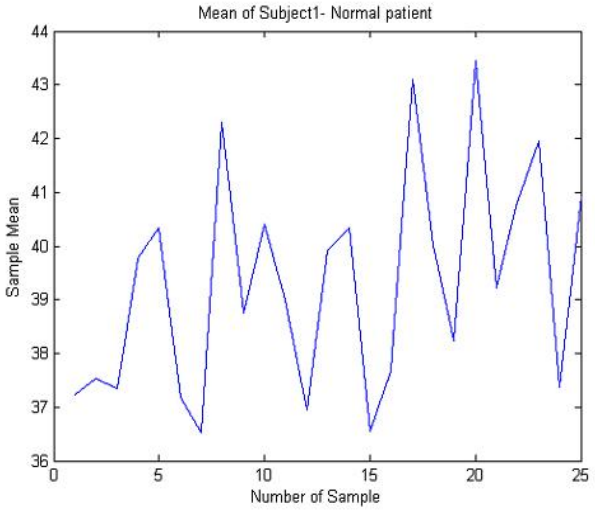

Fig.4. Control Charts for Basis Weight of Subject 1 Mean.

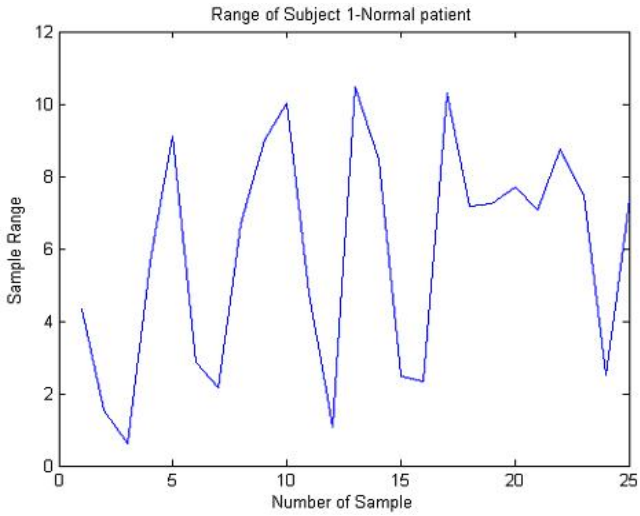

Fig.5.Control Charts for Basis Weight of Subject 1 Range.

Table 3: Sampled data of the dynamic human blood flow of Subject 2

S.No.	Sampled Data					Mean	Range
1	38.2	42.2	45.1	37.0	37.2	40.0	8.1
2	45.8	37.9	36.9	43.6	45.1	41.9	8.9
3	48.0	36.5	41.4	44.4	47.6	43.6	11.5
4	37.9	35.5	37.5	36.7	37.6	37.0	2.4
5	37.0	36.1	36.0	38.2	37.5	37.0	2.2
6	35.6	37.8	37.9	36.8	37.8	37.2	2.3
7	36.1	37.2	37.8	36.0	37.8	37.0	1.8
8	35.9	37.3	36.6	36.9	36.6	36.7	1.5
9	38.2	38.1	37.0	37.2	37.6	37.6	1.1
10	35.1	38.2	36.4	37.4	45.3	38.5	10.2
11	46.0	40.1	36.8	43.9	45.3	42.4	9.2
12	47.3	37.1	38.5	44.6	46.5	42.8	10.1
13	41.2	36.6	44.0	45.7	47.3	43.0	10.6
14	37.7	40.2	44.2	46.3	38.7	41.4	8.7
15	36.9	41.6	45.2	46.1	37.4	41.4	9.3
16	39.7	43.4	45.0	40.5	37.8	41.3	7.2
17	43.6	44.3	46.9	35.3	37.1	41.4	11.5
18	42.4	45.7	38.8	36.1	41.8	40.9	9.6
19	44.0	45.8	37.5	36.2	41.3	40.9	9.5
20	45.8	38.4	37.9	37.6	44.3	40.8	8.2
21	45.9	36.8	37.2	42.8	45.7	41.7	9.1
22	39.3	36.4	36.3	37.5	35.5	37.0	3.8
23	37.6	36.4	37.1	37.6	37.5	37.3	1.2
24	35.8	35.8	37.0	37.9	36.6	36.6	2.1
25	37.8	37.6	37.1	36.7	36.4	37.1	1.4

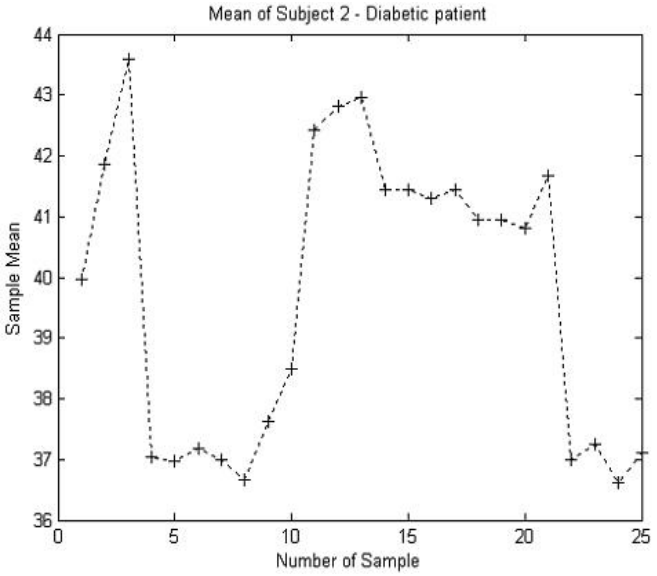

Fig.6. Control Chart for Basis Weight of Subject 2 Mean.

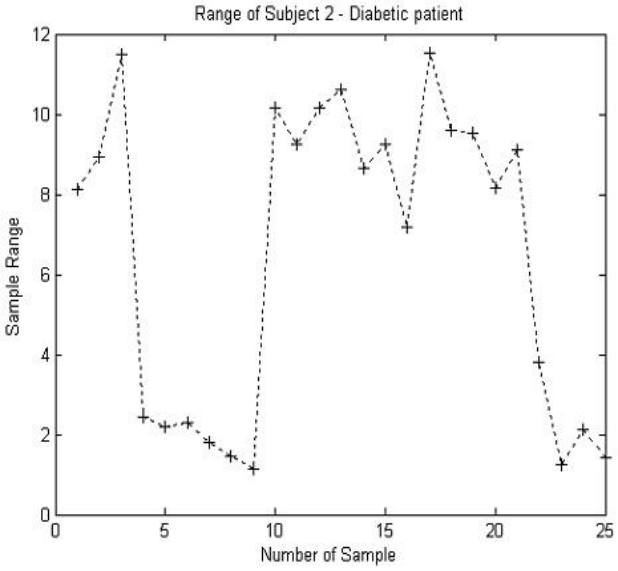

Fig.7.Control Charts for Basis Weight of Subject 2 Range.

6. Conclusion

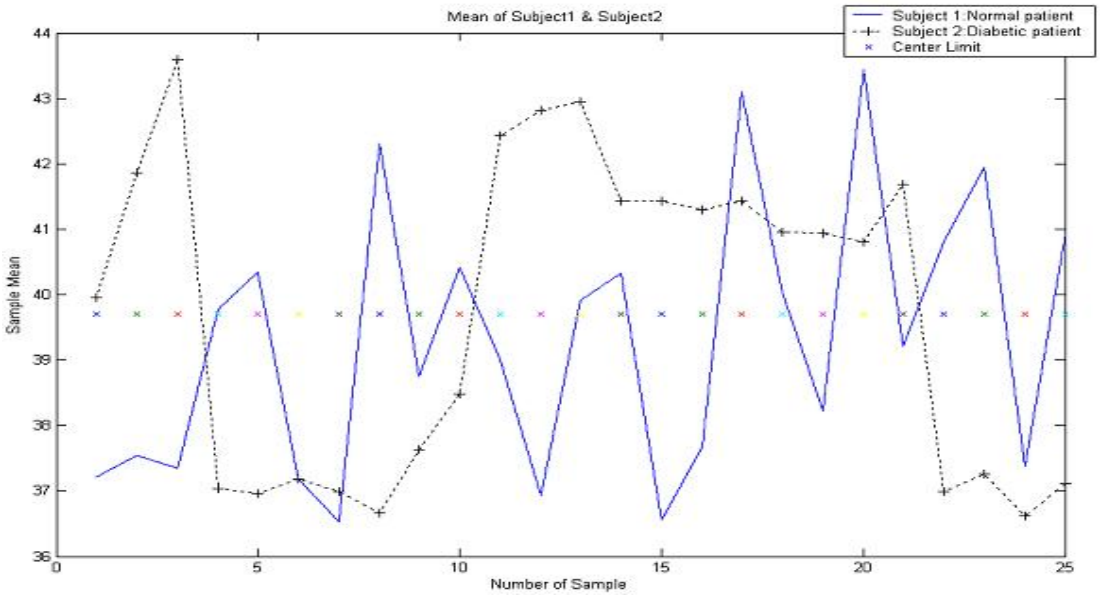

Fig.8. Control Charts for Basis Weight of Subject 1 and Subject 2 Mean

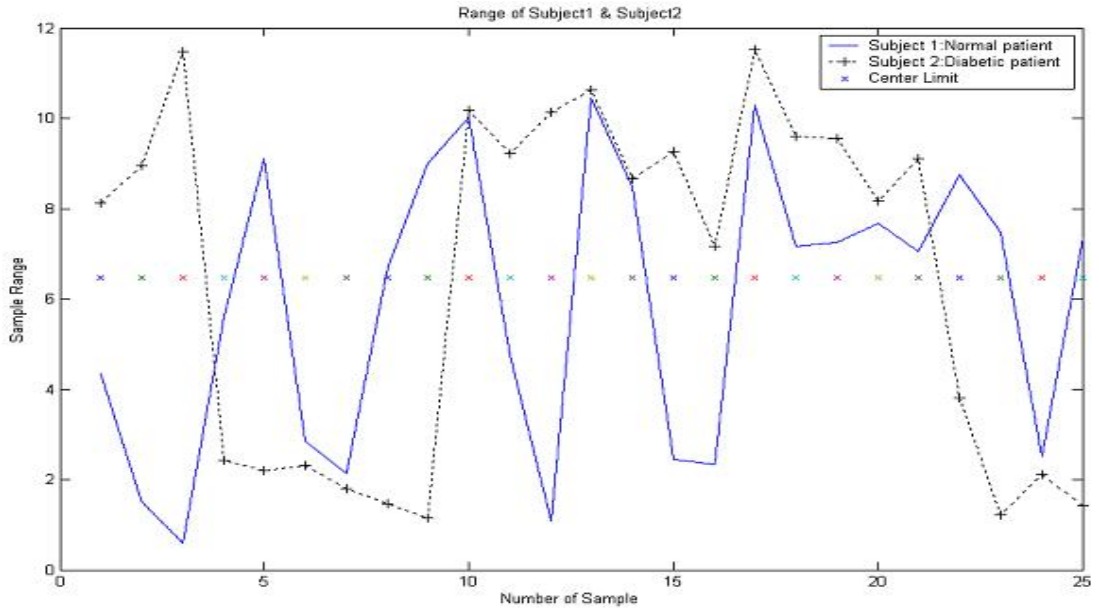

Fig.9. Control Charts for Basis Weight of Subject 1 and Subject 2 Range.

SUBJECT 1

Table 4: Hematology of Subject 1

1	R.B.C	5.17
2	P.C.V	44.8
3	HB A1c	5.4 %
4	MBG	105 mgs/dl

SUBJECT 2

Table 5: Hematology of Subject 2

1	R.B.C	5.21
2	P.C.V	41.3
3	HB A1c	15.8 %
4	MBG	434 mgs/dl

To give a preliminary introduction to estimation the blood glucose level of diabetic and non diabetic patients from the micro circulations. The He-Ne laser operating at 632.8nm wavelength is used. We can compute various associated parameters viz. blood pressure, blood cholesterol and blood glucose from blood flow.

Thus, we came to know that the plot Figure 8 and Figure 9 shown in the continuous line, the blood flow is at normal velocity and the cells are distributed evenly. So that the reflected laser beam are at regular intervals. Similarly the plot shown in dotted line is diabetic patient were the blood flow is not flowing with the normal velocity due to high viscosity and the cells are not properly distributed. The table (4) and (5) showed the hematology values of the subject1 and subject2.

Although the books about traditional quality tools usually do not present this technique, it is extremely important in the diagnosis process of diabetic mellitus, as on the human blood flow mechanism. Even in leading statistical software this control chart is not easily found, or else it is presented by another name.

References

[1] Shewhart, W.A. Economic control of quality of manufactured product. Milwaukee, ASQC Quality Press, 1989.

[2] Burr, J.T. The effects of non-normality on constants for x-bar and R charts. Industrial Quality Control, Milwaukee, v.23, p.563-9, 1967.

[3] Schilling, E.G.; Nelson, P.R. The effect of non-normality on the control limits of x-bar charts. Journal of Quality Technology, Milwaukee, v.8, 1976.

[4] Montgomery, D.C. Introduction to statistical quality control. 3 ed. New York, Wiley, 1996.

[5] Wheeler, D.J. Advanced topics in statistical process control. Knoxville, SPC, 1996.

[6] Dr.B.M.Jayaram,"HbA1c: Impact on diabetic management," Type2 Diabetes and its complication: A preventive program, 2008,pp.85-90.

[7] William F.Ganong, "Review of Medical Physiology," A LANGE MEDICAL Book., 19th Edition, pp.554-560. ISBN-0-8385-8449-7.

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Annexure: A - Factors for Control Limit Calculation

n	A_2	d_2
2	1.880	1.128
3	1.023	1.693
4	0.729	2.059
5	0.577	2.326
6	0.483	2.534
7	0.419	2.704
8	0.373	2.847
9	0.337	2.970
10	0.308	3.078

Source: Montgomery D. C. Introduction to statistical quality control. 3rd ed. New York, John Wiley, 1996.

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