Assessment of Hemoglobin Level of Pregnant Women Before and After Iron Deficiency Treatment Using Nonparametric Statistics

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Abstract
Iron Supplementation is generally recommended during pregnancy to meet the iron requirement of both mother and fetus. When detected early in pregnancy, iron deficiency anemia (IDA) is associated with an increase in the risk of preterm delivery. Deficiency of Vitamin C also causes poor iron absorption leading to IDA. This paper deploys non-parametric statistics to analyse and compare the hemoglobin level of pregnant women before and after consumption of Vitamin C and Sulfas Ferroses. The objective of this study is to compare the hemoglobin level of pregnant women before and after the IDA treatment and assess the association between maternal hemoglobin (Hb) level and pregnancy outcome. Johnson transformation is used to estimate the proportions of women with hemoglobin level out side the required specification limits before and after the treatment. Wilcoxon Rank Sum Test is deployed to compare the hemoglobin level before and after the treatment. The result indicates a significant difference in the hemoglobin level before and after the treatment.

Key words: Anemia, Hemoglobin, Johnson transformation, Performance analysis, Proportion of non-conformance, Wilcoxon Rank Sum Test.

1. Introduction

Due to the increased iron requirements during pregnancy, pregnant women are recognized as the group most vulnerable to iron deficiency anemia (IDA). Anemia, as determined by low hemoglobin or hematocrit, is most common among women in their reproductive years. Until recently, it was assumed that anemia during pregnancy had few untoward sequelaes. In recent years it has been suggested that a proportional relationship between anemia and preterm delivery now exists [1]. Infants born to women with a low Hemoglobin **level** have subsequently resulted in a lower birth weight, height and Apgar scores. In Asia, the prevalence of anemia was estimated to be 44% in non-pregnant and 60% in pregnant women [10]. At least 50% of the anemia cases have been attributed to iron deficiency ([2]; [3]; [12]). Maternal iron deficiency anemia increases the risk of premature delivery and subsequent low birth weight, and may contribute to low iron status and poor health of infants ([1]; [11]; [6]).
It was found that pregnant women with anemia are at a greater risk of perinatal mortality and morbidity ([5]; [9]; [8]). The results which have been gathered and analysed are due to a of trial experiment conducted in Indonesia relating to pregnant women. Specifically candidate mothers were observed over a nine month period and asked to consume 90 tablets of Vitamin C 100 mg and Sulfas Ferroses (SF) 350 mg after their third semester of pregnancy. In this paper we assess the performance of non-normal hemoglobin level data collected before and after treatment. The proportion of hemoglobin measurements falling below the WHO recommended level for either case is estimated using Johnson transformation. We will then use Wilcoxon Rank Sum Test to assess the effectiveness of the Vitamin C and Sulfas Ferroses (SF) treatment.

2. Subjects

The study was conducted among 125 women enrolled in a maternity clinic in Banjarmasin Indonesia. We are using 125 pairs of data collected during February 2007-September 2010. The pregnant women who deliver their baby in the clinic had been monitored during their nine-month pregnancy and each consumed 90 tablets of Vitamin C 100 mg and Sulfas Ferroses (SF) 350 mg after their third semester of pregnancy. The hemoglobin level of the individual patient was measured before and after the treatment. One of the objectives in this research is to analyse the hemoglobin level of these women before and after treatment. We also assess the distribution of these data and take necessary steps to transform the data (before and after treatment) to estimate the proportion of women with hemoglobin level outside WHO recommended lower and upper specification limits {LSL , USL] of 11 and 14.

In section 3.2 we explain the reason for transforming data and propose the transformation model to be adopted. At the start of the study the authors have used statistical package Minitab to fit the commonly used normal distribution function to each set of the hemoglobin data.

For both sets the p-value of the fit was less than 0.01 indicating the measurements of the hemoglobin level do not follow normal distribution. The histograms of the data are presented in Figures 1-2. The summary statistics including skewness, Upper and lower quartiles (Q3 and Q1), mean, standard deviation, minimum and maximum are given in table 1 below.

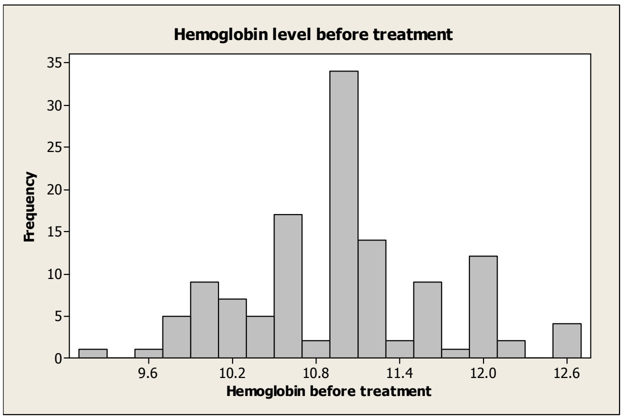

Figure 1: Distribution of the Hemoglobin level measurements before treatment.

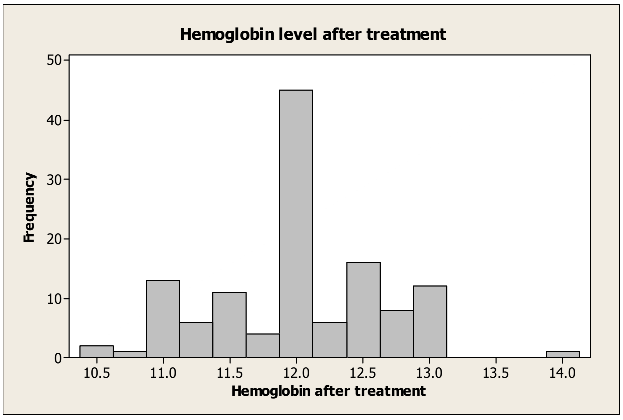

Figure 2: Distribution of the Hemoglobin level measurements after treatment.

Table 1-a: Descriptive Statistics for Hemoglobin level before and after treatment

		N	Mean	St. Dev	Min	Q1
Hb	before	125	10.94	0.7	9.2	10.5
Hb	after	125	12	0.63	10.5	11.5

Table 1-b: Descriptive Statistics for Hemoglobin level before and after treatment

		N	Median	Q3	Max	Skewness
Hb	before	125	11	11.2	12.5	0.13
Hb	after	125	12	12.5	14	-o.o7

3. Method

One of the main objectives of this paper is to estimate the proportion of women with the hemoglobin level outside the WHO lower and upper specification limits (LSL and USL) [13]. This requires the knowledge of the data distribution both prior to the treatment and after the treatment. Figures 1-2 show that none of the data set follows normal distribution. Furthermore, the summary statistics confirm a significant difference between the mean hemoglobin level before and after the treatment with positive skewness coefficient before the treatment and negative after the treatment. It is well documented that the low hemoglobin levels are a growing concern to the medical profession [3], [5]; therefore it is only logical that the aim should be to reduce the proportion of women with Hb level below the LSL. Since the data does not follow normal distribution we have used the Johnson transformation to estimate the proportion of non conforming data. This proportion is estimated using the performance analysis in the statistical package Minitab. We have employed the Wilcoxon Rank sum test which is a nonparametric alternative to paired test to assess the effectiveness of the treatment process undertaken by the clinic.

3.1 Johnson Transformation

Many analyses require an assumption of normality. In cases when data is not normal, one can apply a function to make the data approximately normal and complete the required analysis. In this research we desire to perform a capability analysis on the non-normal hemoglobin data, therefore, we will first transform the data and then apply the performance analysis on the amended data. Depending on the nature of the data, there are many different functions such as square root, logarithm, power, reciprocal or arcsine, that one could apply to transform the data.

The Johnson transformation function is selected from three types of functions in the Johnson system [4]. Because the functions cover a wide variety of distributions by changing the parameters, the statistical package usually finds an acceptable transformation. The Johnson transformation function is complicated, but is well suited for finding an appropriate transformation for our purposes.

3.2 Performance Analysis of Non-normal Data

Process capability analysis is used to ensure that the outcomes of a process are capable to fulfil certain requirements or specifications. Application of process capability analysis is an essential part of the overall quality improvement process. The concept of process capability was introduced by Juran et al.[7]. The two most popular indices used in performance analysis are Cp, Cpk and defined as follows:

$$C_p = \frac{USL - LSL}{6\sigma} \quad (1)$$

$$C_{pk} = \min\left(\frac{USL-\mu}{3\sigma}, \frac{\mu-LSL}{3\sigma}\right)$$

$$C_{pk} = \min\left(C_{pu}, C_{pl}\right) \tag{2}$$

μ and σ are the population mean and standard deviation respectively.

In the capability calculations, we are mainly interested in three points within the process distribution: the upper tail, the point of central tendency and the lower tail. In terms of quantiles, these points for the normal distribution correspond to $X_{0.99865}=\mu+3\sigma$, $X_{0.50}=\mu$ $X_{0.00135}=\mu-3\sigma$ In case of normally distributed data, it is easy to estimate quantile points. But for the non-normal data, it is quite cumbersome to estimate them. In fact when the population is not normal, these quantiles do not necessarily corresponds to $\mu+3\sigma$, μ , $\mu-3\sigma$, respectively. To deal with non-normality; one approach is to transform the non-normal output data to approximately normal data using mathematical functions. In this paper we have used the Johnson transformation to transform the data and used the statistical package Minitab to estimate the capability indices and the proportion of data falling out side the specification limits.

3.3 Non-parametric Wilcoxon Rank Sum Test

The Wilcoxon test is a nonparametric analog of the sample t-test because it does not require the data to come from a normally distributed population, as the t-test does. It is a nonparametric hypothesis test for the median of a single population. The procedure uses the null hypothesis that the population median (η) is equal to a hypothesized value ($H0$: $\eta = \eta_0$), and tests it against an alternative hypothesis, which can be either left-tailed $\eta < \eta_0$), right-tailed ($\eta > \eta_0$), or two-tailed ($\eta \neq \eta_0$). In this paper we apply the Wilcoxon test to the population of the hemoglobin difference of the study group. Since the differences would also be non-normal. The differences are defined as:

Difference = Hb level after treatment – Hb level before treatment;

If the treatment is significantly increasing the hemoglobin level, then we expect the median of the population of differences to be greater than zero. However if the treatment had no significant effect then the population of differences would have a median of zero, i.e., we test the hypothesis:

$H0 : \eta = 0.0$ vs $Ha : \eta > 0.0$

4. Case Study and Discussion

As stated earlier this study has used the hemoglobin measurements of 125 women who were monitored in a maternity clinic in Banjarmasin between January 2005 and December 2010. Each patient was given 90 tablets of Vitamin C 100 mg and Sulfas Ferroses (SF) 350 mg after their third semester of pregnancy. The hemoglobin level of individual patient was measured before and after the treatment. The authors have examined the distribution of each data set (before and after treatment) and presented the results in Figures 1-2.

→The results clearly demonstrate the data does not follow normal distribution. The Johnson transformation was employed to convert the skewed data to approximately normal data. The capability analysis was performed on the data to estimate the proportion of patients whose globins level fall out side the WHO recommended specification limits defined by LSL=11 and USL=14. The WHO anemia classifications based on the hemoglobin level are:

- Hb: 11 gr% : normal
- Hb: 9-10 gr% : mild anemia
- Hb: 9-10 gr% : mild anemia
- Hb: 7 – 8 gr%: medium anemia
- Hb: < 7 gr% : severe anemia

The results of the performance analysis are presented in Figures 3-4. The outputs indicate that if patients had not received the treatment then, approximately 416000 per million would have had anemia (PPM < LSL = 416000). Figure 4 shows the significant reduction of this proportion after the treatment, i.e. PPM < LSL = 32000 (under observed performance).

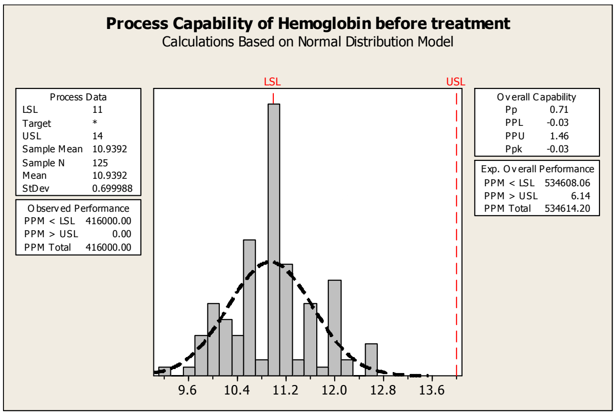

Figure 3: Performance analysis of Hemoglobin measurements before the treatment.

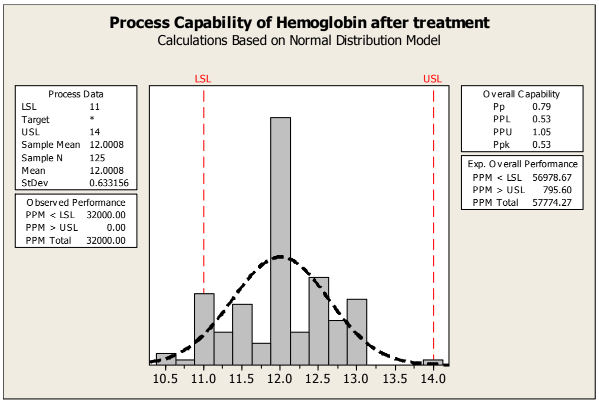

Figure 4: Performance analysis of Hemoglobin measurements after the treatment

We have also employed the non-parametric Wilcoxon Rank Sum test to investigate the effectiveness of the treatment in increasing the hemoglobin level of the women in the study group. Figure 5 presents the box plot comparison of the two data sets. The results of the Wilcoxon Rank Sum test are presented in Table 2 and show that the median of the differences is 1.05 and the 95% confidence interval for the median difference is [1.05 1.10]. The results also indicate that the null hypotheses.

H0: median of differences = 0.0 should significantly be rejected in favour of the alternative;

Ha: median of differences > 0.0 with the p-value of 0.0. Therefore, we can conclude that the treatment has significantly increased the median of the hemoglobin level by 1.05 units. Furthermore, on average we would expect the median to increase between 1.05 to 1.10.

Table 2: Out put for Wilcoxon Signed Rank Test where difference = Hemoglobin after treatment - Hemoglobin before treatment.

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H0: median of differences = 0.0 versus
Ha: median of differences > 0.0
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	N	N for Test	Wilcoxon Statistic
Diff after-before	15625	14587	101319492

	N	P	Estimated Median
Diff after-before	15625	0.000	1.05000

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95% confidence interval for the median of
the differences = [1.05    1.10]
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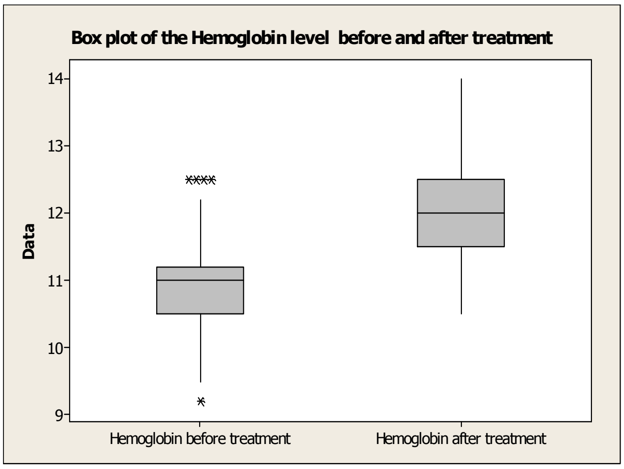

Figure 5: Box plot of Hemoglobin level measurements before and after the treatment.

5. Conclusion

Anemia is an increasingly prevalent factor in the Maternal Mortality Rate (MMR). It has been well established in the research literature that consumption of Vitamin C and Sulfas Ferroses during the pregnancy term reduces the incidence of hemoglobin level <11 which leads to anemia. The paper has investigated the distribution of the hemoglobin measurements before and after the treatment for 125 patients who have been monitored in the clinic. Johnson transformation is used to transfer the non-normal data. Performance analysis is employed to estimate the proportion of anemia patients before and after the treatments. The results show a significant reduction of 416000/1000000 to 32000/1000000 in the proportion after the treatment. The Wilcoxon Signed Rank test is used to assess the effectiveness of the treatment in increasing the hemoglobin level of pregnant women and reducing the maternal mortality rate. The results have showed an increase of 1.05 to 1.10 in the median of the hemoglobin level after the treatment. Therefore, we can conclude that the treatment has been extremely effective in reducing the anemia rate in pregnant women.

Acknowledgement

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