



RESEARCH ARTICLE



Received on: 02-10-2014

Accepted on: 30-10-2014

Published on: 23-11-2014

**Dr Oduola Abiola**

PAP RSB Institute of Health Sciences,  
Univeristi Brunei Darussalam, Jalan  
Tungku Link, Gadong, BE 1410, Brunei  
Darussalam

**Email:** oduola.abiola@ubd.edu.bn



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Conflict of Interest: None Declared !

DOI: 10.15272/ajbps.v4i37.597

## Haematological profile shows that Inbred Sprague Dawley rats have exceptional promise for use in biomedical and pharmacological studies

Nadzirah Md Said and Oduola Abiola

PAP RSB Institute of Health Sciences, Univeristi Brunei Darussalam, Jalan Tungku Link,  
Gadong, BE 1410, Brunei Darussalam.

### Abstract

**Background:** Laboratory or model animals are used in research for cure and improvement of human and animal diseases. Rats particularly the inbred strains are now more widely used laboratory model especially in toxicology and for understanding the pathophysiology of diseases.

**Aim:** To determine the haematological indices of male and female inbred Sprague Dawley rats in health.

**Methods:** An automated haematology analyzer was used to determine haematological indices of whole blood from individual in 20 each of male and female inbred Sprague Dawley rats. Mean, standard deviation, median interquartile range as well as minimum and maximum values for the haematological profile were calculated.

**Findings:** Statistically significant differences for total and differential white blood cells (WBC), red blood cells (RBC) and Haemoglobin (Hgb) levels were observed between male and female rats.

**Conclusion:** Data presented here would be useful as a reference for studies aimed at understanding the pathophysiology of diseases especially neoplasms and haematological disorders; as well as in evaluating alterations in blood parameters in relation to the pharmacological interventions and/or toxicological effects in inbred Sprague Dawley rats.

**Keywords:** Disease pathophysiology; Haematological indices; Inbred Sprague Dawley rats; Pharmacological interventions; Toxicological effects.

### Cite this article as:

Nadzirah Md Said , Oduola Abiola, Haematological profile shows that Inbred Sprague Dawley rats have exceptional promise for use in biomedical and pharmacological studies. Asian Journal of Biomedical and Pharmaceutical Sciences; 04 (37); 2014,33-37.

## INTRODUCTION

Over the years, there have been demands to increase the quality of animals used for research, which show that laboratory, or model animals are widely used in this area with most of them being mice, rats and/or other rodents. These animal models are used for developing new methods and approaches to the cure and improvement of human and animal diseases, disability, and other biological processes.<sup>1,2,3</sup>

The use of laboratory rats (*Rattus norvegicus*) in research has increased steadily as they are preferred because of their short life cycles, inexpensive cost to purchase, easy maintenance in limited space<sup>4</sup> and availability of a large database of their characteristics that are useful in interpreting relevant animal data for humans.<sup>5</sup> The rats particularly the inbred strains are now more widely used as laboratory model in the understanding and studying of diseases.<sup>3,6</sup> Inbred strains are produced by at least 20 generations of subsequent brother-sister matings,<sup>7</sup> and are both homozygous and isogenic: all the individuals are genetically virtually identical.<sup>5</sup> The homozygosity and isogenicity therefore tend to make the inbred animals to be phenotypically uniform. Consequently, this is invaluable in that a given biological effect can be detected with fewer animals, although the uniformity may not be apparent for characters such as body weights, unless very large numbers are studied.<sup>5</sup>

Thus the rat model is being used extensively in physiology, transplantation, immunogenetics and cancer research,<sup>7</sup> and remains the dominant model for the preliminary testing of all forms of therapeutic and chemical toxicities.<sup>4,8</sup> In this area of research, abnormal treatment-related values could represent changes pertaining to the effects of the treatments such as the toxicity's effects, which could be detected by alterations in a series of *in vivo* analysed parameters.<sup>9</sup> Among these parameters are haematology data and they are of great importance in determining such effects. This is because blood plays a major role in the body's transport system and excretion of substances of almost all the body's metabolic processes, and any deviations from normal are detectable in the blood profile.<sup>3</sup> One way of evaluating the haematologic profile is by Full Blood Count (FBC) otherwise called Complete Blood Count (CBC). It yields information about production of all blood cells, the oxygen-carrying capacity through RBC indices, haemoglobin and haematocrit. It also provides information about the immune system through the evaluation of the WBC counts especially along with differential counts.<sup>10</sup> Thus, CBC is one of the most frequently requested tests in clinical medicine<sup>11</sup> with multiple indications such as anaemia, cancer, infection as well as monitoring for side effects of drugs causing blood dyscrasias.<sup>10,11</sup>

Of all the rat models, Sprague Dawley (SD) rats are the most widely used research models in all aspects of biomedical research.<sup>12</sup> The docile nature of the rats provides a variety of health profiles that enable for the needs of specific research. This study therefore presents the haematological profile (erythrocytic and leukocytic indices) of the inbred SD rat model, which was determined using a haematology blood analyser.

## Materials and Methods

### *Animal care and experimental design*

This study was conducted in accordance with the internationally accepted principles for laboratory animal use and care as found in the European Community guidelines (EEC Directive of 1986; 86/609/EEC). The Universiti Brunei Darussalam Research Ethics Committee approved the study prior to its commencement.

Breeding pairs of inbred SD rats were obtained from iDNA Biotechnology, Kuala Lumpur, Malaysia. They were imported into the Universiti Brunei Darussalam Animal House where they were brother-sister mated to produce the rats for this study after a period of acclimatisation spanning several weeks.

Forty inbred SD rats consisting of 20 each of weanling male and female weighing between 117–264g and 82–116g respectively (at the commencement of the study) were used. All the animals were housed 4 per RC1 propylene cage with metal grill top, kept under 12 h light and 12 h dark cycle at 22±1°C and allowed free access to rat chow and water *ad libitum*. The rats were sacrificed by cervical dislocation followed by decapitation after six weeks weighing 357–507 g and 142–187g for male and female respectively. Whole blood was collected into an EDTA contained sterile specimen tube (BD Vacutainer; Beckton, Dickinson and Company USA) for haematological analyses.

### Full blood count

CBC was carried out using an automated analyser: ACT Diff Analyzer (Beckman Coulter USA), which counts and sizes blood cells by detecting and measuring changes in electrical resistance when the cells in the conductive liquid passes through a small aperture of the machine and hence, impedes the current and cause a measurable pulse.<sup>13</sup> The height of the pulse is proportional to the volume of the cells, while the number of pulses indicates particle count and the amplitude of the electrical pulse produced is proportional to the cells' volume.<sup>14</sup> The various parameters that are determined by this machine include total WBC, lymphocyte per cent (LY%), mononuclear cell per cent (MO%), granulocyte per cent (GR%), lymphocyte number (LY#), mononuclear cell number (MO#), granulocyte number (GR#), RBC number, haemoglobin (Hgb), haematocrit (Hct), mean

corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), red cell distribution width (RDW), platelet count (Plt), mean platelet volume (MPV), plateletcrit (pct), and platelet distribution width (PDW).

*Statistical analysis:* Data analysis was carried out using IBM SPSS 20 to determine the mean, standard

deviation (SD), Minimum value (Min.), Maximum value (Max.), Median (IQR); These are shown in Table 1. Independent sample t-test was used to compare values for the haematological indices in male and female rats (Table 2). A 'P value' that is less than 0.05 ( $P < 0.05$ ) is considered to show significant statistical difference.

**Results**

Blood indices	Male (n=20)				Female (n=20)			
	Mean ± SD	Min.	Max.	Median (IQR)	Mean ± SD	Min.	Max.	Median (IQR)
WBC (x 103 cells/μL)	9.04 ± 2.29	5.00	14.45	9.2 (3.46)	6.51 ± 2.08	1.70	12.15	6.3 (2.07)
LY %	83.51 ± 4.02	74.85	88.75	85.0 (6.15)	88.48 ± 2.89	82.65	93.45	88.1 (4.19)
MO %	6.30 ± 2.35	1.95	10.40	6.2 (3.61)	5.82 ± 1.34	3.50	8.40	6.1 (1.73)
GR %	10.31 ± 3.37	6.00	18.40	9.0 (4.29)	5.67 ± 2.19	2.40	9.15	6.1 (4.00)
LY# (x 103 cells/μL)	7.50 ± 1.91	4.30	12.20	7.6 (2.95)	5.74 ± 1.77	1.55	10.00	5.5 (2.04)
MO # (x 103 cells/μL)	0.55 ± 0.25	0.15	1.15	0.5 (0.27)	0.39 ± 0.18	0.10	1.05	0.4 (0.14)
GR# (x 103 cells/μL)	0.94 ± 0.42	0.35	1.70	0.8 (0.61)	0.39 ± 0.23	0.10	1.10	0.4 (0.22)
RBC (x 106 cells/μL)	7.61 ± 0.27	7.10	7.93	7.7 (0.47)	6.86 ± 0.47	5.95	7.81	6.9 (0.57)
Hgb (g/dL)	15.63 ± 0.71	14.25	17.15	15.7 (0.99)	14.71 ± 1.08	12.10	16.75	14.7 (1.05)
Hct (%)	52.33 ± 45.06	39.55	243.65	42.6 (3.12)	39.76 ± 2.71	33.80	44.15	39.7 (3.71)
MCV (fL)	55.61 ± 1.29	53.30	58.00	55.7 (1.85)	56.50 ± 4.81	39.20	60.75	57.7 (1.85)
MCH (pg/cell)	20.58 ± 0.77	19.30	21.65	20.6 (1.40)	22.29 ± 3.78	20.40	38.15	21.6 (0.83)
MCHC (g/dL)	36.19 ± 3.64	21.15	38.35	37.1 (1.31)	37.01 ± 0.89	35.50	38.20	37.2 (1.86)
RDW (%)	12.89 ± 1.16	11.10	16.55	12.7 (1.14)	11.88 ± 1.28	11.00	17.00	11.7 (0.79)
Plt (x 103 cells/μL)	595.23 ± 206.49	253.50	963.50	596.3 (304.00)	516.00 ± 239.84	45.00	937.50	544.8 (333.90)
MPV (fL)	6.31 ± 0.81	3.20	7.25	6.3 (0.57)	6.42 ± 0.54	5.50	8.05	6.5 (0.64)
Pct	0.39 ± 0.15	0.16	0.69	0.4 (0.21)	0.37 ± 0.11	0.16	0.55	0.4 (0.19)
PDW	16.71 ± 0.78	14.20	17.70	16.7 (1.03)	19.37 ± 11.45	15.20	67.95	17.1 (0.93)

**Table 1:** Haematological profile of the male and female inbred SD rats. Values represent the mean ± standard deviation

Blood indices	Male (n=20)		Female (n=20)	
WBC (x 103 cells/μL)	9.04 ± 2.29**		6.51 ± 2.08	
LY %	83.51 ± 4.02		88.48 ± 2.89	
MO %	6.30 ± 2.35*		5.82 ± 1.34	
GR %	10.31 ± 3.37**		5.67 ± 2.19	
LY# (x 103 cells/μL)	7.50 ± 1.91*		5.74 ± 1.77	
MO # (x 103 cells/μL)	0.55 ± 0.25*		0.39 ± 0.18	
GR# (x 103 cells/μL)	0.94 ± 0.42**		0.39 ± 0.23	
RBC (x 106 cells/μL)	7.61 ± 0.27**		6.86 ± 0.47	
Hgb (g/dL)	15.63 ± 0.71**		14.71 ± 1.08	
Hct (%)	52.33 ± 45.06		39.76 ± 2.71	
MCV (fL)	55.61 ± 1.29		56.50 ± 4.81	
MCH (pg/cell)	20.58 ± 0.77		22.29 ± 3.78	
MCHC (g/dL)	36.19 ± 3.64		37.01 ± 0.89	
RDW (%)	12.89 ± 1.16*		11.88 ± 1.28	
Plt (x 103 cells/μL)	595.23 ± 206.49		516.00 ± 239.84	
MPV (fL)	6.31 ± 0.81		6.42 ± 0.54	
Pct	0.39 ± 0.15		0.37 ± 0.11	
PDW	16.71 ± 0.78		19.37 ± 11.45	

Haematological profiles for male and female inbred SD rats are presented in Table 1. They contain mean, standard deviation (SD), Minimum value (Min.), Maximum value (Max.), Median and Interquartile range (IQR). Visually the figures do not appear to show much variation for most of the haematological indices both within and between genders. However when statistically analysed, significant differences in a number of the indices become apparent as shown in Table 2. The differences between the genders are also revealed and are particularly more pronounced in favour of the male with respect to total and differential WBC counts, except for lymphocyte per cent that tends to be in the opposite direction.

**Discussions**

We have used the Beckman Coulter Blood Analyser to determine the haematological indices in inbred SD rats for both genders. While there are several reports on haematological indices of SD rats in the literature, we are not aware of any one that has specifically used inbred SD rats; thus, it could be argued that this study

**Table 2:** Comparison of FBC between male and female inbred SD rats. Values represent the mean ± standard deviation Significant differences at \*  $P < 0.05$  and \*\*  $P < 0.01$

is the first to report haematological indices in inbred SD rats of both genders. Comparative studies of CBC have reported an agreement between the automated haematology analyzer readings and those of standard manual methods especially when used with appropriate controls.<sup>15,16</sup> More importantly however, the Beckman Coulter Blood Analyser that we have used in this study had been reported to give accurate and precise CBC and 5-part differential results.<sup>17</sup> Therefore, the data from this study could be related to those of others especially if they are obtained within these analytical methods and confines.

In the present study, we have observed differences in total WBC, mononuclear percent, granulocyte percent, lymphocyte, mononuclear and granulocyte numbers, RBC, Hgb and RDW between males and females. The differences observed for RBC and Hgb concentration could be related to the different demand for oxygen according to gender.<sup>9</sup> Most of the WBC parameters were higher in male than in female rats, although the lymphocyte percent was higher in the opposite direction. The higher WBC counts in male rats is generally in agreement with previous studies which reported that male rats generally have higher total leukocytes, including lymphocyte and granulocyte counts than their female counterparts;<sup>18,19</sup> these workers observed that this might be due to the influence of sex hormones on blood cell counts. While the observed differences may be due to effect of hormones as suggested, it is interesting that none of the studies including the present one has measured sex hormone levels and/or characterised the oestrous cycle stage of the female rats. Further studies are therefore needed to understand the possible role(s) of sex hormones on the parameters. Thus we intend to characterise the oestrous cycle stages as well as measure the levels of androgens, oestrogen, progesterone and indeed other related hormones in a future study.

In addition, a previous study on blood counts of adult albino rats of the Wistar strain showed high leukocyte counts in males than in females.<sup>20</sup> The values that we observed for the leukocyte count are much lower than in Cameron and Watson's study.<sup>20</sup> The discrepancies could be due to strain differences but more importantly the fact that we used inbred SD strain and possibly other factors such as the level of hygiene maintained in the animal facilities. Notwithstanding, these values are higher in male than in female which to us is significant as it may be suggesting a unique characteristic of the inbred SD rat and deserves further investigations. With respect to other parameters, the range of values reported by Cameron and Watson [1949] are generally similar to those that we observed in the present study despite the differences in methods. This is not

surprising given that SD and Wistar rats derived from crosses involving albino females.<sup>21</sup> Thus, the haematological data of the inbred SD rats could provide reference range values for use in defining any alterations in blood parameters and indices that may represent changes pertaining to pharmacological and/or toxicological effects, as well as for use in other areas of research.

### Conclusions

The similarity of some of the haematological indices of the inbred SD rats obtained in this study with the data of other strains of rats point to its wide applicability with respect to use in related future studies. The unique characteristic of much lower leukocyte counts than in rat models from previous studies suggest that the inbred SD rat model holds promise for studies involving leukocytic disorders in addition to being used in determining the alterations in vivo analysed parameters that may be related to the effects of treatments, particularly in toxicological studies.

### Author's contributions

NMS: Carried out laboratory experiments and statistical analysis as well made first draft of manuscript.

OA: Conceptualized, designed the study, supervised laboratory experiments, revised and finalized manuscript.

### Conflict of interest statement

None declared.

### Funding sources

This study was financially supported by PAPRSB Institute of Health Science, Universiti Brunei Darussalam, Brunei Darussalam.

### Acknowledgements

We are grateful to Mr Lai Kuan Hai for helping with the animal husbandry.

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