Available online www.ijpras.com

International Journal of Pharmaceutical Research & Allied Sciences, 2018, 7(2):191-199



Research Article

ISSN: 2277-3657 CODEN(USA): IJPRPM

Monitoring the Cardiovascular Parameters (HR, RR, PBP) Under Pressure Situation

Sami AbdulJabbar Rashid¹, Mustafa Maad Hamdi², Ahmed Shamil Mustafa²

¹Department of Electrical, Electronics and Systems, Faculty of Engineering, Universiti Kebangsaan Malaysia (UKM), Malaysia

²Department of Computer Engineering Techniques, Al-Maarif University College, Iraq

ABSTRACT

Clinical physiological parameters are one of the most important fields in healthcare innovation. Many mobile applications and devices have been designed and programmed for this purpose. Each one has been dealing with one parameter or more. Each device or software has been covering a part of monitoring, or has been designed for a specific purpose like monitoring cardiovascular parameters while doing cardio training. In this project, it was tried to monitor the physiological clinical parameters under pressure using only PPG signal. The idea was to calculate the heart rate, respiration rate and pulse pressure for all subjects in two situations. The first one was a normal case, and the results were compared with standards to approve that the algorithms used were suitable, and the second one was being under pressure to determine the effects of pressure position on the human's physiological parameters. The results showed that the heart rate was highly affected by the pressure position. The respiration rate was affected also but not highly. Finally, the pulse pressure was not affected by the pressure position because it is the difference between the systolic and diastolic blood pressure.

Key words: Blood Pressure (BP), Heart Rate (HR), Respiration Rate (RR), Pulse Pressure, PPG, Clinical, Monitoring.

INTRODUCTION

Nowadays, health care is very important among all people. And, as Ghamri et al. (2017) has declared, the prevalence of cardiovascular diseases (CVD) which is one of the main health issues, has been increasing in developing and developed nations during the last decade. And, Suastuti et al. (2018) stated that the prevalence of obesity and its complication such as coronary heart disease, diabetic, hypertension, and hyperlipidemic is increasing nowadays. Also, cardiovascular diseases affect life expectancy and damage the quality of life. Therefore, one of the factors that affect the quality of life is the health literacy (Marzangi et al, 2018). Hence, people try to check their health status by themselves instead of going to hospitals for check-up. Many devices have been implemented for this issue. Some of them are portable, reliable and easy to use. Modern technology has grown this point by programing applications for health care monitoring using smart phones rather than fixed devices. It is easier for patients to use many applications on only one device instead of using many devices, each for a special application. In addition to personal use, these applications are good for doctors or any one in charge. They make their work easier and faster. The most popular applications have been used to measure:

- a- Heart rate
- b- Respiratory rate
- c- Blood Pressure
- d- Oxygen saturation level

They are most probably regarded as physiological parameters [1]. PPG signal is most widely used to calculate the above parameters. PB can be estimated depending on PPG signal. Changing in BP will affect the shape of PPG signals. The heart rate (HR) is one of the important parameters for monitoring the clinical cardiovascular parameters. HR is the average of heart pulses per minute. By monitoring HR continuously, it is possible to get an indication about the heart itself. The force of blood that travels through the arteries is called Blood Pressure (BP). There are two measurements to PB: Systolic Pressure, which measures the highest contracts of the heart, and Diastolic Pressure which measures the lowest contracts of the heart. BP is one of the physiological parameters that is used to monitor the health condition of the patients. It gives an indication about various cardiovascular terms, which is important to determine the clinical parameters, and do medical researches. Either invasive or non-invasive, it can be used to calculate the Blood Pressure. Invasive techniques are used for continuous monitoring of Blood Pressure. The noninvasive techniques include the Korotkoff and Oscillometry methods [2]. The accuracy readings of non-invasive are very good because they are confined to only one point at a time. Of course, the subjects affect the readings. Pulse Wave Velocity (PWV) is directly related to the BP [3]. In non-invasive technique, PWV is an excellent way to monitor the BP. The problem is that it is not easy to measure the PWV using clinical equipment. Therefore, Pulse Transit Time (PTT) is used instead of PWV. The relationship between the PTT and BP is opposite, which means when BP increases, PTT will decrease. The aim of this research was to collect the PPG signal in two cases, one in normal situation and the other under pressure situation. In this project, the effects on the characteristics of the signals were studied, and a program was implemented for calculating and monitoring the cardiovascular parameters under pressure case. The parameters of this research were Heart Rate (HR), Respiration Rate (RR) and Pulse Blood Pressure (PBP). The tissues in the human body are hidden under the skin, the thickness of the skin is different from one place to another. The soft skin allows the light to transmit through it. Because the color of the blood is red, the most useful wavelength that should be used must be red. The Photoplethysmograph (PPG) acquires the information that can be collected by transmitted signal [4]. A source of light is considered as a guide to a place that the data must be collected. Not all the light is transmitted, but just a part of the light is reflected by the skin. There is no exact value of the rate of light that is transmitted, and it mostly depends on the location. Fig. 1 shows the reflection of the light source from the body. Only the reflected part from the vessel contains information, the others are useless.

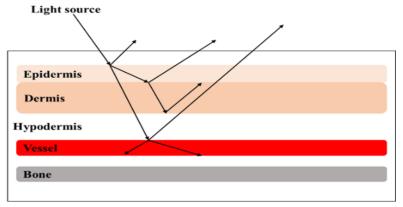


Figure 1. Reflection of light source

The signal that is collected contains two main components. The first one is the static signal or DC, that comes from static elements in human body such as, bone and dermis, etc. the second part is the dynamic signal or AC which is the reflected light from vessels. The vessel blood contour changes due to the heart pulsation, and the PPG is the useful signal to represent it.

Clinical applications of ppg signal

Various clinical devices are based on PPG signal such as :

- i- Monitoring the physiological parameters (Heart Rate, Oxygen Saturation, Blood Pressure and Respiration Rate).
- ii- Vascular Assessment (Arterial Compliance, Arterial Disease and Ageing, Endothelial Function and Venous Assessment).
- iii- Autonomic Function (Thermoregulation and Vasomotor Function, Neurology, Orthostatic Intolerance and further Cardiovascular Variability Assessments).

A brief description of the most popular clinical settings that depend on PPG signal has been provided.

A. Blood Oxygen Saturation

One of the most advanced significant technology in clinical monitoring is Pulse oximetry [5]. It measures the PPG to obtain information about oxygen saturation in blood as well as the heart rate [6]. Different clinical settings like hospitals, veterinary clinics and sport medicine depend on this application. During 1990, Pulse oximetry became an international standard for anesthesia monitoring. The oxygen saturation can be calculated by shining infrared red light through the vascular tissue. The amplitude of AC signal is very sensitive to the changes in oxygen saturation. The oxygen saturation can be calculated from the amplitude ratio, and the DC component in PPG. The PPG signal changes with each heart beat because of the blood volume in arterial. The technique relies on a peripheral pulse that should be presented by the main limitation of the pulse oximetry. Dyshaemoglobinaemias can affect the saturation readings of the oxygen. That means, at low levels of saturation the accuracy may fall off [7]. To solve the problem of artefact movement that affects the reliability of measurement, advanced computer algorithms have been developed. One of the most popular algorithms is the Massimo SET technology [8]. Pulse oximeters can use both the transmission and reflection modes to measure SpO2 operation [9]. To cover the problem of associated finger pulse loss, central body measurement sites have been investigated which include monitoring of oxygen saturation [7]. In noninvasive measurement, another model was developed in pulse oximetry. This model uses PPG signal that is applied by external artificial perturbations [10].

B. Heart Rate (HR)

One of the most important parameters of physiological characteristics is the heart rate. It is used in wide range of medical settings such as ambulatory patient and hospital based monitoring. The beat of heart is synchronous with the AC component of the PPG signal, for that it can be a good source for information of heart rate. Cardiac arrhythmia and movement artifact can make a real problem by reducing the confidence in the rate parameter. To improve the heart rate detection, many algorithms have been investigated. Zero crossing and digital filtering are examples of these algorithms; they are used for separating respiratory and heart rate from PPG signal that has been collected from ear [11]. Another device for heart rate and respiration which is based on PPG, has been described. This device has been used for monitoring the neonatal care unit, and testing the ECG and PPG signals [12]. 77% of measurements were obtained by high quality ECG signal. By adjusting the offset of PPG signal, the heart rate will show only 1% false for both negative and positive beats. PPG signal is the most popular signal that is used by the sophisticated algorithms to extract the heart rate information. This information includes both time and frequency techniques [13]. To measure the heart rate accuracy, two signals should be collected from the same place in different situations. In this case, a study hand is used to collect data first in rest, and then under movements. The two approaches that show a significant improvement in both time and frequency domain are Fast Fourier Transform (FFT) and Weighted Movement Average (WMA). By applying new computer algorithms, the heart rate error reduced to 6 beats per minute compared to classical algorithms which is 11 bpm for FFT and 16 bpm for WMA. A new technology is used to measure the heart rate by Bland and Altman [14]. This technology works by the demonstration between radial piezoelectric, pulse oximetry, and the radial artery [15].

C. Respiration Rate (RR)

The respiration rate is the physiological monitoring of the number of breathing intervals per minute. The respiration rate is used in many clinical instrumentations like anesthetics, sleep study assessments, neonatal, and critical care. By using PPG signals that are collected from sensors attached to skin, it is possible to monitor breathing because of the respiration variation. The PPG signal contains low frequency respiratory induced intensity variations (RIIV) which is well documented [16]. The contributions of the venous return to the heart, include RIIV which is caused by the changes in the sympathetic tone control and alternations in intra thoracic pressure of the blood vessels. Until now, the RIIV physiological mechanisms have not been not fully understood. During the mainly thoracic breathing, the lower respiratory rates observed higher tidal volumes with the highest RIIV amplitude. [16] tested the coherence and CO2 reference against thoracic impedance measurements. They investigated the complex phase relationship between pressure and RIIV. Many other researches were done to understand the lower frequency components of PPG signal. [16] studied the variations of the finger PPG signal to induce the respiratory. This study was observed under arm BP cuff pressurized with high SBP. The aim of this study was to give further evidence for autonomic nervous system involvement. Other researcher groups investigated various RIIV extraction algorithms. [12] used pattern recognition of neural network algorithm to extract RIIV from the reflection PPG measurement mode. This technique gave good results with low error. [15] implemented zero phase digital filter to extract the breathing interval (BI) from children.

To estimate the respiratory rate of the PPG signal, wavelet transform was automation facilitated [17]. Another study was done on breathing with changing in pulse timing characteristics. PTT was used to track arousals during obstructive in that study. The results of this study gave as useful clinical non-invasive measurement of inspiratory [18]. The changes in PTT significantly induced the slow-paced breathing and deep inspiratory challenges in autonomic testing.

D. Blood Pressure (BP)

One of the important parameters for clinical measurement is the arterial Blood Pressure (BP). Surrogate measurements is an example of beat-to-beat PB tracking. Many noninvasive PB measurements based on PPG signal approaches have been done. Below, a summary of them has been provided. In 1980s, FinaresTM technology was introduced. This technology worked by measuring a continuous beat to beat basis of the arterial pressure waveform from the finger. This method was built in PPG sensor with inflatable finger cuff. This method worked depending on the dynamic unloading on the walls of finger arterial. Many studies have been published based on this technology, some of these publications have been comparative studies, some of them have been methodological; the most popular ones have been the review [19]. Automatic function testing and anesthetic monitoring are the main clinical applications that depend on this technology. The BP can be estimated from Pulse Arrival Time. The accuracy of this method was approved by comparing it with the conventional arm blood pressure measurement. This approach is useful for BP monitoring at home. This method works depending on Noninvasive BP measurement [20].

E. Pulse Blood Pressure

There are two numbers given regarding BP. The systolic blood pressure (SBP) is the higher number which indicates the maximum pressure of heart, and the diastolic blood pressure (DBP) which is the lower number which indicates the amount of pressure in arteries. Both numbers have been measured within every heartbeat. The pulse blood pressure is the numeric difference between the SBP and DBP. For example, when the measurement of BP is 130/90 mmHg, the pulse blood pressure is 40. The range of 30 to 40 are considered as normal range for healthy people. Higher number of pulse blood pressure gives an indication about a problem with heart. If the pulse blood pressure is over 60, it means that there is a cardiovascular disease. In general, a greater than 40 mmHg pulse blood pressure is abnormal. On the opposite side, low pulse blood pressure means that the heart is poor. The major benefit of the elevated pulse blood pressure is stiffness of the aorta which is the largest artery in human body. The higher blood pressure means the lower pulse blood pressure.

RSULTS AND DISCUSSIONS

A. Preprocessing

Before starting with the results, the prepressing that is done on the signal should be focused. The collected signal was a raw signal that contained all information that was not needed at all. In addition to that, it contained noise that occurred either by the sensor or the movement within data collection, or other factors. The signal also contained DC part which was not important in the current project. The first step was normalizing the signal using sampling frequency equal to 500 Hz. The second step was filtering the signal to remove the noise. For this project, FIR band pass filter was used with order of 2500 and cut-off frequency [0.001, 0.04]. The cut-off frequency was determined by applying Shannon Nyquist formula. The third step was to remove the DC part from the collected signal by detrending it. Fig. 2 shows the filtered signal compared to the original signal, both were detrended to make the comparison easier.

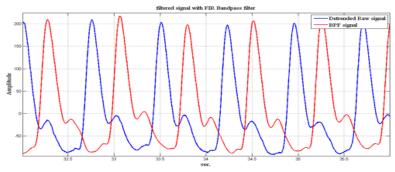


Figure 2. Filtered PPG Signal

As can be seen, the blue signal is the original, and the red is filtered. It can be noticed that the red one is more smooth and cleaner. There was a shifting between the two signals because theoretically they should match each other. This shifting occurred because of the effect of filter.

B. Calculating Heart rate (HR)

The heart rate is the number of heart pulses per minute. Generally, the range of heart rate for normal people is between 40 to 120 pulse per minute. This section has been divided into three parts; the first one has demonstrated the heart rate for all subjects in normal case, the second part has calculated the heart rate for all subjects under pressure, and finally the third part has compared the results of two cases to conclude the effect of pressure situation on heart rate. Because PPG signal was used, the HR was the difference between the pulses of the signal. Fig. 3 shows the detection of maximum peak for each pulse in the signal.

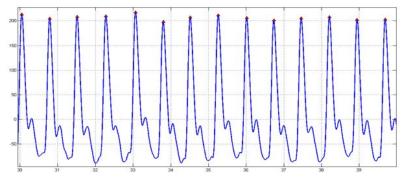


Figure 3. Maximum Peak Detection

Fig. 3 shows 10 seconds of PPG signal detecting the maximum peak for each pulse. As mentioned before, the HR is the difference between the pulses. So, the number of HR from figure above can be easily counted. Counting by hand showed that there was 13 HR within 10 seconds. That means, for one minute, there were roughly about 80 pulses which is a normal range for a middle aged healthy subject. Fig. 4 shows the HR for one subject in a normal case.

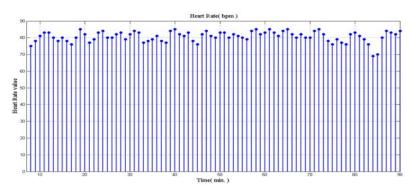


Figure 4. HR Values for One Subject

Fig. 4 shows the HR for 90 seconds for one subject. To calculate the HR for all subjects, the mean was taken for HR values of each subject which have been stored in the table. The overall results of HR for all subjects are shown in Fig. 5.

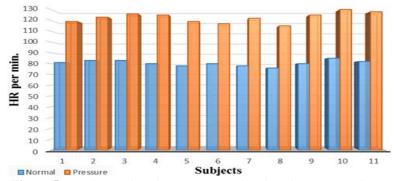


Figure 5. HR Comparison between Normal and Under Pressure Cases

Form the figure, it can be noticed that the HR values for all subjects are between 76 and 85 pulse per minute which is normal. These results can be obtained by calculating the HR for each subject separately along with the recoded signal and the stored results, then taking the mean value for each subject, and storing it in a table. Same procedure was done on the signal that was collected under pressure. Generally, most of human beings' heart rate increases when they get under pressure. But, the amount of increase is different from one subject to another. Some people reach the danger rate; some of them can manage themselves and stay in normal range. The pressure itself also affect the heart rate. For example, the pressure on someone at an exam hall is not like the one who is at a hospital, and waiting for a dangerous surgery.

From the figure, it can be noticed that all the values have been increased. Some of them are still in normal range, and others are higher than normal range but very close to normal. This is because of the pressure that has been used in testing. And, because it is not easy to collect data from person who is under high real pressure, the data in this study was collected before and after the exam.

From the figure, it is easy to distinguish the effect of pressure on the heart rate. Almost all people suffer from increasing the heart rate when they get under pressure. This experiment has shown that even a normal daily pressure affects heart rate. It means that there is need to monitor this parameter to be sure about human's health. As mentioned, the range of the increase is different from one person to another which depends on the person himself, and is also affected by the pressure of the situation.

C. Calculating Respiration rate (RR)

The respiration rate is the number of breathing per minute. The average range of respiration for normal people in rest is between 3 to 20 breathes per minute. It depends on the age and other parameters. The respiration for children is higher than young people, and it is very low for old people. The respiration rate is affected by many criteria like training or running. In this project, the pressure was examined to determine how it is affecting the respiration rate. The section has also been divided into three parts; the first normal case has been examined to approve that our algorithm is giving us correct results compared to the standard readings. The second part has calculated the respiration rate for all subjects under pressure situation, and finally, the third part compared the results to conclude the effect of pressure on the respiration. Calculating the respiration rate is not as easy as calculating HR, the respiration is more complicated. The way of calculating the RR is by applying polynomial AR model on the PPG signal to extract the polynomial parameters, after that, calculating the RR will be started. Of course, dealing with polynomial parameters may contain real and imaginary parts. So, this point should be taken into account. After calculating the RR, the values were stored in an array for each subject. Fig. 6 shows an example of RR for one subject.

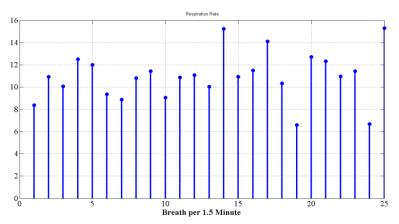


Figure 6. Respiration Rate (RR) for one subject

Fig. 6 shows the respiration rate for one subject in rest or a normal case for one minute and half. The number of breath was found to be equal to 25 breaths in one minute and half that means the RR was around 16 respirations per minute which was normal. By taking the mean for the RR for each subject, the overall RR for all subjects in normal case was built. Fig. 7 shows the overall RR.

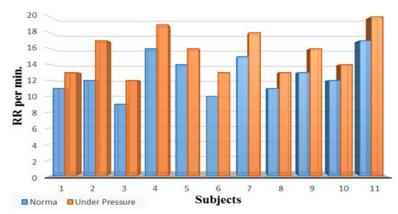


Figure 7. RR Comparison between Normal and Under Pressure cases

Form the figure, it can be noticed that all results are in the normal range because the signals were collected from healthy people at rest. The respiration rate increased in several situations for example when playing games or doing cardio training. The reason of the increase in the respiration is that the brain needs more oxygen to continue working normally. So, the people starts breathing faster to gain more oxygen. Fear or any troubles in physiological indicators causes the need for more oxygen to keep the body working normal. In this project, the effect of pressure on the respiration rate was tested. We know that when anybody gets under pressure, he or she breathes faster than normal but we do not know how much faster.

From the figure it can be noticed that there is an increase in the values of respiration rate, but this increase is little comparing to the normal case. That is because the pressure was not high enough and the number of subjects was small. The better way is to compare the results side by side to see the real differences between them. The other thing is that in both cases, they were still in normal range. That led to the point that the effect of pressure did not affect respiration, from this point of view, it was not a dangerous parameter. According to the literature, the respiration rate has been highly more affected by body movement like training and playing than pressure.

D. Calculating Pulse Pressure

The pulse blood pressure is different from blood pressure. The pulse pressure is the difference between systolic and diastolic values in each pulse of PPG signal. Despite the BP, it is easy to calculate the pulse pressure from one PPG signal continuously. By applying a simple code on a continuous recorded signal, we can calculate the pulse pressure. The benefits of calculating the pulse pressure is that it gives an indication about the heart health. The way of calculating the pulse pressure is by segmenting the recorded PPG signal to one cycle, then detecting the systolic and diastolic at each segment, finally calculating the difference between them and store the results in array. Fig. 8 shows the way of calculating the pulse pressure for one segment.

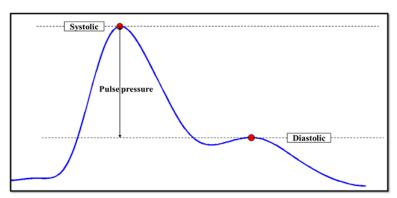


Figure 8. Calculating pulse pressure

The standard pulse pressure for normal healthy people is about 40mmHg. As usual, two tests were done; one at a normal case, and the second under pressure to see the effect of pressure on the heart. Fig. 9 shows the pulse pressure values for all subjects.

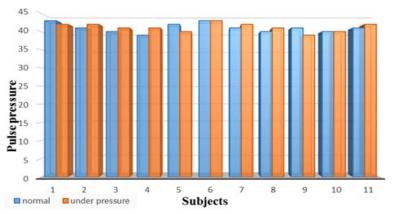


Figure 9. Pulse Pressure Comparison

From the figure, it is easy to notice that all the results are normal, because the subjects of this study were young and they did not have problems with heart or pressure. The results were between 39mmHg to 43mmHg. The figure also shows that the values of pulse pressure are still at normal range. That means the pressure would not affect the heart. The impressive thing about the results, shown in Fig. 9, is that for some subjects the pulse pressure was higher at normal case and for the others, it was lower, and some of them were equal. The reason justifying these results is that the pulse pressure was affected by systolic and diastolic. In this test, there was no difference between them. Even if the blood pressure increased under the pressure, the range between systolic and diastolic was still the same, or there was a small difference between them.

CONCLUSION

In this project, it was tried to monitor the physiological clinical parameters under pressure using only PPG signal. More than 20 subjects were invited to do the test, but the signals of only 11 of them were good enough to do the experiments. The challenges faced in this project were the data collection and programming the code. Another challenge was the topic itself, because the authors are engineers, we did not have lots information about the clinical parameters of human beings and what really affect them. The idea was to calculate the heart rate, respiration rate and pulse pressure of all the subjects in two situations. One test was done in normal case, and the results were compared with standards to approve that the algorithms used were suitable, and the second one was done under pressure to determine the effects of pressure position on the human's physiological parameters. The results showed that heart rate was highly affected by the pressure position. The respiration rate was also affected but not highly. Finally, the pulse pressure was not affected by the pressure position because there was a difference between the systolic and diastolic blood pressure. Finally, many things were learnt from this project such as coding in MATLAB, cardiovascular parameters, and clinical physiological monitoring.

REFERENCES

- 1. M. Lansdown, "A method of using induced waves to study pressure propagation in human arteries", [J]. Circ. Res, 1957, 5:594-601, 1957.
- 2. Y. Zhang, "Blood Pressure Devices", IEEE/EMBS International Summer School on Medical Devices and Biosensors (ISS-MD), 2004.
- 3. H. C. Bazzet and N. B. Dfeyer, "Measurement of pulse wave velocity", [J]. Am. J. Physiol, 1922, 63:94-115, 1922.
- 4. M. Maguire and T. Ward, "The Photoplethysmograph as an instrument for physiological measurement", Department of Electronic Engineering, NUI Maynooth, 2002.
- 5. Webster J. G., "Design of Pulse Oximeters, Bristol", Institute of Physics Publishing, 1997.
- 6. Aoyagi T. and Miyasaka K., "Pulse oximetry: its invention, contribution to medicine, and future tasks Anesth", Analg, 94 (Suppl. 1) 51–3, 2002.
- 7. Kyriacou P. A., "Pulse oximetry in the oesophagus Physiol", Meas. 27 R1–35, 2006.

- 8. Hayes M. J. and Smith P. R., "A new method for pulse oximetry processing inherent insensitivity to artifact", IEEE Trans. BME 48 452–61, 2001.
- 9. Mendelson Y. and Ochs B. D., "Noninvasive pulse oximetry utilizing skin reflectance Photoplethysmography", IEEE Trans. BME 35 798–805, 1998.
- 10. Echiadis A., Crabtree V. P. and Smith P. R., "VENOX Technology Implementation", Loughborough University Department of Electrical and Electronic Engineering ESC Division Research Report 31–4, 2005.
- 11. Nakajima K., Tamura T. and Miike H., "Monitoring of heart and respiratory rates by photoplethysmography using a digital filtering technique", Med. Eng. Phys. 18 365–72, 1996.
- 12. Johansson A. and Oberg P. A., "Estimation of respiratory volumes from the photoplethysmographic signal", experimental results Med. Biol. Eng. Comput. 37 42–7, 1999.
- 13. Yan Y. S., Poon C. C. and Zhang Y. T., "Reduction of motion artifact in pulse oximetry by smoothed pseudo Wigner-Ville distribution", J. Neuroeng. Rehabil. 2005.
- 14. Bland M., "An Introduction to Medical Statistics", 2nd edn (Oxford: Oxford University Press), 1995.
- 15. Foo J. Y. and Wilson S. J., "Estimation of breathing interval from the photoplethysmographic signals in children", Physiol. Meas. 26 1049–58, 2005.
- 16. Nilsson L., Goscinski T., Johansson A., Lindberg L. G. and Kalman S., "Age and gender do not influence the ability to detect respiration by Photoplethysmography", J. Clin. Monit. Comput. 20 431–6, 2006.
- 17. Leonard P. A., Douglas J. G., Grubb N. R., Clifton D., Addison P. S. and Watson J. N., "A fully automated algorithm for the determination of respiratory rate from the Photoplethysmogram", J. Clin. Monit. Comput. 20 33–6, 2006.
- 18. Pitson D. J., Sandell A., van den Hout R. and Stradling J. R., "Use of pulse transit time as a measure of inspiratory effort in patients with obstructive sleep apnoea", Eur. Respir. J. 8 1669–74, 1995.
- 19. Imholz B. P. M., Wieling W., van Montfrans G. A. and Wesseling K. H., "Fifteen years' experience with finger arterial pressure monitoring: assessment of the technology Cardiovascular", Res. 38 605–16, 1998.
- 20. Yao S. T., Hobbs J. T. and Irvine W. T., "Ankle systolic pressure measurements in arterial disease affecting the lower extremities", Br. J. Surg. 56 676–9, 1969.
- 21. K. Ghamri, R. Ghamri, E. Alofi. Knowledge of cardiovascular risk factors among medical students at king Abdulaziz university. *J Adv Pharm Edu Res* 2017; 7(4):524-530.
- 22. Marzangi A, Ahangarzadeh Rezaei S, Ghareagaji Asl R. (2018). "Health literacy and its relation to quality of life in people with heart disease", *International Journal of Pharmaceutical and Phytopharmacological Research*, 8(3), pp.25-32.
- 23. Suastuti, N, G, M, A. Bogoriani, N, W. Putra, A, A,B.(2018). Activity of Hylocereus Costarioensis's Extract as Antiobesity and Hypolipidemic of Obese Rats. *International Journal of Pharmaceutical Research & Allied Sciences*, 7(1):201-208.