ISSN 2229-5518

IS 'BLOOD PRESSURE MEASUREMENT' & DIAGNOSIS – Resulting in HEART PROBLEMS & FATALITIES? – Urgent Need to Revisit Conventional Understanding

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Fluid Thermal Technologies

Abstract — Since the time of Harvey, who suggested the important link between 'blood pressure' and cardiovascular diseases and Korotkov, who later on proposed its measurement using Sphygmomanometer, 'blood pressure' is considered as the most important parameter in diagnosis from hypotension to hypertension and various other diseases. In the recent past, engineers have joined hands with medical professionals to apply all types of sensing techniques and measurement instrumentation (often times ignoring or not worrying about measurement uncertainty!) for helping doctors set standards for quantifying disease symptoms and help assess human health. However, a fluid dynamicist can only wonder, how doctors can measure the unsteady/turbulent, 'blood pressure' inside such complex geometries (anatomy) of living beings, when an engineer cannot measure static pressure reasonably accurately, even in simple, steady pipe flows made of nonliving matter! Could one evade the seriousness of the issue by a mere suggestion that the term 'blood pressure' used in medicine is a misnomer? In fact, it is not only a misnomer but medical evaluations based on such measurements could also lead to mal/wrong diagnosis due to large uncertainties in measurement, questions concerning standards, calibration, etc. Such wrong diagnosis could further lead to unnecessary or wrong medication prescriptions, even resulting in fatalities. The fundamental question being, what is the basic standard for 'blood pressure' for diagnosis? How did one set and accept 70-120 or numbers close to them as the standard for normal 'blood pressure' and base all diagnosis with incorrect or highly unreliable measurement and standard? This paper raises serious concerns regarding 'blood pressure' measurement and challenges the use of 'blood pressure' as a key parameter and its "gold standard" in medical diagnosis as well as treatment including surgery.

Index Terms— Blood Pressure, Gold Standard, Hypertension, Sphygmomanometers, Cannula, Uncertainty

1 INTRODUCTION

Blood is the fluid which circulates throughout the entire body of human beings and animals and transports nutrients to sustain life. The main driving force is not gravity but the static pressure generated by the heart. The static pressure generated by the pumping action of the heart has to overcome the fluid dynamic resistance and the gravitational force in some parts of the artery and the veins. Hence, blood pressure is required to drive blood throughout the cardio-vascular system. However, what this paper is questioning is the fundamental understanding of the science of Blood Pressure measurement in human beings and the application of its gold standard for diagnosing human health and prescribing medications, which could be leading to fatalities arising from heart and associated problems.

In the human heart, the static pressure is generated in two stages. The right ventricle along with the right atrium and the tricuspid and pulmonary valves act as the first stage pump and produces enough pressure to pump the bad blood collected from various organs by the venous system into the lungs for cleaning it up during the Oxygen – Carbon dioxide mass exchange diffusion process. The cleansed blood is brought back into the 2nd stage of the pump consisting of the left ventricle, through the left atrium and the Mitral valve and pumped during the systolic phase to all organs of the body through the Aortic valve. Thus heart can be modeled as a 2 stage pump with lungs acting as an inter-stage mass/species exchange device. There is no doubt that blood circulation is maintained by the static pressure developed by the heart and hence blood pressure is a very important parameter for understanding the state of health of a human being.

It is the most important piece of information used by most physicians in many countries not only for diagnosis but also to assess the physiological and mental state of human beings both in medicine and veterinary science. Blood cannot flow without a driving force. Kotchen [2011] has given an excellent extensive review of translational research connecting blood pressure to cardiovascular diseases through hypertension and the associated physiological and neurodynamic mechanisms. The driving force or pressure is generated by the heart in two stages, as described above. However, the cardio vascular and pulmonary system through which the blood flows is a very complex piping system. One simple example is the carotid artery with its bifurcations. Kang, Tang and Liu (2016) have employed the Lattice-Boltzman method for computing the blood flow in the stenosed artery, and showed the effect of stenosis on blood flow through the braches. Hence, it is obvious that the impact of stenosis, which could form due to various physiological and even neurological reasons could affect the blood pressure in the arterial system. Following Hamad's (2015) work, one could conclude that such stenosis, depending on the size, upstream velocity profile and the local rheological characteristics could further influence the blood pressure. Dasi, Morshed, and Forleo (2013) have presented research findings relating to blood clot formation by hemolysis from shear thinning. Such blood clots could in turn lead to additional stenosis, thus influencing the blood pressure.

The presence of the heart and the lungs in the circuit, which are the main organs responsible for the cardio-pulmonary circulation and the purification of the blood makes the system even more complex. This increased anatomical complexity increases the resistance to blood flow and requires the heart to generate a greater pressure to drive blood through the system. The pumping action by the heart as well as the breathing action of the lungs are intermittent and not continuous. They synchronize in such a fashion as to enable an efficient cleaning process in the lungs. In fact, the respiratory distress being talked about in COVID 19 and MERS patients is likely to affect the synchronism in some patients and could lead to various outcomes/diseases caused by impure blood. It could also curtail the mechanisms responsible for production of antibodies and development of immunity The suggested modeling of heart as a 2 stage pump is based on analogy with mechanical pumps {see Shiva Prasad [2009] and Bellur and Shiva Prasad [2015]}. This analogy can be extended to assess the health of heart just like the operation of a mechanical pump. It also leads one to identify the maximum (systolic) and minimum (diastolic) pressures generated in the heart as the most important characteristic defining a healthy blood flow and the human being's overall health. Everyone knows that human beings cannot function with very little blood flow and leads to death when it completely ceases to flow. Hence, there is no doubt that "Blood Pressure" has become a very important parameter defining the health of a human being and doctors use its gold standard (70 – 120, 80 – 130 or a close by range, depending on the group of medical practitioners) in medical diagnosis. However, they have not addressed the fundamental questions concerning its measurement. The setting up of the 'Gold Standard' is attributable {see NHBPEP Report (2004)} to the push by some insurance companies, several decades ago for setting standards for assessing the health of human beings by linking it to cardiovascular health and hence blood circulation and pressure. This motivated research in the 19th century to develop some technique for measuring blood pressure and gave birth to the science of sphygmomanometry. The science of fluid mechanics has advanced considerably since the 19th century. However, unfortunately not much attention has been paid to questioning the art & science of blood pressure measurement. One should note that there is no dearth for papers on the topic of Blood Pressure measurement; one of the important issue which was debated in various forums was the use of Mercury manometers and its associated harmful effect on humans. The United Nations through its development program has produced a manual {see UNDP Report (2013)} offering guidance for maintaining and calibrating non-mercury type sphygmomanometers. Although the present authors have been thinking about the problems in the measurement of blood pressure since quite some time, they started publishing their views in scientific forums, only since 2013{see Bellur and Shiva Prasad (2013)} and have faced a big challenge to get it published in an archival journal as perhaps it might generate an appreciable level of turbulence/turmoil in the medical world. However the senior author was heartened to note recently, that it has at least created a big stir in the biomedical world leading to sponsorship and funding for an "Indo-US Grand Challenge Initiative on Affordable Blood Pressure Measurement Technologies". However, the senior author is still waiting to get an assessment of his views concerning the present day status of Blood Pressure Diagnosis/ Medication Prescription and its consequences by the World Medical Association. In fact, the seriousness of improper diagnosis of Blood Pressure can be understood from some of the papers (Gurpreet, S. W. and Vekat S. R., 2018) which correlate the increasing incidence of heart problems in many countries attributable to blood pressure. In India, according to the statistics published in a May 2018 article (Swagata Yadavar 2018 in IndiaSpend Magazine) about 30% of the fatalities are attributable to Hypertension (also see Raghupathy A., 2014 and Paul K. W. et al, 2017).

2 WHAT IS BEING MEASURED AS BLOOD PRESSURE?

Reliable pressure measurement, particularly measurement of static pressure in mechanical devices like even simple piping systems is extremely difficult. It is the static pressure which is responsible for generating the pressure gradient to drive the blood flow and hence that is the one which needs to be measured in human beings also! The old way of measuring pressure in any mechanical device is by tapping fluid into a manometer and comparing it with the atmospheric pressure acting on the exposed limb. In human beings, one cannot think of tapping blood by drilling hole into an artery or vein. Or else, one cannot think of employing the modern method of sticking a pressure transducer flush with the inner surface of an artery or vein, however small and thin the transducer is. The other method of introducing static tubes with multiple holes into an artery (intra-arterial) is also extremely difficult and highly erroneous, when used in human subjects, although one type of measurement of blood pressure using a Cannula employs this method.

This impossibility or at least difficulty in direct measurement of blood pressure has encouraged measuring something else and calling it as blood pressure! The measurement of blood pressure done in the arm, wrist or finger does not represent blood pressure. It is actually a measurement of the response of the mass of human tissue, muscle, skin and sometimes nerves, veins secondary arteries also, to the flow of blood in a very small artery and does not represent the blood pressure at all as the mechanical impedance of the mass surrounding the artery is very large and varies in a spatiotemporal manner (even circumferentially also) and depends on anatomy, physiology and even neuromechanics. All indirect blood pressure measuring devices irrespective of whether they use auscultatory or oscillatory technique do not at all measure blood pressure and whatever they measure has large uncertainty also {see Bellur and Shiva Prasad (2013)}.

3.1 UNCERTAINTY IN BLOOD PRESSURE MEASUREMENT

Essentially there are 2 broad categories of measurement; the Direct measurement involves inserting a small tube with circumferential holes, called 'Cannula' {see Fig. (1)}, inside major arteries or in the aortic chamber itself and connecting the tube to a manometer or pressure transducer to measure the static pressure.

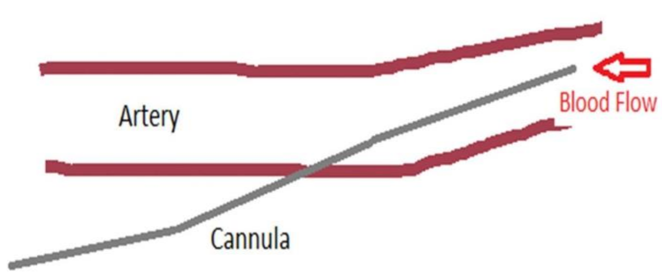

Fig. (1): Sketch showing Direct Measurement of Blood Pressure in an Artery

The major issues are that the sensor is highly invasive and completely alters the flow field, and the measurement is highly sensitive to the flow direction. Unless the tube is always aligned with the flow direction, it will measure a component of the dynamic pressure also, thus making the static pressure measurement highly erroneous. The alignment is extremely difficult because of the flexibility of the human artery and the surrounding organ as well as the inaccessibility of the measurement location. In fact, measurement of static pressure in steady flow inside pipes (as in curved pipes) using sensors is itself highly erroneous not only due to the invasiveness, but also due to the difficulty in alignment with the flow direction. The unsteadiness in blood flow adds more to the difficulty in blood pressure measurement.

The indirect measurement using sphygmomanometer {see Fig. (2)} is done in two ways – Auscultatory or Oscillatory.

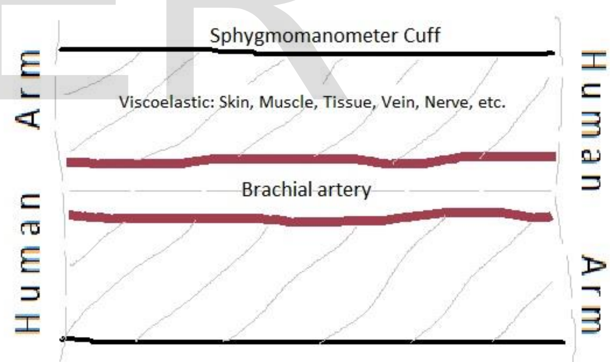

Fig. (2): Sketch showing Indirect Measurement of Blood Pressure using Sphygmomanometer

In the former, the cuff is initially squeezed to completely block the artery, and then released to allow blood to flow. The blood pressure is measured by listening to the Korotkoff's sound at the start of blood flow corresponding to the systolic phase and the disappearance of the sound during the diastolic phase and noting the pressures corresponding to those events. The large uncertainty in measurement is not the only issue. The location of blood pressure measurement is another important parameter which adds to the uncertainty, as the blood pressure could vary with location not only in magnitude but also in phase relative to the systolic and diastolic events. This is because of pulsations which are generated by the interaction of the dynamics of the valve motion with the dynamics of blood flow through the complex cardiopulmonary-arterial flow system. It should be treated as analogous to the piping pulsation in complex mechanical piping systems. In fact, there is also an additional physical mechanism (structural dynamics) present in human blood flow due to the flexible or compliant nature of the arterial system, which could generate additional frequencies in the flow and make the pulsations more complex for measurement or prediction. In fact, the importance of compliance on hemodynamics lead to developing techniques for measurement of arterial stiffness by Pannier [2002]. Also, this complex interaction of physics raises questions not only concerning the fundamental understanding of Korotkoff's sound but the use of stethoscope itself for diagnosis of various heart and lung problems like atrial fibrillation, arrhythmia, palpitation, COPD, pneumonia, heart murmur, etc.

Measurement uncertainty due to human error, anatomical differences due to age or otherwise, physiology, white coat hypertension, health condition, the type of instrument used, calibration of the instrument, size of the cuff {see Bakx et al. (1997)} etc., have all been researched and discussed reasonably extensively by prior authors. Also, Kuzborska (2016) has studied the influence of age and gender on the strength of blood vessels and its enormous consequential effect on local arterial blood pressure. Very little discussion has occurred concerning the uncertainty arising from fluid dynamic causes.

3.2 UNCERTAINTY - FLUID DYNAMIC ISSUES

To understand the errors arising from fluid dynamic reasoning, one should consider the complexity of the flow geometry, the compliant nature of the geometry and the turbulent nature of the flow. The arterial geometry itself is a complex piping network, with varying cross section, bends, branches, compliant - porous walls and varying internal roughness. In addition, irrespective of the location of measurement, and particularly in the arm (most common location), the artery is surrounded by other secondary arteries, tissue, fluid material, veins, nerves, skin, etc. Note that the cross section of the artery is not always circular, but varies from perhaps a nearly circular cross section to an ellipsoidal section with varying ratio of major to minor axis during auscultation. Hence the static pressure distribution around the circumference varies and is unpredictable. Also, note that the brachial artery is not centrally placed with respect to the arm cross section {see Fig. (3)} and the large asymmetry in its location implies asymmetrical compliance, stiffness or impedance of the arm mass around the artery. The authors have neither found any reasonably accurate direct measurement or simulation of blood flow in human beings nor comparable experimental or analytical fluid dynamic simulations in engineering systems. Any rigorous analytical computation using CFD (Computational Fluid dynamics) is extremely complex, as it will involve considering the flow as not only 3 dimensional, unsteady and turbulent but also involving fluid structure interaction with a structure involving asymmetry and compliance or stiffness varying spatially as well as temporally. In addition, in many cases, one might have to consider arterial blood flow to consist of more than one species. Further, boundary conditions for computational simulation become highly subjective as it cannot be obtained accurately in human subjects.

The auscultation process does not ensure uniform pressure distribution inside the volume of the cuff, while the sensing and measurement of pressure is done at one location in the cuff

ISSN 2229-5518

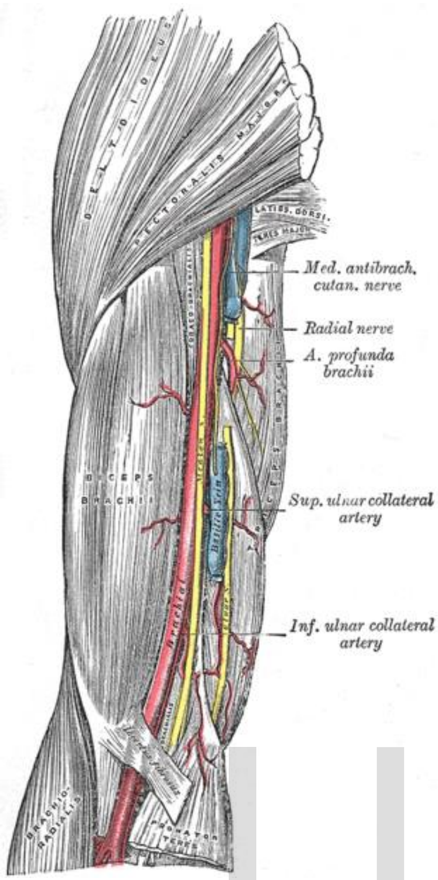

Fig. (3): Brachial Artery (Ref: Wikipedia-from Vandyke Carter & Henry Gray, Anatomy of the Human Body, 1918)

where the air is tapped through a tube to an analog or digital sensor and display device. During auscultation, the closing or extent of closing of the artery and the variation of cross sectional shape of the artery depends on the magnitude of pressure inside the cuff and the turbulent static blood pressure inside the artery. Also the Korotkoff's sound depends on the manner of opening of the artery, which in turn depends on the internal and external pressure distribution around the circumference of the artery. One can also surmise various ways of opening with single or even multiple jets. This could completely affect the spectral characteristics of the Korotkoff's sound. Also as described in an earlier section, one should keep in mind the wave interference analogous to piping pulsation in mechanical systems, arising from the interaction of valve dynamics, piping acoustics and structural dynamics and the presence of other acoustic waves emanating at various branches, both upstream and even downstream and their interaction with the systolic and diastolic waves, which could also result in the spectral variation of the Korotkoff's sound. Even the rate of variation of the opening could have an impact on the sound heard through the stethoscope. The length of the cuff coupled with the compliance could influence the actual location where the artery closes and the shape of the Ventury tube during opening and hence the Korotkoff's sound itself. One cannot easily ignore all these errors arising from fluid dynamic causes by simply dubbing them as minor errors, basing it on the fact that there are no data to prove its significance at least in the context of human blood pressure measurement. As far as engineering systems are concerned, the author suggests developing experimental/analytical models by simplifying the problem into several subsystem studies.

If one were to use the oscillatory method, where is the need for the cuff itself and also to pump the cuff to a pressure higher than the estimated blood pressure? Also, what is the pressure to be set inside the cuff? Does it depend on the volume of the cuff? The other problems discussed, unrelated to the cuff, still remain in the Oscillatory method.

Due to the various reasons described above, the measurement uncertainty could be greater than 40% - 60% in many cases. It is important to note that just because, the nurses or sometimes doctors, who measure blood pressure get repetitive readings, the errors due to various reasons given above including the tendency to make a guess based on the patient's history (bias), inclination for getting repetitive readings, etc., cannot be ignored.

4 CAN BLOOD PRESSURE BE MEASURED?

Force or pressure can best be measured in situ, using Newton's 3rd law of motion as it does not get transported like energy. Pressure expresses itself as momentum and the transport of momentum can experience large impedance, whose magnitude depends on the media. In a human body, the radial impedance (around an artery) itself, behaves in a spatiotemporal fashion depending on the anatomy, physiology and neuromechanics. Also, unlike engineering systems, one cannot drill a hole or put a thin, flexible, pressure sensor flush with the inner surface of the artery to measure blood pressure! In addition, one of the other important issue is the question concerning the use and application of Korotkoff sound even to the Stethoscope. Pan et al (2018) have reported errors in blood pressure measurement depending on the location of stethoscope around the brachial artery. Although, the authors have not done a thorough literature search concerning the use of stethoscope (Ref: www. Wikepedia.org) by medical doctors at least for preliminary diagnosis and treatment of heart and lung ailments like hypertension, hypotension, murmur, atrial fibrillation arrhythmia, COPD, etc., I doubt whether all mechanisms (heart valve dynamics, cardiopulmonary piping acoustics, and structural dynamics of not only the arterial subsystem and the heart but also the entire cardiopulmonary system) involved in generating additional sound/noise by wave interference and the consequent spatiotemporal variations of pressure/sound are being considered in such diagnosis. In addition, the use of stethoscope introduces issues related to interfacial mechanics also.

The proper question to be asked is whether blood pressure can be measured at all, irrespective of the technique and the instrument used? It is very important to note that direct measurement using a cannula is the only technique which can measure blood pressure. However, that method is extremely difficult for obtaining even any reasonably accurate, quantitative measure of the blood pressure. Hence it cannot be used for establishing any standard for diagnosis. The indirect measurement using sphygmomanometer cannot be correlated or has very poor correlation with the actual blood pressure in the artery.

One could argue that although direct measurement might be unreliable, the certainty can be improved and a quantitative measure established by employing a large sample of measurement. A large sample cannot help establish a meaningful measure of blood pressure for establishing a measurement standard due to a wide variation in the blood pressure depending on the individual's anatomy, physiology and neuromechnics. Also, as mentioned above, it is also location dependent. One should note that measuring blood pressure inside the Aorta cannot solve the problem. Further, it cannot be done always and even measuring inside the Aorta incorporates all of the measurement difficulties outlined above in addition to greater complexity introduced by three dimensionality and turbulence involving a large extent of separated flow also. Similarly, one should note that measuring blood pressure at a finger-tip has serious issues concerning the basic nature of the flow which could contain regions of stagnation and recirculation. Finally, when the measurement techniques themselves are highly questionable and have large uncertainty, no refinement or increase in sampling can improve the creation of standards and hence the age old blood pressure standards are highly questionable. This raises a serious concern regarding the measurement of Blood Pressure and its use in medical diagnosis.

There is another fundamental issue, whether one should measure the static pressure of the flowing fluid (blood) or wall static pressure and if so, where? Either way, accurate and easy measurement, is almost impossible, although the latter parameter is comparatively easier to measure in engineering systems.

One could demonstrate the large errors and uncertainty in the sphygmomanometer measurements by a highly simplified simulation of brachial artery and arm by using a plastic tube embedded in a thick soft rubber pipe (spongy material), connecting the tube to a pressure source and measuring wall static pressure inside the tube and on the outer wall of the pipe at the same or close axial location using pressure transducers. Although one cannot simulate the artery, arm and their (compliance, physiology and neuromechanics) impedances, it could serve as a simple tool for demonstration. One could vary the material and hence impedance of the tube and pipe to demonstrate the effect of anatomy to some extent. This could be tried and expanded as a research project from undergraduate to Ph. D. level by performing measurements by varying the parameters for material, geometry, diameters, fluids to generate the pressure source, etc.

5 CONCLUSION

THIS PAPER HAS RAISED THE FOLLOWING IMPORTANT ISSUES/ALARM:

1) Blood pressure cannot be measured by indirect techniques using sphygmomanometer. Also, direct measurement with a Cannula cannot be used for any quantitative assessment.

2) The established standard/s for Blood Pressure is highly questionable.

3) The use of Blood Pressure as a Gold Standard in medical diagnosis as well as treatment including surgery needs serious and urgent rethinking.

4) Since systolic and diastolic pressures are closely connected with heart health & human health, wrong diagnosis and use of unnecessary or wrong medication is bound to affect heart health by affecting the elasticity and the resilience of the heart muscles and even arteries.

5) Hence incorrect measurement of blood pressure and improper medication could lead to many other illnesses and fatalities due to their side effects. Could the large number of deaths from heart failure/diseases alone be linked to side effects of improper blood pressure medication?

Such medication induced side effects cannot be merely dismissed by saying that no measurement is perfect and medical and even engineering sciences involve trial and error, as heart is the main engine driving and sustaining the human body.

6 ACKNOWLEDGMENT

The second author likes to acknowledge Dr. Pravas R. Mahapatra for reading an earlier version of the manuscript along with the reviewer comments and rebuttals of the 2017 submission to the ASME Journal of Biomedical Engineering and for the friendly discussion concerning this highly controversial issue, which obviously many medical doctors and even some biomedical engineers hesitate to discuss and oppose publication of this important and serious issue.

7 REFERENCES

1. Kotchen, T. A., 2011, "Historical Trends and Milestones in Hypertension Research, A Model of the Process of Translational Research", *Hypertension,* 58, pp. 522-538.

2. Kang, X., Tang, W. and Liu, S., 2016, "Lattice Boltzmann Method for Simulating Disturbed Hemodynamic Characteristics of Blood Flow in Stenosed Human Carotid Bifurcation", J. Fluids Engrg. 138(12), 8 pages.

3. Hamad, K. J., 2015, "The Flow Behavior of a Biofluid in a Separated and Reattached Flow Region" J. Fluids Engrg. 137(6), (8 pages).

4. Dasi L. P., Morshed K. N., and Forleo M., 2013, "Phenomenology of Hemolysis in Turbulent Flows" *ASME 2013 Summer Bio Engrg. Conf.*, Paper No. SBC2013-14843, pp. V01AT05A020; 2 pages

5. Shiva Prasad, B. G., 2009, "Fluid Mechanics of Human Heart & Positive Displacement Pump – What can be Learnt from the Analogy?", Oral

Presentation, *5th Annual Dayton Engineering Sciences Symposium,* Dayton, USA.

6. Bellur, V. P., and Shiva Prasad, B. G., 2015, "'Blood Pressure' – Is it Just a Misnomer?", Oral Presentation, *11th Annual Dayton Engineering Sciences Symposium, Dayton*, USA.
7. National High Blood Pressure Education Program (NHBPEP), 2002: *Working Meeting* on Blood Pressure Measurement, National Heart, Lung, and Blood Institute (NHLBI) and American Heart Association (AHA), Natcher Conference Center, NIH, Bethesda, Maryland.
8. Guidance on Maintaining and Calibrating non-Mercury Clinical Thermometers and Sphygmomanometers, *UNDP Global Health Care waste Project, https://www.google.com/#q=GUIDANCE+ON+ MAINTAINING+AND+ CALBRATING+NONMERCURY+CLINICAL+THERMOMETERS+AND+*SPHYGMOMANOMETERS.
9. Bellur, V. P. & Shiva Prasad, B. G., 2013, "'Blood Pressure' – Are we Measuring the Pressure of Blood?", Oral Presentation, *9th Annual Dayton Engineering Sciences Symposium,* Dayton, USA.
10. Pannier, B.M., Avolio, A. P., Hoeks, A., Mancia, G. and Takazawa, K., 2002, "Methods and devices for Measuring Arterial Compliance in Humans", *American Journal of Hypertension,* 15, pp. 743-753.
11. Bakx c., Oerlemans G., van den Hoogen H., van Weel C., and Thien T., 1997, "The Influence of Cuff size on Blood Pressure Measurement", *Journal of Human Hypertension,* Vol.11, pp. 439 – 445.
12. Kuzborska, Z., 2016, "Influence of Age and Gender on the Strength of Blood Vessels", *CBU International Conference on Innovations in Science and Education, Prague,* Czech Republic, March 23-25.

13 Pan F, Chen F, Liu C, Yang Z, Liu Z and Zheng D, "Quantitative Comparison of Korotkoff Sound Waveform Characteristics: Effects of Static Cuff Pressures and Stethoscope Positions". *Ann. Of Biomedical Engrg.* 2018 Nov; 46(11):1736-1744.

14 Gurpreet S. Wander & Venkat S. Ram, Global Impact of 2017 American Heart Association/American College of Cardiology Hypertension Guidelines - A Perspective from India, *Circulation.* 2018; 137:549–550.

15 https://www.indiaspend.com/high-blood-pressure-killed-1-6-mn-indians-in-2016-but-most-are-unaware-of-its-dangers-94201/ Reported by Swagata Yadavar, *IndiaSpend Magazine*, May 29, 2018.

16 Raghupathy Anchala, Nanda K. Kannuri, Hira Pant, Hassan Khan, Oscar H. Franco, Emanuele Di Angelantonio, and Dorairaj Prabhakaran, "Hypertension in India: a systematic review and meta-analysis of prevalence, awareness, and control of hypertension", *J. of Hypertension*, 2014 Jun; 32(6): 1170–1177.

17 Paul K. Whelton, Robert M. Carey, Wilbert S. Aronow, Donald E. CaseyJr, Karen J. Collins, Cheryl Dennison Himmelfarb, Sondra M. DePalma, Samuel Gidding, Kenneth A. Jamerson, et al, "2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines", *Hypertension*, Vol. 71, No. 6, 2017.

18 https://www.wikipedia.org