THE POSSIBLE LINK BETWEEN HYPERTENSION AND OSTEOARTHRITIS

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ABSTRACT

Background: The prevalence of hypertension and osteoarthritis increase with age and are frequent comorbidities. Both share another thing in common; hypertension is a vascular disease while the final pathogenesis of osteoarthritis is vascular. Hypertension is associated with a higher likelihood of vascular end-organ event (cerebral, cardiac, microvascular and renal outcomes). Osteoarthritis final pathway is a perfusion abnormality of the synovium, articular cartilage and subchondral bone. That presupposes another end organ vascular event.

Objective: To assess the prevalence of hypertension and osteoarthritis in patients attending an orthopaedic clinic, evaluate and explore commonality and possible aetiological linkages. Null hypothesis: Hypertension has no link with large joint osteoarthritis.

Methods: A retrospective review of 788 case files of patients seen in an orthopaedic clinic between January 2019 and March 2020. Five hundred and sixteen patient files had complete data and were selected for the study. The raw data were entered on a data sheet. The patient's age, gender, weight, height, and BMI were all extracted and recorded. The Mean Arterial Blood Pressure (MAP) (calculated from the average BP value) was the main independent variable. The average BP value was taken by averaging at least three BP readings taken on different visits. The dependent variable was osteoarthritis of any major joint. Osteoarthritis was diagnosed radiologically. For statistical analysis, the study carried out the frequencies, means, Pearson correlation, odds ratio and multivariate linear regression.

Results: The overall prevalence of hypertension in the sample was 36%. Similarly, the prevalence of osteoarthritis was 17%, but much higher in the hypertensive cohort (25%, $P < 0.001$). The mean systolic and diastolic blood pressures increased with age in men and women, although 36% of the hypertensives were below 40 years. Osteoarthritis showed to be a strong risk factor (OR = 2.2). Other risk factors included male gender (OR = 1.7), and diabetes mellitus (OR = 1.7), and overweight (OR = 2.7). Stepwise logistic regression revealed large joint osteoarthritis to be a moderate predictor of hypertension (R = 0.4, $P < 0.001$).

Conclusion: The study reveals the risk factors of increasing age, overweight, diabetes, and osteoarthritis as significant correlates and risk factors for hypertension in the orthopaedic patient cohort. All patients attending orthopaedic outpatient clinics should have their BP taken. BP measurements should be mandatory in the elderly particularly those with osteoarthritis. Orthopaedic surgeons should have some knowledge on how to manage uncomplicated hypertension. Null hypothesis: Large joint osteoarthritis has no link with hypertension.

Key words: Prevalence, Hypertension, Osteoarthritis, Relative-risk, Cardiovascular risk

INTRODUCTION

The current definition of hypertension (HTN) is Systolic Blood Pressure (SBP) values of 130 mmHg or more and/or Diastolic Blood Pressure (DBP) of more than 80 mmHg (1).The reported (2) risk of becoming hypertensive (BP>140/90 mm Hg) during a lifetime exceeds 90% (3). Essential hypertension is a rise in BP from an unknown cause that increases the risk for cerebral, cardiac, and renal events. Hypertension and ageing, obesity, diabetes mellitus, and hyperlipidaemia are known and clustered together as cardiovascular risk factors (3). Hypertension is classified as pre-hypertensive (systolic BP >120 or diastolic BP > 80 mmHg), and stage I (systolic BP ≥140 or diastolic BP ≥ 90 mmHg) and stage II (systolic BP ≥160 or diastolic BP ≥ 100 mmHg) (4). These stages are also commonly referred to as mild, moderate and severe. Mild to moderate hypertension is more common than severe hypertension and most of the burden of hypertensive disease is attributed to moderate rather than severe hypertension (5).

Hypertension is an independent risk factor for stroke (6), type 2 diabetes (7), and obesity (8). The three conditions occurring together form

the components of the metabolic syndrome, a clustering of conditions that reflect over nutrition and sedentary lifestyles (9). One of the consequences of obesity is osteoarthritis, perhaps, from the joint strain that leads to articular cartilage incongruences and loading and abnormal wearing. Patients with painful orthopaedic conditions such as trauma, arthritis, tendonitis and back pain tend to mask away non-orthopaedic chronic diseases unless the physician directly asks for that information. Yet, some are candidates for major surgery with the potential for end-organ decompensation with devastating outcomes. Although hypertension, like the other twin brothers, obesity and type 2 DM have long-term control goals, immediate control of high BP is of immediate concern. Hypertension is a significant risk factor for causing coronary events such as stroke, heart failure, peripheral arterial disease, dissecting aneurysms, chronic kidney disease, and increased mortality. Therefore, hypertension should be controlled before major elective surgery to decrease cardiovascular events, cerebrovascular events, bleeding, and increased mortality (10).

Whether the BP is currently well controlled or not in a hypertensive the status of key organs must be assessed to check for any damage that may have occurred over time. An ECG, echo, lipids, and creatinine levels become mandatory before major surgery, However, adequate control of hypertension before the patient is subjected to the stress of surgery and anaesthesia (11).

The present study provides detailed information on the distribution of blood pressure and the prevalence of hypertension in patients attending an orthopaedic clinic. From this group of patients, some were admitted for various types of orthopaedic procedures. The relationships and associations between hypertension and general comorbidity are shown. The results are relevant to clinical practice and public health approaches to reducing the burden of postoperative complications, particularly cardiovascular, renal and cerebrovascular, commonly encountered in elderly patients after major surgery.

The associations also give an insight into the intricate relationships within the metabolic syndrome, throwing open the question of whether control of one could lead to control of all, and whether trialling of possible pharmaceutical substances to determine any potential for reversal or deceleration of the osteoarthritic cascade. Interest has been raised on renin-angiotensin enzyme inhibitors or blockers as possible modulators in the perfusion of critical joint tissues.

That would replace the widely used chondroitin/glucosamine compounds that have been shown to have doubtful benefits.

MATERIALS AND METHODS

Data source

A retrospective review of 788 case files of patients seen in an orthopaedic clinic between January 2019 and March 2020. Five hundred and sixteen patient files had complete data and were selected for the study. The raw data were entered on a data sheet. The patient's age, gender, weight, height, and BMI were all extracted and recorded. All patients had their BP recorded every time they attended the clinic. All the blood pressure readings were from the arm (cubital artery). Recorded were the Systolic (SBP), Diastolic (DBP) and Mean Arterial Pressures (MAP). Any patient with SBP readings of >130mmHg or DBP of >80 mmHg (confirmed with a standard sphygmomanometer with an appropriate cuff size) were considered hypertensive. However, for the study, a cut-off MAP of 100 was used as the segregating criteria. Blood pressure readings were done on an electronic blood pressure monitor (Intellective, model KAK 289, Chinese).

The dependent variable was osteoarthritis of any major joint while hypertension (MAP) was the primary predictor. Osteoarthritis was diagnosed radiologically, and graded according to Kellgren-Lawrence classification (12). Only patients with obvious arthritis (> grade 2), showing moderate osteophytes, definite joint space narrowing and some sclerosis were included.

The sample was divided into two groups, the hypertensive cohort (Group 1), and those without hypertension (Group 2). The secondary variables were other most frequent comorbidities (obesity, diabetes mellitus, and hyperacidity, cardiac disease, allergies/asthma and history of malignancy). These were included as possible confounders for hypertension. Apart from patients with large joint arthritis (hip, knee and shoulder), the other presenting orthopaedic conditions such as musculoskeletal trauma, infections, inflammatory conditions, and degenerative spine (low back pain), were treated as secondary predictor variables.

Exclusion criteria included hypertensives secondary to other conditions and all moribund patients and non-walkers. Excluded too were patients with overt depression. Included were all other ambulant patients ages between 20 and 70 years.

Definitions

(i)   Hypertension in this study only refers to essential hypertension.
(ii) Hypertension was defined as patients with a MAP of >100 with or without the use of antihypertensive medication.
(iii) Obesity was defined as a BMI of more than 30 kg/m^2 and above (13).

Statistical analysis

Data were analysed using SPSS 20.0 (SPSS, Inc., Chicago, IL). The means were compared between the groups, and significance was tested with independent t-tests and nonparametric tests for frequencies. Pearson correlation moment was performed to establish relationships between the variables, and the odds ratio was used to calculate the risk posed by other conditions. Binomial logistic regression was applied to model the relationship between the categorical variable (osteoarthritis) and the determinants. The confidence interval was assessed at 95% (P <0.05).

RESULTS

Out of the 788 files examined, 272 (35%) were excluded for the incompleteness of data leaving 516 cases for analysis. The prevalence of hypertension in the sample was 185 (36%), of which 117 (63%) were newly diagnosed. The remaining 68 were known hypertensives. The prevalence of arthritis was 17% and different between the two groups, a difference that was statistically significant (25% vs 13%, P = 0.0006). There were more male hypertensives than females (ratio 4:3, P <0.001), (Table 1).

Table 1
Prevalence of arthritis

	Group 1	Group 2	Total (N)	(%)	Chi square
Osteoarthritis	46	43	89	17	0.0006
No osteoarthritis	139	288	427	83	
Total	185	331	516		
Male	111	116	227	44	<0.001
Female	74	215	289	56	
Total	185	331	516		

Mean systolic and diastolic blood pressures increased with age in men and women, but a significant proportion of young patients, 36%, of patients below 40 years had raised blood pressure. There was a negative moderate correlation between age and hypertension (-0.4), which was statistically significant (p <0.01). Men had a higher prevalence of hypertension (42%) than women (30%), a difference that was statistically significant (<0.001). The correlation between gender and hypertension was poor (-0.2, p <0.01), despite a strong Odds Ratio of 1.7 (males are 1.7 times more likely to develop hypertension than females), (Table 2).

Only the most frequent comorbidities encountered in the study were analysed. These were obesity, diabetes mellitus, hyperacidity, cardiac disease, allergies/asthma, and previous history of malignancy. The study noted that as a person's weight increases the frequency of hypertension also increased. Out of the 12 underweight patients, only 1 (8%) was hypertensive compared to 42% of the obese patients. The mean BMI was 27.6 in the non-hypertensive cohort and 31.9 in the hypertensives group, although the difference was not statistically significant (p = 0.552). Pearson correlation returned a poor negative association (-0.2) between overweight and hypertension. The Odds ratio for an overweight person to develop hypertension was 2.7. The other conditions to show a strong OR were a previous history of malignancy (7.3), cardiac disease (4.2), and diabetes mellitus (1.7), (Table 3).

The spectrum of orthopaedic conditions was compressed to seven groups for statistical analysis. These groups were acute trauma, infections, inflammatory conditions, degenerative spine, and joint osteoarthritis. Infrequent conditions were lumped together as other conditions. The risk of hypertension was only found in patients with arthritis (OR = 2.2). The frequencies of these conditions and the relative risk are shown in Table 4.

Table 2
Hypertension, arthritis and age

Age (years)	Hypertension	Arthritis	% Hypertensive	% Arthritic
20-29	11	0	6	0
30-39	36	3	19	3
40-49	49	26	26	29
50-59	48	37	26	42
>60	41	23	22	26
Total	185	89	100	100
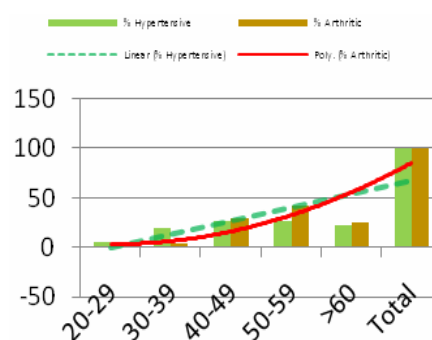
Table 3
Hypertension and other comorbidity

Description	No.	Normal BP	Hypertension	(%)	OR
Obese	184	106	78	42	2.7
Diabetes mellitus	62	33	29	47	1.7
Hyperacidity	92	73	19	21	0.4
Cardiac disease	7	2	5	71	4.2
Allergies/asthma	22	17	5	23	0.5
History of malignancy	5	1	4	80	7.3
Other comorbidities	17	10	7		
None	127	89	38	30	0.7
Total frequencies	711	439	272	100	

Table 4
Frequencies of presenting orthopaedic diseases and the risk factor for hypertension

Description	No.	Normal BP	Hypertension	(%)	χ^2	OR
Degenerative spine	175	110	65	37	0.435	1.1
Joint osteoarthritis	89	43	46	52	0.513	2.2
Acute trauma	95	64	31	33	0.001	0.8
Inflammatory conditions	46	29	17	37	0.004	1.1
Infections	21	13	8	38	0.876	1.1
Other conditions	90	68	16	19		
Total frequencies	516	331	185			

Logistic regression

Binomial logistic regression estimated the probability of having osteoarthritis occurring in patients with hypertension. In this model, the Cox & Snell (R^2) or Nagelkerke (R^2) methods returned a variation in the dependent variable (osteoarthritis) ranging from .234 to .447. The R^2 value indicates how much of the total variation in the dependent variable could be explained by any of the independent variables, meaning only 23-45% of osteoarthritis could be explained by the presence of any of the correlates, and was statistically significant (Table 5).

Table 5
Model summary and coefficients

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	323.881	.234	.447

Omnibus tests of model coefficients

	Chi-square	df	Sig.
Step	135.611	8	.000
Block	135.611	8	.000
Model	135.611	8	.000

Category prediction

The estimated probability of the event occurring must be greater than or equal to 0.5 (better than even chance, cut value is .500), which means that the probability of a case being classified into the "yes" category must be greater than .500. From the ensuing table, the sensitivity, specificity, positive predictive value and Negative predictive value could be deducted, (Table 6).

Table 6
Classification table

Observed			Predicted		
			Osteoarthritis		Percentage Correct
			Yes	No	
Step 1	Map	Yes	22	40	35.5
		No	11	435	97.5
	Overall percentage				90

a The cut value is .500

The calculated values were:
- Sensitivity (the percentage of cases that had osteoarthritis correctly predicted by the model) was 67%.
- Specificity (the percentage of cases that did not have osteoarthritis and that were also correctly predicted as such) was 92%.
- The positive predictive value (which is the percentage of correctly predicted cases of osteoarthritis compared to the total number of cases predicted to have osteoarthritis was) 35%.

- The negative predictive value (the percentage of correctly predicted cases without osteoarthritis compared to the total number of cases predicted as not having osteoarthritis) was 98%.

Variables in the equation

The variables in the equation table show the contribution of each independent variable to the model and its statistical significance, (Table 7).

Table 7
Variables in the equation

	B	S.E.	Wald	df	Sig.
Age	-.072	.014	26.979	1	.000
Gender	.355	.349	1.037	1	.309
Obesity	-.092	.032	8.307	1	.004
Hypertension	-.020	.015	1.811	1	.178
Diabetes	.454	.606	.561	1	.454
Hyperacidity	.068	.647	.011	1	.916
LBP	20.176	2784.434	.000	1	.994
MSK Inflammation(1)	-19.766	5535.188	.000	1	.997
Constant	28.942	5535.188	.000	1	.996

From these results only age and obesity were statistically significant p <.001 and p = 0.004 respectively. Hypertension return was not statistically significant (p = .178) and therefore, together with diabetes, hyperacidity, back pain and musculoskeletal did not add significantly to the model.

In conclusion, a logistic regression was performed to ascertain the effects of age, weight, gender, obesity, hypertension, hyperacidity, musculoskeletal inflammatory conditions and Low Back Pain (LBP) on the likelihood the patient developing osteoarthritis of any of the three major joints (shoulder, hip and knee). The logistic regression model was statistically significant, $\chi2(8)$ = 135.611 p< 0.001. The model explained 45% (Nagelkerke R^2) of the variance in osteoarthritis and correctly classified 90% of cases.

DISCUSSION

The reported prevalence of hypertension varies worldwide. One survey in 2012 showed very low prevalence in rural India (5%) and very high in Poland (70%). The same survey reported a prevalence of between 19-23% in rural areas and 24-38% in urban centres in sub-Saharan Africa (14). In Kenya, various studies showed a prevalence of 23-29% (15-17). Jenson *et al.* (18) reported a prevalence of 33% in Mombasa. This study has returned a prevalence rate of 36%.

For osteoarthritis, the prevalence rates varied greatly between different surveys and the joint under study. A Chinese study showed a prevalence rate of knee osteoarthritis of 22% among the middle-aged and the elderly (19). A large systematic review and meta-analysis on the prevalence of osteoarthritis in the lower middle-and low-income countries of Africa and South Asia showed a pooled prevalence of 16.05% (20). In the Middle East, the figures were quite low (7-9%) (21). In this study, the cumulative prevalence of osteoarthritis was 17%.

The study shows in greater detail the previously described positive relationships between ageing and systolic BP (22), BMI and hypertension (23), Type 2 DM and hypertension (24), and hypertension and osteoarthritis. Orthopaedic surgeons need, therefore, to be aware that more than 50% of their elderly patients (>50 years) are likely to have high BP. The same applies to patients who are obese (42%), those with osteoarthritis (52%). It is difficult to unequivocally comment about patients with history of cardiac disease and history of malignancy which returned high prevalence's (72% and 80% respectively) as their numbers were few. However, a systematic review and meta-analysis of 30 observational studies demonstrated an odds ratio for the association between hypertensive disease and perioperative cardiac outcomes of 1.35 (1.17–1.5). Such patients were reported to be more prone to perioperative ischaemia, arrhythmias, and cardiovascular liability. The recommendation in that study for the patients with markedly elevated preoperative BP was to maintain intraoperative arterial pressure within 20% of their normal (25).

Osteoarthritis (OA) is a joint disease characterised by perfusion abnormalities and neovascular invasion to the subchondral bone, synovium and articular cartilage. Although the articular cartilage is bathed and nourished by the synovial fluid, that aspect alone may not be sufficient to sustain it when perfusion to the synovium is denigrated. There is great contrast between the synovium of a young healthy knee

and that of an end-stage osteoarthritic knee. The former looks cherry red while the latter has the dark grey colour. Radiographic and symptomatic evidence from observational studies shows that hypertension may be a risk factor for knee osteoarthritis (26).

Apart from local vascular disturbance, systemic vascular pathology has been suggested in the aetiology of osteoarthritis (27). According to this theory, hypertension disrupts joint homeostasis by increasing intraosseous pressure that eventually results in ischaemic hypoxia that causes tissue damage, triggering subchondral bone and osteochondral junction remodelling. It has also been shown that systemic activation of the renin–angiotensin and endothelin systems can locally affect the signalling pathways that govern joint disease (27).

In addition, a link between OA and metabolic syndrome has been suggested. Metabolic syndrome is described when an individual is obese, hypertensive and has dyslipidaemia (9,28). A fourth component of type 2 diabetes mellitus caused by insulin resistance joins the triad. In a recent meta-analysis, Lo *et al.* (29) suggests an intimate relationship between hypertension and osteoarthritis but not necessarily chronic joint pain. That finding stimulated requirement for more research to the cellular and molecular pathogenesis of osteoarthritis and development of therapy strategies.

In this study, a binomial logistic regression was run to predict osteoarthritis from hypertension amongst other comorbidities. Apart from the high odds ratio (OR 2.2), which indicate a double risk factor, there was a moderate negative correlation of 0.386 (39%), P<0.001. The R^2 values of 0.45 (Nagelkerke R^2), however, indicate how much of the total variation in the dependent variable (osteoarthritis) could be explained by the other variants including hypertension. Note that 34% of hypertensive patients could be explained by obesity alone, p< 0.001.

Apart from osteoarthritis, the other comorbidities among hypertensive patients with significant relative risks (OR > 1) were a history of malignancy (OR 7.3), cardiac disease (OR 4.2), obesity (OR 2.7), and diabetes mellitus (OR 1.7). Although the numbers were small, patients with a history of malignancy (>5 years) showed the highest relative risk to hypertension, although the risk of hypertension was much lower in patients with musculoskeletal tumours (OR 0.9). Previous studies have showed hypertension as the most common comorbidity encountered in patients with malignancy (30) after chemotherapy.

The prevalence before chemotherapy is similar to that in the general population, but a much higher rate is observed after the initiation of certain chemotherapeutic agents such as angiogenesis inhibitors, alkylating agents, and immunosuppressants (31,32).

The association between elevated arterial pressure and cardiovascular disease has already been intimated. The risk of cardiovascular events in the general population increases steadily with increasing MAP. The individuals at greatest risk of suffering a cardiovascular event (heart failure, atrial fibrillation, chronic kidney disease, heart valve diseases, aortic syndromes, and dementia, in addition to coronary heart disease and stroke) because of hypertension are those with the highest arterial pressures (25,33,34).

The other comorbidity that showed a high relative risk was obesity. Obesity, particularly visceral obesity is associated with an increased cardiovascular risk and earlier onset of cardiovascular morbidity (35). Although many studies have established this strong relationship between obesity and hypertension, the relationship has not been clearly established. There has been a suggestion of a complex interaction of demographic, genetic, hormonal, renal, and haemodynamic factors. Age, race, and gender acting as modulators between the two (36). It has been suggested that hyperinsulinemia, which is characteristic of obesity, contributes to the probability of developing hypertension by activating the sympathetic nervous system and causing sodium retention. That is reported to enhance the pressor effect of insulin and blunting of the vasodilator action in obese subjects (36,37).

CONCLUSIONS

The high prevalence of hypertension in the population is a major public health problem. The rise in the prevalence of osteoarthritis appears to keep pace, just like the prevalence of obesity and diabetes mellitus. The three comorbidities (diabetes, hypertension and obesity) maximally increase the risks of cardiovascular incidences in the general population and after major surgery. Their relationships with osteoarthritis require being enlightened as surgery for arthritis is major and stressful. Finally, the close association between hypertension and osteoarthritis would be a point of study, particularly the emerging research on endothelium-targeted strategies with the use of the renin-angiotensin system modulators as a potential treatment for osteoarthritis.

REFERENCES

1. Iqbal, A.M. and S.F. Jamal, Essential hypertension, in Stat Pearls [Internet]. 2022, Stat Pearls Publishing.

2. Messerli, F.H., Williams, B. and Ritz, E.Essential hypertension. *The Lancet.* 2007; **370**(9587): 591-603.

3. Avgerinos, K..I., Spyrou, N., Mantzoros, C.S. and Dalamaga, M, Obesity and cancer risk: Emerging biological mechanisms and perspectives. *Metabolism.* 2019; **92**: 121-135.

4. Prabahar, K. Comparison of prescription patterns of antihypertensives in the geriatric population with JNC 8 guidelines. *J Applied Pharma Sci.* 2021; **11**(10): 88-92.

5. Borzecki, A., Kader, B. and Berlowitz, D. The epidemiology and management of severe hypertension. *J Human Hypertension.* 2010; **24**(1): 9-18.

6. Kario, K., *et al.,* Morning hypertension: the strongest independent risk factor for stroke in elderly hypertensive patients. *Hyperten Res.* 2006; **29**(8):581-587.

7. Kim, M.-J., *et al.,* Hypertension is an independent risk factor for type 2 diabetes: the Korean genome and epidemiology study. *Hyperten Res.* 2015; **38**(11): 783-789.

8. Diaz, M. Hypertension and obesity. *J. Human Hyperten.* 2002; **16**(1): S18-S22.

9. Samson, S.L. and Garber, A. J. Metabolic syndrome. *Endocrinol Metabol Clin.* 2014; **43**(1):1-23.

10. Aronow, W. S. Management of hypertension in patients undergoing surgery. *Annals Translational Med.* 2017; **5**(10): 227.

11. Lapage, K.G. and Wouters, P. F. The patient with hypertension undergoing surgery. *Current Opinion Anaesthesiol.* 2016; **29**(3):397-402.

12. Kohn, M.D., Sassoon, A.A. and Fernando, N.D. Classifications in brief: Kellgren-Lawrence classification of osteoarthritis. *Clin Orthop Related Res.* 2016; **474**(8):1886-93.

13. Friedman, N. and Fanning, E.L. Overweight and obesity: an overview of prevalence, clinical impact, and economic impact. *Disease Management.* 2004; **7**(Suppl 1): S-1-S-6.

14. Hendriks, M.E., *et al.,* Hypertension in sub-Saharan Africa: cross-sectional surveys in four rural and urban communities. *PloS One.* 2012; **7**(3): e32638.

15. Joshi, M.D., *et al.,* Prevalence of hypertension and associated cardiovascular risk factors in an urban slum in Nairobi, Kenya: a population-based survey. *BMC Public Health.* 2014; **14**(1):1-10.

16. Olack, B., *et al.,* Risk factors of hypertension among adults aged 35–64 years living in an urban slum Nairobi, Kenya. *BMC Public Health.* 2015; **15**(1):1-9.

17. Mohamed, S.F., *et al.,* Prevalence, awareness, treatment and control of hypertension and their determinants: results from a national survey in Kenya. *BMC Public Health.* 2018; **18**(3):1-10.

18. Jenson, A., *et al.,* Assessment of hypertension control in a district of Mombasa, Kenya. *Global Public Health.* 2011; **6**(3): 293-306.

19. Sun, X., *et al.,* Osteoarthritis in the middle-aged and elderly in China: prevalence and influencing factors. *Intern J Environ Res Public Health.* 2019; **16**(23):4701.

20. Yahaya, I., *et al.,* Prevalence of osteoarthritis in lower middle-and low-income countries: a systematic review and meta-analysis. *Rheumatol Intern.* 2021; **41**(7):1221-31.

21. Hamood, R., *et al.,* Prevalence and incidence of osteoarthritis: A population-based retrospective cohort study. *J Clin Med.* 2021; **10**(18):4282.

22. Black, H. The paradigm has shifted to systolic blood pressure. *J Human Hyperten.* 2004; **18**(2):S3-S7.

23. Koliaki, C., Liatis, S. and Kokkinos, A. Obesity and cardiovascular disease: revisiting an old relationship. *Metabolism.* 2019; **92**:98-107.

24. Viigimaa, M., *et al.,* Macrovascular complications of type 2 diabetes mellitus. *Current Vascular Pharmacol.* 2020; **18**(2):110-116.

25. Howell, S., Sear, J. and Foex, P. Hypertension, hypertensive heart disease and perioperative cardiac risk. *Br J Anaesthesia.* 2004; **92**(4):570-583.

26. Zhang, Y.-M., Wang, J. and Liu, X-G. Association between hypertension and risk of knee osteoarthritis: A meta-analysis of observational studies. *Medicine.* 2017; **96**(32):

27. Ching, K., *et al.,* Hypertension meets osteoarthritis—revisiting the vascular aetiology hypothesis. *Nature Reviews Rheumatol.* 2021; **17**(9):533-549.

28. Le Clanche, S., *et al.,* Inter-relations between osteoarthritis and metabolic syndrome: A common link? *Biochimie.* 2016; **121**:238-252.

29. Lo, K., *et al.,* Association between hypertension and osteoarthritis: a systematic review and meta-analysis of observational studies. *J Orthopc Translation.* 2022; **32**:12-20.

30. Małyszko, J., *et al.,* Hypertension in malignancy–an under appreciated problem. *Oncotarget.* 2018; **9**(29):20855.

31. Cohen, J.B. *et al.,* Hypertension in cancer patients and survivors: epidemiology, diagnosis, and management. *Cardio Oncology.* 2019; **1**(2):238-251.

32. Mouhayar, E. and Salahudeen, A. Hypertension in cancer patients. *Texas Heart Inst J.* 2011; **38**(3):263.

33. Fuchs, F.D. and Whelton, P.K. High blood pressure and cardiovascular disease. *Hypertension.* 2020; **75**(2):285-292.

34. Whelton, S.P., *et al.,* Association of normal systolic blood pressure level with cardiovascular disease in the absence of risk factors. *JAMA Cardiol.* 2020; **5**(9):1011-18.

35. Leggio, M., *et al.,* The relationship between obesity and hypertension: an updated comprehensive overview on vicious twins. *Hyperten Res.* 2017; **40**(12):947-963.

36. Mikhail, N., Golub, M.S. and Tuck, M.L. Obesity and hypertension. *Progress Cardiovas Dis.* 1999; **42**(1):39-58.

37. Kotsis, V., *et al.,* Mechanisms of obesity-induced hypertension. *Hyperten Res.* 2010;. **33**(5):386-393.