

**ROLE OF SWETHA PARPATI IN THE MANAGEMENT OF ACUTE
HYPERTENSION/HYPERTENSIVE CRISIS****Dr. Sarwar Hussain Ansari¹, Dr. MD Haidar², Dr. Rajarshi Chaudhuri^{*3}**^{1,2}2nd Year PG Scholar, Dept. of Panchakarma, I.P.G.A.E. & R. at SVSP, Kolkata.³Lecturer Dept of Panchakarma, I.P.G.A.E. & R. at SVSP, Kolkata.Article Received on
13 October 2020,Revised on 03 Nov. 2020,
Accepted on 24 Nov. 2020

DOI: 10.20959/wjpr202015-19286

Corresponding Author*Dr. Rajarshi Chaudhuri**Lecturer Dept. of
Panchakarma, I.P.G.A.E. &
R. at SVSP, Kolkata.**ABSTRACT**

In Ayurveda, the study of the therapeutic uses and effects of drugs means Pharmacotherapy is described under the branch of Rasashastra. This article aims for the assessment of role of Swethaparpati in management of Raktagata vata/Acute Hypertension. Hypertension (HTN or HT), also known as high blood pressure (HBP), is a long-term medical condition in which the blood pressure in the arteries is persistently elevated. Long-term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral arterial disease, vision loss, chronic kidney disease, and dementia. Raktagata Vata means

involvement of Rakta (blood) by vitiated Vayu. According to Ayurveda, the main function of Rakta is "Jivana (life)." Hence, it has been mentioned as a "Jivana" (life). When Rasa-Rakta Dhatu (plasma and blood) remains in their normalcy and cardiovascular system, mainly Sira (veins), Dhamani (arteries), and Hridaya (heart) stay put standard and perform their functions as a rule. Any abnormality of Rasa Rakta Dhatu affects the normal circulation of Rasa Rakta and ultimately results in the abnormality of the blood pressure by making additional pressure or less pressure on the Rakta Vahinies (arteries). In our sastra there is no direct reference regarding the management of acute case of Hypertension except oral intake Rudraksha in the form of kwatha churna or vati but according to modern science as we know drugs like Furosemide, Nifedipine, Labetalol etc is the drug of choice in such condition. According to the references the ingredients used for the preparation of Swethaparpati are Suryakshara, Sphatika and Navasagara, Tankana and Karpura. Here a detailed review of literature has been collected regarding the potential of the above mentioned individual ingredients along with the recent research updates regarding individual ingredients used in the production of Swetha

Parpati. So we given Swethaparpati as Mutral & Swedajanan dravya in the dose of 500mg stat dose with normal water in our outdoor patients to assess the effectiveness of Swethaparpati in case of acute Hypertention/Raktagata vata.

Shweta Parpati uses

Mutrala (diuretic), Swedjanaan (promotes sweat), Ashmari (urinary calculi), Mutrakriccha (urinary disorders), Mutraghata (urinary obstructions) etc.

Dose: 5-10 Ratti (625-1125 mg)

Anupana-Sheetajala, NarikelaJala, Sharkarayuktajala.

Effect on Tridosha: Balances Vata and Pitta.

Ingredients of Swethaparpati with their quantity and melting point^[1]

S. No.	Name of ingredient	Quantity	Melting point
1.	1 Suryakshara	20 Karsha	334* C ^[2]
2.	2 Sphatika	5 Karsha	92-95* C ^[3]
3.	3 Tankana	3 Karsha	743*C ^[4]
4.	4 Karpura	3 Karsha	175* C ^[5]
5.	5 Navasagara	3 Karsha	338* C ^[6]

Therapeutic uses of individual drugs (ingredients) of Swethaparpatias per Rasatarangini

Name of Drug/Ingredient	Therapeutic Use of Purified Drug
1) Suryakshara (Potassium nitrate)	Vidagdhaajeerna (indigestion), Asmari (urinary calculi), Mutrakrichra (urinary diseases), Agnimandya (loss of appetite), Panduroga (iron deficiency anaemia), Prameha (urinary disorders/diabetes mellitus) ^[7]
2) Sphatika (Potash Alum)	Visarpa (erysipelas), Switra (vitiligo), Vranaropana (heal the wound), Netraroga (eye disorders), Vishamajwara (chronic fever), Grahani (Sprue/IBS), Rudirasravrodhini (stops bleeding). ^[8]
3) Navasagara (Ammonium chloride)	Gulma (gaseous tumour of abdomen), Adhmana (fullness of abdomen), Mukhasosha (dryness of mouth), Vrishchikavishanashaka (antidote of poison of scorpion), Hridroga (heart disorders), Netrya (cures eye ailments), Kushta (skin disorders). ^[9]
4) Tankana (borax)	Adhmana (fullness of abdomen), Sthavaravishanashaka (pacifies poison caused by plants), Vrananasahana (cures the wound), Moodagarbhapravarthaka (expels malformed foetus), Balya (provides strength). ^[10]

Research carried out on Swethaparpati**1. Role of Shwet Parpati in Mutrakrichra (Dysuria)^[11]**

Shwetaparpati Contains-Shudhasora 16 parts, Shuddhkankshi 2 parts, Shuddhanavsadar 1 part and prepared by method of Parpatikalpana. All the ingredients of Shwetparpati are Mutrala (Diuretic) in nature. This study was a randomized controlled clinical trial. The other group was given placebo treatment to see whether the results obtained were by chance or due to the drug.

2. Effect of Swethaparpati in Mutrakrichra: An Article Review^[12]

It is an effort done to assess the mode of action of the drug considering the potential of each ingredient, Suryakshara, Sphatika and Navasagara. Detailed review of literature including the recent research works done on the single ingredients is included. In diuresis one more thing to be tested symptomatically is potassium depletion, which other diuretics make, whereas in Shwethaparpati it is absent. The action of the drug based on the alkalinity/acidity is also tried.

3. An observational clinical study on the management of Mutrakrichchra (lower urinary tract infection).^[13]

Study was conducted on 40 patients who were administered with the combination of Gokshurachurna, Pashanabhedadi kashaya and Shwetaparpati for the duration of 15 days. Out of 40 patients 23 (57.3%) got complete relief and 17 (42.5%) got marked relief from the parameters considered for the assessment of result which was statistically highly significant with P value 0.000.

Research Updates of Individual Drugs of Swethaparpati**Suryakshara and Sphatika^[12]**

These two drugs contribute K⁺ ion which acts as an alkalinizer is the drug used in all conditions of dysurea. Urinary tract alkalinizer; produces an alkaline load that increases urinary pH and raises urinary citrate by augmenting citrate clearance without measurably altering ultra filterable serum citrate; produces urine that is less conducive to crystallization of stone-forming salts.

Tankana^[13]

It induces menstruation in women suffering with amenorrhea or oligomenorrhea (scanty menstrual flow); it is useful in uterine infections.

Karpura^[14]

Diuretic and keeps the urinary system free of bacterial infestations. (Companies like Dhootpapeswar, Baidyanath, IMPCL are manufacturing Swetaparpati on the reference mentioned in Sidhayogasangraha and AFI).

HYPERTENSION/RAKTAGATA VATA**INTRODUCTION**

Hypertension is a common disease in present era. Every fifth person is found hypertensive. Most adults develop it, in later half of their life.^[15] It is one of the most frequent cause for cardiovascular, cerebrovascular and renovascular mortality and morbidity.^[17]

The adverse effects of hypertension principally involve the blood vessels, central nervous system, retina, heart and kidneys, and can often be detected clinically.^[15] It is very well established that in case of untreated hypertension mortality and morbidity increase several fold and that control of it, reverse this to a great extent. So that hypertension must be treated and controlled.^[18]

More than 50% of the deaths and disabilities from heart disease and stroke together kill more than 12 million people each year. It has been predicted that by the year 2020 there will be a 75% increase in the global cardiovascular disease burden occurring, The situation in India is rather more alarming, it has been predicted that there would be a 111% increase in the cardiovascular deaths in India by 2020. Therefore cardiologist has already drawn considerable attention to the WHO and various health administrations to develop effective strategies for Hypertension Prevention Programme.^[15]

Various *Ayurvedic* scholars have coined different names for hypertension such as: *Raktagata Vata*, *Siragata Vata*, *Avrita Vata*, *Dhamani Prapurana*, *Rakta Vikshepa*, *Vyana Prakopa*, *Raktamada*, *Uchharaktachapa*, *Vyana Atibala* etc.^[15*]

In each of these terms, different points of view have been adopted, but no one has denied the fact that in hypertension, the main pathogenesis occurs in *Rakta* along with the blood vessels. This being the only factor in common, many previous authors have given separate views on the *Ayurvedic* pathogenesis of this condition. As modern science is well advanced in understanding hypertension, we must understand all that is known about this disease and suitably correlate it to *Ayurvedic* principles for better understanding.

There is an urgent need to develop personalized medicine through traditional Ayurvedic medicine; a shift from single target single intervention approach to integrative system biology i.e. holistic approach. In modern medicine anti hypertensive drugs lower the high blood pressure but do not eradicate the risk of cardio-cerebroreno-ophthalmo-vascular involvement, But Ayurvedic therapy can minimize the risk factor in a better way. In Ayurvedic texts there is no clear pronounciation of Hypertension; but it might be present from the time, when life is existing in the universe because diseases like Pakshaghata (Stroke), Mutraghata(Renal failur) and Hridroga(Heart disease) are very well explained in our texts which are common complications secondary to Hypertension.^[19]

Regulation of Blood Pressure in Ayurveda

Blood pressure is not described in any of the Ayurvedic classics. Blood pressure is an important phenomenon for the normal functioning of blood circulation, and physiology related to blood circulation is described by Ayurvedic Scholors. The regulation of Blood pressure is carried by Myocardial contractility, that pump the heart continuously and ejects the blood, helps in maintaining normal Blood pressure.

In Ayurveda regulation of Blood pressure can be understood by functions of PranaVayu, Vyana Vayu, Sadhaka Pitta, Avalambaka Kapha, Rasa and Rakta Dhatu which are situated in Hridaya.(Heart). According to Ranjit Rai Desai, vitiation of Vata, Pitta, and Kapha (Premordial factors), asthi meda etc. affects blood pressure Kapha vitiation (avalambak kapha) increases cardiac strength but due to sluggishness of kapha, it decreases the kapha and on other hand Pitta (sadhak pitta) and Vata(vyan vata) vitiation increases blood pressure. Here one thing must be clarified that term for blood circulation is not the rakta samvahana (transportation of blood) but rasanudhavana (Circulation of Plasma) Ayurveda belives that rasa(plasma) is the circulating medium and not the rakta(blood).^[20]

Niadana/Etiology of Raktagata vata/Hypertension

- ❖ Essential Hypertension is idiopathic where exact etiology of the rise in blood pressure is not yet clear. There are many pre disposing factors which causes hypertension is mention as follow.
- ❖ Alcohol intake (Madyapan)
- ❖ Salt intake (Lavan)
- ❖ Sedentary life style (Ati Snighda, Madhur & Divaswap)
- ❖ Mental Stress. (Krodha, Bhaya, Shok)

- ❖ Physical Strain (Shrama)
- ❖ Seasonal variations (Rutu Sandhi)^[21]

Nidanarthkara Roga

- Madhumeha (Diabetes),
- Sthoulya (obesity),
- Hridroga (Heart disease),
- Vrika roga (Renal disease) are the precipitating diseases to form secondary hypertension.^[21]

Samprapti/Pathogenesis of Raktagata vata/Hypertension in Ayurveda

- ❖ Ati lavana sevana (Excessive salt intake),
- ❖ Madyapana (Alcohol consumption)
- ❖ Snigdha bhojana (oily diet)
- ❖ Divaswap (day time sleep) and
- ❖ Manovighata (Mental accident) leads to vitiation of Shonita (blood). But Shonita being Dhātu (tissue) is not capable of vitiating Doshas (pre-mordial factors of body) independently. The Doshas present in the Shonita which are involved indirectly in the manifestation of high blood pressure. The over use of salt, alcohol vitiates the Sadhaka pitta and Shonita (blood). Sedentary habits vitiate the Avalambaka kapha and psychological stress induces vitiation of Prana vayu. Initially Prana vayu gets prakopa. Since Prana vayu has influence on Hridaya (heart), vitiates Hridaya and its residing components like Vyana vayu, Sadhaka pitta, Avalambaka kapha. Shonita is also involved as it is located in hridaya. Prakupita (vitiating) Avalambaka kapha induces exaggerated contractility of the heart, while aggravated Vyana vayu leads to increased gati (speed), the force of ejection of blood from Hridaya. These events result in forceful expulsion of blood through dhmanis (blood vessels), ultimately leading to increased resistance in vessels ensuring High blood pressure.

Symptomatology (Lakshanas)

Hypertension is asymptomatic in most of the cases but the symptoms can be seen in accelerated or sustained or Malignant Hypertension.

- ❖ Headache (Shirorukh)
- ❖ Tiredness (Shrama)

- ❖ Irritability (Krodhaprachurata)
- ❖ Raised body temperature (Jwara)
- ❖ Dizziness (shirobhram)
- ❖ Vomiting (Klama)
- ❖ Altered consciousness (tamasaatidarshan)
- ❖ Seizures (Kampa)
- ❖ Visual Disturbances (Akshiraga)
- ❖ Focal neurological signs (Ardita)
- ❖ Urinary symptoms (Raktameha)
- ❖ Delirium in Hypertensive (Shiro Bhrama)
- ❖ Delirium in encephalopathy (Mada)
- ❖ Stupor (Moorchha)
- ❖ Coma (Sanyasa)^[22]

Table 1: Classification of blood pressure for adults aged ≥ 18 years.^[23]

BP Classification	Systolic BP (mmHg)	Diastolic BP (mmHg)
Normal	<120	<80
Prehypertension	120–139	80–89
Stage 1 hypertension	140–159	90–99
Stage 2 hypertension	≥ 160	≥ 100

Table 2: Classification of blood pressure for adults.^[24]

Category	Systolic BP (mmHg)	Diastolic BP (mmHg)
Optimal	<120	<80
Normal	120–129	80–84
High normal	130–139	85–89
Grade 1 hypertension (mild)	140–159	90–99
Grade 2 hypertension (moderate)	160–179	100–109
Grade 3 hypertension (severe)	≥ 180	≥ 110
Isolated systolic hypertension	≥ 140	<90

Box 1. Factors influencing prognosis of hypertension Risk factors^[25]

Level of systolic and diastolic blood pressure.

- ❖ Men aged >55 years.
- ❖ Women aged >65 years.
- ❖ Smoking.
- ❖ Dyslipidaemia.
- ❖ Family history of premature cardiovascular disease (men aged <55 years, women aged <65 years).

- ❖ Abdominal obesity (abdominal circumference ≥ 102 cm for men, ≥ 88 cm for women).
- ❖ C-reactive protein ≥ 1 mg/dL.

Target organ damage

- ❖ Left ventricular hypertrophy (LV mass index >125 g/m² in men, >110 g/m² in women)
- ❖ Carotid intima-media thickness ≥ 0.9 mm or atherosclerotic plaque Serum creatinine >1.3 mg/dL in men,
 >1.2 mg/dL in women.
- ❖ Microalbuminuria.

Diabetes mellitus

- ❖ Fasting plasma glucose ≥ 126 mg/dL.
- ❖ Postprandial plasma glucose ≥ 200 mg/dL.

Associated clinical conditions

- ❖ Cerebrovascular disease (transient ischaemic attack, stroke, haemorrhage).
- ❖ Heart disease (angina, myocardial infarction, heart failure)
- ❖ Renal disease (diabetic nephropathy, serum creatinine >1.5 mg in men, >1.4 mg in women, proteinuria >300 mg/24 hours)
- ❖ Peripheral vascular disease
- ❖ Advanced retinopathy (haemorrhage, exudates, papilloedema)

Causes of hypertension

The various causes of hypertension are listed in Box 2. Primary (essential or idiopathic) hypertension is systemic hypertension of unknown cause that results from dysregulation of normal homeostatic control mechanisms of blood pressure in the absence of detectable known secondary causes. Over 95% of all cases of hypertension are in this category. Secondary hypertension is systemic hypertension due to an underlying disorder. It accounts for $<5\%$ of cases of hypertension.^[26]

Box 2. Causes of Hypertension**1. Primary (essential or idiopathic).****2. Secondary Renal.**

- Renal parenchymal.
- ❖ Acute glomerulonephritis.

- ❖ Chronic nephritis.
- ❖ Polycystic disease.
- ❖ Diabetic nephropathy.
- ❖ Hydronephrosis.
- Renovascular
- ❖ Renal artery stenosis.
- ❖ Intrarenal vasculitis.
- Renin-producing tumours.
- Renoprival.
- Primary sodium retention (Liddle syndrome, Gordon syndrome).

Endocrine

- ❖ Acromegaly.
- ❖ Hypothyroidism.
- ❖ Hyperthyroidism.
- ❖ Hypercalcaemia (hyperparathyroidism).
- Adrenal
 - i. Cortical
 - ❖ Cushing syndrome
 - ❖ primary aldosteronism
 - ❖ congenital adrenal hyperplasia
 - ❖ apparent mineralocorticoid excess (liquorice)
 - ii. Medullary
 - ❖ Pheochromocytoma
 - Extra-adrenal chromaffin tumours.
 - Carcinoid.
 - Exogenous hormones:- estrogen, glucocorticoids, mineralocorticoids, sympathomimetics, tyramine containing food, monoamine oxidase inhibitors.

Systolic hypertension

1. Increased cardiac output.
 - ❖ Aortic valvular insufficiency
 - ❖ Arteriovenous fistula
 - ❖ patent ductus arteriosus

- ❖ Thyrotoxicosis
- 2. Rigidity of aorta
- 3. Iatrogenic hypertension

Laboratory investigation^[27]

Laboratory investigations should be directed at providing evidence of additional risk factors, searching for secondary hypertension and assessing presence or absence of target organ damage. They include routine tests, recommended tests (based on recent studies) and specific tests for extended evaluation of hypertensive complications and causes of secondary hypertension.

- **Routine tests:**—electrocardiogram (ECG) – plasma glucose (preferably fasting) – serum total cholesterol – serum high-density (cholesterol) lipoprotein (HDL)– fasting serum triglycerides – serum uric acid – serum creatinine – serum potassium – haemoglobin and haematocrit – urinalysis (dipstick test and urinary sediment examination).
- **Recommended tests:**—echocardiogram – carotid (and femoral) ultrasound – C-reactive protein – microalbuminuria (essential in diabetics) – quantitative proteinuria (if dipstick is positive) – funduscopy (in severe hypertension).
- **Extended evaluation (domain of the specialist):**—complicated hypertension: tests of cerebral, cardiac and renal function – search for secondary hypertension: measurement of renin, aldosterone, corticosteroids, catecholamines, arteriography, renal and adrenal ultrasound, computed tomography (CT) and brain magnetic resonance imaging (MRI).

Clinical trial

A patient Mr Ramesh rajbhar, Age- 55years, was came in our OPD with complaining of pain in multiple big joints like knee joint. He has a past history of Hypertension but he takes irregular medication, during general examination we got Systolic Blood pressure 200mm of Hg & Diastolic Blood pressure 120mm of Hg. We adviced him totake 500mg Sweta parpati as a stat dose with normal water. After 45mins patient passed urine for 2 times, then we checked BP and got Systolic BP 180mm of Hg & Diastolic BP 100mm of Hg. Again we checked BP after an interval of 30mins, we got Systolic BP 140mm of Hg & Diastolic BP 90mm of Hg. Such type of trail was done on two more patients and we got same types of results as mentioned above.

CONCLUSION

As we know Ayurveda is a science of life. It deals with health promotion of a healthy person and cured the diseased one. Various such types of clinical trials requires to established our science in modern era. I will try to continue this clinic trail in future for the betterment of humanity.

REFERENCES

1. Jivram Kalidasshastri; Rasodharatantra (1st Ed); Kathiyawad; Shri Rasashala Aushadhaashram; 1931.
2. Wikipedia org. [Online]. Available from: https://en.wikipedia.org/wiki/Potassium_nitrate-334 [Accessed 16 July 2017].
3. Wikipedia org. [Online]. Available from: https://en.wikipedia.org/wiki/Potassium_alum [Accessed 16 July 2017].
4. Wikipedia org. [Online]. Available from: <https://en.wikipedia.org/wiki/Borax-743> [Accessed 16 July 2017].
5. Wikipedia org. [Online]. Available from: [https:// en.wikipedia.org/wiki/Camphor-175](https://en.wikipedia.org/wiki/Camphor-175) [Accessed 16 July 2017].
6. Wikipedia org. [Online]. Available from: [https:// en.wikipedia.org/wiki/Ammonium_chloride-338](https://en.wikipedia.org/wiki/Ammonium_chloride-338) [Accessed 16 July 2017].
7. Sri Sadanandasharma. Talakadi Vigyaniya Ekdasha Taranga. In: Kashnathshastri(ed.) Rasatarangini. Varan asi: MotilalBanarasidas; 197. p.181-183.
8. Sri Sadanandasharma. Ksharavisheshadi Vigyaniya Chaturdasha Taranga. In: Kashnathshastri (ed.) Rasatarangini. Varanasi: Motilal Banarasidas, 1971; p. 5- 7.
9. SriSadanandasharma; Ksharatrik Vigyaniya Trayodasha Taranga; In Kashnathshastri (Ed.) Rasatarangini; Varanasi, Motilal Banarasidas, 1971; p.79-81.
10. Sri Bhavamisra. Bhavaprakasa Nighantu (6Ed.); Chaukham bhabharati Academy; Varanasi, 1982.
11. Bhujbalanna sahib ashok, Wasniksumedh, Dhalaperupali. Role of Shweta ParpatiIn Mutrakrichra (Dysuria); Ayurveda medical Journal, 2015; 1(6): 427-431.
12. Dr Geethubalakrishnan, Dr Vineeth P K; Ramesh N V.; Effect of Swetha Parpati In Mutrakrichra: An Article Review; Journal Of Medical Pharmaceutical And Allied Sciences, 2017; 1(1): 588-595.
13. PriyaBhat, Gajanana Hegde. An observational clinical study on the management of Mutrakrichchra (Lower Urinary Tract Infection). Ayurpharm Int J Ayur Alli Sci., 2014;

- 3(10): 275-281.
14. Shaikh SM, Doijad RC, Shete AS, Sankpal PS; A Review on Physicochemical evaluation of Ayurvedic mineral drug Tankan Bhasma; Pharma Tutor, 2016; 4(4): 23-27.
 15. Ambulkar P, Chand T, Rao S, Dwivedi L., Makardhwaj as a Boon in Hypertension (Vyan Bala Vaishmya): A Clinical Evaluation, Proceedings in National Seminar on Preventive Cardiology in Ayurveda. Rashtriya Ayurveda Vidyapeeth Publication, New Delhi. India, 2010; pp. 295-300.
 16. Madhumati Dhamle Post Graduate Thesis on – the study of Yojana-Chatushka of Charaka and Yojana for the management of Raktashrita Vyadhi (hypertension) Department of Basic Principles, Institute of Post Graduate Teaching and Research in Ayurveda (2001).
 17. Tripathi A, Clinical evaluation of Shankhapuspi compound in Hypertension, Proceedings in National Seminar on Preventive Cardiology in Ayurveda. Rashtriya Ayurveda Vidyapeeth Publication, New Delhi, India, 2010; pp. 309.
 18. Yadav B, Sehrawat D, Prasad M, Ghosh S, A clinical study on factors affecting prevalence of Hypertension (Raktagatvat): Proceedings in National Seminar on Preventive Cardiology in Ayurveda. Rashtriya Ayurveda Vidyapeeth- Publication, New Delhi, India, 2010; pp. 269-278. mainly in the developing countries.
 19. Shukla N, Shukla CP, A Comparative study of Sarpagandhavati and Vachadiyoga in the management Essential Hypertension; Proceedings in National Seminar on Preventive Cardiology in Ayurveda, R.A.V. Publication, New Delhi India, 2010; pp.251-258.
 20. Desai R, Ayurvediya Kriyasharir, Chaukhamba Surbharati Prakashan, Varanasi, India, 2010.
 21. Tripathi B, Samhita C, Adhyaya S, In: Chakarpani & Charak Chandrika (Eds.), Chaukhamba Surbharati Prakashan, Varanasi, India, 2012; 24(5-10): P-430.
 22. Tripathi B, Samhita C, Adhyaya S., In: Chakarpani & Charak Chandrika, 24(11-17) P-430.
 23. Chobanian AV et al. Seventh report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure. Hypertension, 2003; 42: 1206–1252.
 24. Kaplan NM. Kaplan's clinical hypertension. 8th ed. Philadelphia, Lippincott Williams and Wilkins, 2002.
 25. Stamler J, Wentworth D, Neaton JD. Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222

- primary screeners of the Multiple Risk Factor Intervention Trial (MRFIT). JAMA, 1986; 256: 2823–2828. OS.
26. Kaplan NM. Kaplan's clinical hypertension. 8th ed. Philadelphia, Lippincott Williams and Wilkins, 2002.
27. Chobanian AV et al. Seventh report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure. Hypertension, 2003; 42: 1206–1252.