



Female Gender and Patient Outcomes Female Gender... Is It Really A Risk Or A Boon?

Authors

Srilata Moningi, Narmada Padhy, Abhiruchi Patki, Gopinath Ramachandra

Email: srilatanims@gmail.com, Mobile: 9848352882

Abstract

Men and women both face health problems. Barring certain subtle differences in endocrinology and reproductive physiology, the rest of the systems function nearly same in both, yet the incidence and presentation of certain diseases in women is different than men. This article discusses in detail this array of differences, ranging from difference in life expectancy in both, incidence of critical illness or cardiac arrest, to differences in incidence and outcome of various types of surgeries and medical illnesses with an aim to arrive at a possible scientific explanation as to why this difference exists.

Keywords: Women; Physiology; Incidence; Outcome.

Female gender is the most susceptible character and a social stigma in Indian paradigm. The famous quote "MEN ARE FROM MARS AND WOMEN FROM VENUS" is true to its words. There are some subtle differences between males and females and some of them are enumerated here. Males are more prone to inhalation toxic exposure purely, due to occupation. This also includes higher rate of injuries including accidents. Life style habits like cigarette smoking, drinking, late night parties, rash driving are more prevalent in males though the difference is getting marginal in urban places. Females, on the other hand, working both at home and work place are more strained. Nutritional deficiencies are more common in females compared to males, especially in under developed and developing countries. This may be attributed to the cultural disbeliefs and taboos like gender inequalities. The background of hormonal difference and the basic neural network plays a crucial role in these differences. The

estrogen hormone in females is protective whereas testosterone has got opposite effects. Other minor differences include the attitude, emotional aspect and limited access to resources and services behind the health benefits and its outcomes.

Males and females both face health problems. Do these differences define the outcome in health based practice? Are these outcomes differing in different sub categories of health? Evidence shows inconsistent findings in the outcome. There are enough evidence spurring from critical care, cardiac and trauma patients. But very sparse literature was reported with respect to neurosurgery, orthopedic and abdominal surgeries. In this article, we will discuss the female gender and its outcome in different subspecialities of surgery and medicine.

Overall, the average life expectancy is 71 years as per the 2013 census (World Fact Book). The life expectancy of females exceeds males in the world population as a whole. This is more than 80 years

on an average, especially in developed countries. The average difference in the life expectancy in males and females comes down as we go down the trend of developing and underdeveloped countries. This is attributed mainly to the increased maternal mortality ratio, cultural taboos and the prevailing gender inequalities. On the other side, the increasing life expectancy in females not only attributes to the hormonal effects but also to the decreasing social discrimination.

In India, the life expectancy showed a big leap by 8.6 years in both males and females since 1990. This has been the top 25 biggest gains in life expectancy worldwide. This Indian surge is more than the average global increase noted. (Indian Express: Tuberculosis, heart disease top causes of death in India: report; dated 18th Dec, 2014)

As per WHO, the females outnumber males in developed countries. In India, the sex ratio among children declined from 927 girls per 1,000 boys in 2001 to 914 in 2011 in contrast to the decreasing social discrimination. The World Economic Forum ranked India as second from last (132nd out of 134 nations) in terms of gender equity in health.

The leading causes of death in males and females as per the global health estimate, 2012 data are ischemic heart disease and stroke followed by COPD and lower respiratory infections. The predominant cause of death among the first 2 leading causes: in males – ischemic heart disease and in females – stroke followed by the other. The scenario in India showed a death toll in females mainly due to infectious diseases like diarrhea compared to males where IHD played a major role.

Maternal mortality ratio: Despite India's upcoming rapid economic growth, maternal mortality ratio is comparatively still high, 140 per 1,00,000 live births. India missed the target of 109 of 2016 census, thus indicating a requirement of drastic step for social and health uplift of females to hit the target. This was reported in the newspaper THE ASIAN AGE dated Oct 25th, 2015.

Cardiac

Literature has shown inconsistent findings with the outcome and female gender. Kim et al did a systematic review of gender differences in mortality after coronary artery bypass graft surgery (CABG) (23 studies) and percutaneous coronary interventions (PCI) (48 studies) from 1985 to 2005 (Medline search).^[1] Gender was found to be an independent risk factor for complications following both CABG and PCI. Greater incidence of complications and mortality followed revascularization in females. Later in 2012, Lehmkohl et al did a prediction outcome for mortality following CABG surgery (1559 patients).^[2] Age, physical function and postoperative complications are found to be risk factors for early mortality following CABG surgery in females. A recent article published by Rawa et al shows a low survival rate at 6 months in females aged 70-80 years and no difference at 1 month in patients undergoing coronary revascularization.^[3] Proper pre-operative assessment, optimization of modifiable risk factors, anticipation and programmed approach for anesthetic management of high risk patients would benefit in decreasing the mortality outcome in female patients.

Vallakati et al studied the impact of gender on outcome after atrial fibrillation ablation by analyzing 18 studies with 8745 patients in total. They opined that the incidence of recurrence after ablation was higher in females by 19%.^[4] Later, after 1 year, these findings were supported by another study by Perrot et al on 1121 patients coming for atrial flutter ablation. They concluded that apart from female gender, history of atrial flutter prior to ablation were independent predictors of recurrence after ablation.^[5]

Regarding congenital heart disease in adults and outcome, females had a better outcome compared to males. They attribute this to the overall protective role of estrogen.^[6] On the other hand, some studies have shown no change in mortality with gender. Though, the incidence of pulmonary hypertension was higher in women, aortic outcomes, endocarditis, arrhythmias and requirement for

automatic implantable cardioverter defibrillator was lower.^[7]

Critical Care

Long back in 1999, Eachempati et al reported female gender as an important risk factor for increased mortality in critically ill patients with documented infection.^[8] The same scenario prevailed even after 10 years of established health care systems.^[9] But in 2010, a study by Akgun et al reported no effect of gender on health care in older medical intensive care patients, as tested by The Therapeutic Intervention Scoring System-28^[10]. Then, there followed a series of mixed results with respect to critical care and outcome. Nachtigall et al reported no difference in the outcome with respect to gender in surgical ICUs. Rather, they reported an increased mortality in female patients with sepsis.^[11] Mahmood et al analyzed 2,61,255 patients and reported decreased mortality in female patients less than 50 years and no difference in mortality after 50 years with respect to gender. With sub-group analysis, females had increased mortality in CABG and decreased mortality in COPD patients. But, no difference in mortality was shown in patients with CAD, sepsis or trauma.^[12] With respect to epidemiology, Sakr et al reported more male admissions compared to females and even the prevalence of sepsis was lower in females. But the incidence of ICU mortality was more with female patients with severe sepsis.^[13] The most current study by Samuelsson et al has not shown any advantage by pre-menopausal females following ICU healthcare. Rather, male patients used more ICU resources compared to females per admission.^[14]

Trauma

Schoeneberg et al studied severely injured patients with matched pair analysis and reported that early mortality was higher in women candidates. With extended hospital stay, survival rate was better in females due to less prevalence of sepsis. But overall mortality rate did not show any significant

difference and there was a falling trend in mortality in females with increasing age.^[15]

Leitgeb et al have not shown any significant difference with gender and outcomes in patients with traumatic brain injury.^[16]

Cardiac Arrest

Karlsson et al analyzed 1667 patients who had out of hospital cardiac arrest and reported that male rather than female gender was associated with survival but did not show any significant difference with neurological outcome. The incidence of adverse events like hypokalemia, hypomagnesemia and blood loss requiring transfusion was more in females whereas pneumonia is common in males.^[17]

Neurosciences

Stroke: Females carry higher risk for poor outcome and early mortality following non traumatic cerebral hemorrhage.^[18]

Parkinson's disease: Females due to the gonadotrophin profile and its effect on the nigrostriatal system, usually have delayed onset of symptoms of Parkinson's disease. And delayed diagnosis is as usual attributed to the low educational status of the population.^[19]

Cerebral Aneurysms

Cerebral aneurysms are more prevalent in older females. But the 3- month outcome following aneurysmal SAH is the same for both men and women.^[20] This is explained by the hormonal influences and variations in aneurysmal wall shear stress. Further, internal carotid artery (ICA) aneurysms are more common in females and anterior cerebral artery (ACA) aneurysms in males. The incidence of multiple aneurysms is more in females.^[21]

Cognition

Women with mild cognitive impairment (MCI) declines twice faster than men with MCI. Women undergoing surgery with general anesthesia declines faster in terms of cognition, brain volume

and functional status when compared to men as reported by Alzhiemers international association in 2015.

Lungs

There is a Strong association between the use of biomass cooking fuels and tuberculosis among women. Results of this study are intended to provide evidence to policy makers, community leaders and the general public on the importance of implementing gender oriented interventions that decrease the use of biomass fuels in poor communities in developing countries^[26]

Vascular Surgery

Overall, there is limited evidence to highlight the differences in outcome based on gender after carotid endarterectomy. Female patients are associated with higher embolic potential and relatively stable plaques which determine the difference in the outcome between male and female patients.^[22] With respect to gender differences and abdominal aortic surgery, females present at an older age. They are symptomatic with smaller AAA diameters and hence, undergo surgery earlier than males. As a result of less favorable vascular anatomy in females, the incidence of perioperative complications was reported high.^[23]

There is a gender disparity in the outcomes of lower extremities peripheral arterial disease .Female gender is an important risk factor that influences the outcomes of vascular interventions; however, these effects vary between different high-risk groups and procedures. Gender effect on mortality dissipates in elderly patients. Prompt recognition of the associations between gender and various risk factors of cardiovascular disease and aggressive modification of these risk factors in female patients may improve gender-related difference in the outcomes of vascular disease.^[24]

Liver

This is an established fact that female patients are more prone to some of the liver diseases,

commonly acute liver failure, autoimmune hepatitis, benign liver lesions, primary biliary cirrhosis, and toxin-mediated hepatotoxicity.^[25]

On the other hand, mortality is increased in men presenting with chronic liver disease and cirrhosis. Though alcoholism is more prevalent in males, alcohol induced liver injury is more severe in female patients with chronic consumption.

A recent meta-analysis reported increased prevalence of non alcoholic fatty liver disease in young males and this increased with increasing body mass index.^[26]

A recent study by Saverio Bell et al has shown that female liver recipients are independent risk factors for graft loss following liver transplantation in chronic HCV patients. The fall in estrogen levels following menopause promotes fibrosis, thus induces graft loss.^[27]

The number of female patients coming for liver transplants has shown a declining trend despite a protocolized approach in selection and planning . Further research is recommended to unearth the shortcomings and increase female awareness for the same.^[28]

Renal

Females display a more passive course of kidney disease. This is attributed to the nephroprotective effects of estradiol by attenuating glomerulosclerosis and tubulo interstitial fibrosis.^[29] But there is no data per se with regards to abdominal surgery and elective neurosurgery.

Another interesting fact to add: Cleanliness is next to God. Generally, clean home and clean surroundings, the credit always goes to female counterparts. This is again proved in one of the studies where washing after patient contact was more frequent with female staff compared to male medical staff in intensive care practice.^[30]

This review of evidence based literature gives us an overall picture of females and their outcome differences in health practice. But we have not included gender differences with pain perception. There is confirmed evidence that if standard living conditions are kept normal for both the sexes,

females have a longer life span compared to males. Though there is no significant difference in the outcome between genders with most of the specialities. Renal disease and some studies have shown a non-virulent course in females and this was attributed to the protective effects of estradiol.

There are some other generalized differences between males and females which may affect the outcome. These are listed as below:

1. Females because of their less capability to enforce for their rights, they are less likely to receive definite treatment options.
2. They have longer waiting times:
 - a) longer door-to-doctor times and
 - b) longer door-to-image times
3. Underestimating or misunderstanding a woman's risk: this is a common problem.
4. The style of description of symptoms: the symptoms are presented in a more narrative way and the emotional aspect is more than the actual presenting symptom; this diverts the attention of the doctor and leading to delay in diagnosing the actual problem per se. This may also be attributed to the specific neural network seen in the female brain.
5. Cultural prejudices: "My son is everything". This is a practical taboo in most of the Indian families. This also leads to undiagnosis or delay in diagnosis. Another great example of social prejudice: in some districts of Nepal, the Achman tribe women are made to sleep in cowsheds, sometimes sharing with cows during the period of menstruation.
6. Even in medical practice, though a good number of workforces in health care practice are females, discrimination towards women still prevails.

7. Nutritional deficiency like iron deficiency is more common in women, especially in developing and underdeveloped countries.
8. Decreased awareness in females, mainly because of low education policies.

Measures to Improve the Outcome

- 1) Improving nutrition of the down trodden females – enhances the immunity and fighting power of females to withstand health problems.
- 2) Life style modifications:
 - a. Exercise
 - b. Healthy living
 - c. Cutting down – smoking, addiction habits
 - d. Dietary restrictions for sugar sweetened carbonated beverages and following healthy eating habits like 6-8 servings of veggie and fruit bowls daily have decreased the coronary calcium score significantly.^[31,32]
- 3) The modifiable risk factors like obesity, smoking, etc. associated with the candidate needs to be identified. Measures should be taken to improve the outcome by targeting these risk factors.
- 4) Awareness of the developing and upcoming health infrastructure like breast screening and PAP smear should be kept in mind. Regular screening and follow up with timely and proper medications will help in improving the outcome.
- 5) Utmost important factor which may contribute for a healthy outcome is female gender per se.

References

1. Kim C, Redberg RF, Pavlic T, Eagle KA. A systematic review of gender differences in mortality after coronary artery bypass graft surgery and percutaneous coronary interventions. *Clin Cardiol* 2007;30:491-5.
2. Lehmkuhl E, Kendel F, Gelbrich G, Dunkel A, Oertelt-Prigione S, Babitsch B,

- et al. Gender-specific predictors of early mortality after coronary artery bypass graft surgery. *Clin Res Cardiol* 2012;101:745-51.
3. Arif R, Farag M, Gertner V, Szabo G, Weymann A, Veres G, et al. Female Gender and Differences in Outcome after Isolated Coronary Artery Bypass Graft Surgery: Does Age Play a Role? *PLoS One* 2016;11:e0145371.
 4. Vallakati A, Reddy M, Alla V, Janga P, Atkins D, Bommana S, et al. IMPACT OF Gender On Outcome After Atrial Fibrillation Ablation: A Meta-Analysis. *J Am Coll Cardiol* 2013;61.
 5. Brembilla-Perrot B, Girerd N, Sellal JM, Olivier A, Manenti V, Villemin T, et al. Risk of atrial fibrillation after atrial flutter ablation: impact of AF history, gender, and antiarrhythmic drug medication. *J Cardiovasc Electrophysiol* 2014;25:813-20.
 6. Zomer AC, Ionescu-Ittu R, Vaartjes I, Pilote L, Mackie AS, Therrien J, et al. Sex differences in hospital mortality in adults with congenital heart disease: the impact of reproductive health. *J Am Coll Cardiol* 2013;62:58-67.
 7. Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, Vliegen HW, et al. Gender and outcome in adult congenital heart disease. *Circulation* 2008;118:26-32.
 8. Eachempati SR, Hydo L, Barie PS. Gender-based differences in outcome in patients with sepsis. *Arch Surg* 1999;134:1342-7.
 9. Combes A, Luyt CE, Trouillet JL, Nieszkowska A, Chastre J. Gender impact on the outcomes of critically ill patients with nosocomial infections. *Crit Care Med* 2009;37:2506-11.
 10. Akgun KM, Murphy TE, Araujo KL, Van Ness PH, Pisani M. Does gender impact intensity of care provided to older medical intensive care unit patients? *Crit Care Res Pract* 2010;2010:404608.
 11. Nachtigall I, Tafelski S, Rothbart A, Kaufner L, Schmidt M, Tamarkin A, et al. Gender-related outcome difference is related to course of sepsis on mixed ICUs: a prospective, observational clinical study. *Crit Care* 2011;15:R151.
 12. Mahmood K, Eldeirawi K, Wahidi MM. Association of gender with outcomes in critically ill patients. *Crit Care* 2012;16:R92.
 13. Sakr Y, Elia C, Mascia L, Barberis B, Cardellino S, Livigni S, et al. The influence of gender on the epidemiology of and outcome from severe sepsis. *Crit Care* 2013;17:R50.
 14. Samuelsson C, Sjoberg F, Karlstrom G, Nolin T, Walther SM. Gender differences in outcome and use of resources do exist in Swedish intensive care, but to no advantage for women of premenopausal age. *Crit Care* 2015;19:129.
 15. Schoeneberg C, Kauther MD, Hussmann B, Keitel J, Schmitz D, Lendemans S. Gender-specific differences in severely injured patients between 2002 and 2011: data analysis with matched-pair analysis. *Crit Care* 2013;17:R277.
 16. Leitgeb J, Mauritz W, Brazinova A, Janciak I, Majdan M, Wilbacher I, et al. Effects of gender on outcomes after traumatic brain injury. *J Trauma* 2011;71:1620-6.
 17. Karlsson V, Dankiewicz J, Nielsen N, Kern KB, Mooney MR, Riker RR, et al. Association of gender to outcome after out-of-hospital cardiac arrest--a report from the International Cardiac Arrest Registry. *Crit Care* 2015;19:182.
 18. Ganti L, Jain A, Yerragonda N, Jain M, Bellolio MF, Gilmore RM, et al. Female Gender Remains an Independent Risk Factor for Poor Outcome after Acute Nontraumatic Intracerebral Hemorrhage.

- Neurology Research International 2013;2013:219097.
19. Martínez-Rumayor A, Arrieta O, Sotelo J, García E. Female gender but not cigarette smoking delays the onset of Parkinson's disease. *Clinical neurology and neurosurgery* 2009;111:738-41.
 20. Kongable GL, Lanzino G, Germanson TP, Truskowski LL, Alves WM, Torner JC, et al. Gender-related differences in aneurysmal subarachnoid hemorrhage. *J Neurosurg* 1996;84:43-8.
 21. Ghods AJ, Lopes D, Chen M. Gender differences in cerebral aneurysm location. *Front Neurol* 2012;3:78.
 22. den Hartog AG, Algra A, Moll FL, de Borst GJ. Mechanisms of gender-related outcome differences after carotid endarterectomy. *J Vasc Surg* 2010;52:1062-71, 71 e1-6.
 23. Szmuda T, Sloniewski P, Baczalska A, Cabala M, Czapski B, Gorczynski A, et al. The pneumatization of anterior clinoid process is not associated with any predictors that might be recognised preoperatively. *Folia Morphol (Warsz)* 2013;72:100-6.
 24. Vouyouka AG, Egorova NN, Salloum A, Kleinman L, Marin M, Faries PL, et al. Lessons learned from the analysis of gender effect on risk factors and procedural outcomes of lower extremity arterial disease. *J Vasc Surg*;52:1196-202.
 25. Guy J, Peters MG. Liver disease in women: the influence of gender on epidemiology, natural history, and patient outcomes. *Gastroenterol Hepatol (N Y)* 2013;9:633-9.
 26. Anderson EL, Howe LD, Jones HE, Higgins JP, Lawlor DA, Fraser A. The Prevalence of Non-Alcoholic Fatty Liver Disease in Children and Adolescents: A Systematic Review and Meta-Analysis. *PLoS One* 2015;10:e0140908.
 27. Belli LS, Romagnoli R, Nardi A, Marianelli T, Donato F, Corradini SG, et al. Recipient female gender is a risk factor for graft loss after liver transplantation for chronic hepatitis C: Evidence from the prospective Liver Match cohort. *Dig Liver Dis* 2015;47:689-94.
 28. Oloruntoba OO, Moylan CA. Gender-based disparities in access to and outcomes of liver transplantation. *World J Hepatol* 2015;7:460-7.
 29. Silbiger SR. Raging hormones: gender and renal disease. *Kidney Int* 2011;79:382-4.
 30. van de Mortel T, Bourke R, McLoughlin J, Nonu M, Reis M. Gender influences handwashing rates in the critical care unit. *Am J Infect Control* 2001;29:395-9.
 31. Chun S, Choi Y, Chang Y, Cho J, Zhang Y, Rampal S, et al. Sugar-sweetened carbonated beverage consumption and coronary artery calcification in asymptomatic men and women. *Am Heart J* 2016;177:17-24.
 32. Miedema MD, Petrone A, Shikany JM, Greenland P, Lewis CE, Pletcher MJ, et al. Association of Fruit and Vegetable Consumption During Early Adulthood With the Prevalence of Coronary Artery Calcium After 20 Years of Follow-Up: The Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Circulation* 2015;132:1990-8.