



## From the Editor

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This is a special double issue this year that is rich with research papers from the region.

There is one particular paper of interested which is the result of regional collaboration of Middle East Primary Care Network MEPCRN. The MEPCRN paper's aim was to determine the prevalence of burnout, and of associated factors, amongst family doctors (FDs) in the Middle East. Methodology. A cross-sectional survey of FDs was conducted using a custom-designed and validated questionnaire which incorporated the Maslach Burnout Inventory Human Services Survey (MBI-HSS) as well as questions about demographic factors, working experience, health, lifestyle and job satisfaction. MBI-HSS scores were analysed in the three dimensions of emotional exhaustion (EE), depersonalization (DP) and personal accomplishment (PA). Seven hundreds questionnaires were distributed in 5 Middle Eastern countries, and 500 were returned to give a response rate of 71%. As far as burnout, 44% of respondents scored high for EE burnout, 30% for DP and 28% for PA, with 15% scoring high burnout in each of the three measurements. A little more than 33% of doctors did not score high for burnout in any dimension. High burnout was observed to be emphatically connected with a few of the variables under concentrate, particularly those relative to respondents' nation of home, occupation fulfillment, expectation to change work, sick leave usage, the misuse of liquor, tobacco and psychotropic medication, more youthful age and male sex. The authors concluded that burnout is by all accounts a typical issue in FDs over the Middle East and is connected with individual and workload pointers, and particularly work fulfillment, aim to change work and the abuse of liquor, tobacco and medicine. The study survey has all the earmarks of being a substantial instrument to quantify burnout in FDs. Proposals for changes of employment conditions and future research are needed for further exploring the issue.

A paper from Saudi Arabia tried to estimate the prevalence of Diabetic Retinopathy among Newly Diagnosed Type 2 Diabetes Mellitus Patients in Abha City, Saudi Arabia. All newly diagnosed diabetic type 2 patients attending primary health care centers in Abha during the period of study (39 PHCCs) were referred to ophthalmology department in Abha General Hospital for diabetic retinopathy screening until the required sample size was reached. The study included 393 newly diagnosed type 2 diabetic patients. Their age ranged between 21 and 96 years with a mean of 52.9 and standard deviation of 11.8 years. Female patients represent (242)61.6% of them. The prevalence of diabetic retinopathy among newly diagnosed type 2 diabetic patients was (13)3.3%. All of DR cases were classified using Friedman's standards as background or non-proliferative diabetic retinopathy. The authors concluded that the prevalence of retinopathy in newly diagnosed type 2 diabetes mellitus patients was found to be relatively low in this study compared to international studies.

A paper from Riyadh studied the effect of different concentrations of ginger and its extracts on kidney functions and glucose in rats. Six weeks Wister Albino rats divided in to six groups each had ten rats: control group (C), diabetic group (DC), while other groups were fed by addition of ginger Freeze-dried or extract concentration (0.5% - 2%) respectively (DGL, DGH, DGEL, DGEH). Diabetes was induced by an intraperitoneal injection of streptozotocin (50 mg/kg of body weight) The results showed that DGH, DGEL and DGEH groups had less weight than the two control (C, DC) groups. The DGEL and DGEH group showed statistically lowered food intake compared with the C and DC group. Ginger and its extracts caused an increase in glucose level. With regard nitrogen blood urea (NBU) and urea, the DGL, DGEL and DGEH groups had no significant differences when compared with the C and DC groups. With regard to creatinine and uric acid there were no significant differences among all groups. This study recommends intake of the low dose of ginger (0.5%) and the high dose of the ginger extract (2%) for improvement of the kidney tissue of diabetic patients.

A paper from Yemen evaluated the prevalence of metabolic syndrome in Yemeni patients with hypothyroidism. A total of 350 patients with past history or newly diagnosed hypothyroidism (diagnosed as having high TSH, and or low FT4 and FT3) (patients group) and 100 healthy euthyroid volunteers as (control group) attending the outpatients medical clinics at Al-Kuwait University hospital in Sana'a city. The patients and control groups were under go complete history and clinical examination included measurement of blood pressure and waist circumference. Among these patients 233 (66.6%) of hypothyroid patients had subclinical and 117(33.4%) had overt hypothyroidism. MS was significantly higher

in hypothyroid (37.4%), (76.3%) in patients with subclinical and 31 (23.6%) in patients with overt hypothyroidism, than in euthyroid group (17%). The commonest occurring metabolic syndrome defined criterion in hypothyroid patients was central obesity 89(67.9%), high blood pressure 88 (67.1%), reduced high density lipoprotein (61%), high serum triglyceride (59.5%) and raised fasting blood glucose (54.9%). The authors concluded that prevalence of MS is high among Yemeni patients with hypothyroidism and central obesity was the commonest co-morbidity. These findings highlight an urgent need to develop strategies for prevention, detection, and treatment of MS that could contribute to decreasing the prevalence of cardiovascular morbidity and mortality in hypothyroid patients.

A review paper from Pakistan looked at the Prevalence and determinants of Unintended Pregnancy. A range of electronic databases was searched for studies conducted in developing countries and published between 1990 and 2015. English-language publications were searched using relevant keywords, and reference lists were hand searched. A systematic review was carried out for all the quantitative studies which met the inclusion criteria. The quality of selected studies was assessed using Newcastle-Ottawa Scale. Twenty-two papers were included in the review. Average prevalence of unintended pregnancy was estimated to be 35% ranging from 13% to 82%. The predictors of unintended pregnancy were found to be, socio-demographic factors include women's age, women's education, parity, birth order and interval, previous pregnancy intention, age at the time of marriage, socioeconomic status, marital status, religion, caste, and ethnicity. The authors concluded that the main correlates were found to be age, parity, educational and economic status. This means that undertaking outreach in poor countries might be helpful in fulfilling the needs of Family planning for these women. Furthermore, community-based distribution of family planning methods or counseling should be targeted to the illiterate older aged women of reproductive age with poor socioeconomic status.

In the special education section, a surgical education on anal abscess and fistula focused on the general practitioner approach in term of diagnosis, office surgery, when to refer, and what underlying conditions to look for.

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# Frequency of Job-Related Burn-out in Family Physicians working in General / Family Practice in the Middle East

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## Abstract

**Introduction:** The aim of this study was to determine the prevalence of burnout, and of associated factors, amongst family doctors (FDs) in the Middle East.

**Methodology:** A cross-sectional survey of FDs was conducted using a custom-designed and validated questionnaire which incorporated the Maslach Burnout Inventory Human Services Survey (MBI-HSS) as well as questions about demographic factors, working experience, health, lifestyle and job satisfaction. MBI-HSS scores were analysed in the three dimensions of emotional exhaustion (EE), depersonalization (DP) and personal accomplishment (PA).

**Results:** Seven hundred questionnaires were distributed in 5 Middle Eastern countries, and 500 were returned to give a response rate of 71%. As far as burnout, 44% of respondents scored high for EE burnout, 30% for DP and 28% for PA, with 15% scoring high burnout in each of the three measurements. A little more than 33% of doctors did

not score high for burnout in any dimension. High burnout was observed to be emphatically connected with a few of the variables under concentrate, particularly those relative to respondents' nation of home, occupation fulfillment, expectation to change work, sick leave usage, the misuse of liquor, tobacco and psychotropic medication, more youthful age and male sex.

**Conclusions:** Burnout is by all accounts a typical issue in FDs over the Middle East and is connected with individual and workload pointers, and particularly work fulfillment, aim to change work and the abuse of liquor, tobacco and medicine. The study survey has all the earmarks of being a substantial instrument to quantify burnout in FDs. Proposals for changes of employment conditions and future research are needed for further exploring the issue.

**Key words:** Burnout, Middle East, general practice, job satisfaction.

## Background

The practice of medicine is inherently stressful. Physicians must continuously respond to the needs of patients and their families, routinely interact with the most intense emotional aspects of life and expend their own emotional resources to provide care and caring to others. Each day, physicians are called on to cope and adapt with stresses characteristic of their role. Extensive 'withdrawals' from emotional reserves are required, while emotional 'deposits' may be infrequent and few. For some, each day becomes increasingly more difficult as coping mechanisms prove inadequate and emotional reserves become depleted (1).

Burnout is generally characterized as loss of eagerness for work, sentiments of negativity, and a low feeling of individual achievement. There have been inquiries concerning the utilization of these criteria, in any case. Burnout is a reaction to chronic, job-related stress. It is an emotional state that may be accompanied by a number of physical and behavioural changes. It is a construct used to describe negative changes in the attitudes, moods, and behaviours of individuals in reaction to stresses at work. The sources of burnout in physicians are maladaptive coping habits, which are fostered by the medical training system. Postgraduate training in medicine involves long hours, excessive workloads, sleep deprivation, changing working conditions, peer competition, self-denial, and social isolation from the 'real world' (2).

Those physicians who manage to survive their training years find that their expectations often do not conform to reality. Instead of the ideal life they envisioned, they find numerous new sources of stress waiting for them. Many arrive at this point with their sense of self-worth completely tied to their productivity. A growing practice would seem to be a sign of success and gratification but may actually require a physician having to work faster and longer to meet demands. Under these conditions, the practice may become routine and tedious. The rapidly increasing body of medical knowledge and technology make it difficult to keep up to date, and there is an increasing pressure to focus on the disease rather than the patient (3).

It is estimated that between 30-40% of physicians suffer from burnout at a level sufficient to affect their personal or professional performance. Prevalence rates for depression and stress (anxiety and burnout) have been reported for British general practitioners, Canadian and American emergency room physicians, American Internists, American family practice residents, Spanish and Canadian general practitioners (4).

A national overview distributed in the Archives of Internal Medicine in 2012 reported that US doctors endure more burnout than other American workers (5). This year, in the Medscape Physician Lifestyle Report, 46% of all doctors reacted that they had burnout, which is a generous increment since the Medscape 2013 Lifestyle Report, in which burnout was accounted for in marginally under 40%

of respondents.. A few studies have recommended that a low feeling of individual achievement is not connected with burnout, in any event in men (6,7).

In other studies , essentially including the statements "I feel burned out from my work" and "I have become more callous toward people since I took this job" appears to be a valid method for measuring burnout (8, 9). Given the vagueness in characterizing and measuring burnout, the criteria utilized as a part of the Medscape review to survey burnout in our doctor individuals give helpful data on the present condition of doctor morale which, tragically, is low.

An article distributed in the Journal of General Internal Medicine reported burnout rates running from 30% to 65% across specialties, with the most elevated rates brought about by doctors at the front of care, such as, emergency medicine and primary care (10). The 2015 Medscape study results mirror this same example, with the most elevated burnout rates found in critical care (53%) and emergency medicine (52%), and with half of all family doctors, internists, and general surgeons reporting burnout. Of considerably more worry, among internists and family doctors who reacted to the Medscape overview, burnout rates ascended from around 43% in 2013 to half in both gatherings, a flat out expansion of 7% however a 16% ascent in frequency in only 2 years. In a year ago's Medscape Physician Compensation Report, family doctors and internists were two of the specialties most likely to say they would choose medicine again, but also two of the specialties most likely to say they would not choose their own specialty again.

Other studies have demonstrated that the pervasiveness of burnout in essential consideration doctors (PCPs) has expanded over the earlier decade in the United States as well as in Europe (7, 11). The minimum worn out doctors as indicated by our study are dermatologists (37%), therapists (38%), and pathologists (39%). As far as we can tell no one has yet documented rates of burnout in general practice in the Middle East.

## Aims and Objectives

Burnout can be prevented by psychological or social interventions. The aim of this study is to quantify burnout in Middle-Eastern FPs/GPs (Family Doctors/General Practitioners), and try to identify factors which predict burnout in the study population.

### Objectives

The objective of this study is to perform a survey of burnout in General Practice/Family Medicine, with the participation of Middle-Eastern FPs/GPs. We may then investigate the frequency of burnout in FPs/GPs and to identify risk factors contributing to the development of such burnout.

## Study population - Methods - Research Plan

Randomly assigned FPs/GPs from participant countries were asked to participate in this study. The randomisation and sample selection process was co-ordinated by a key FP/GP in each Country, selected from the participants of project meeting, or their delegates. Each Country was expected to provide up to 100 completed questionnaires to the co-ordinating doctors (authors) for analysis.

Participating doctors were asked to complete a questionnaire that had two parts, and which had been piloted successfully and validated (12) (Table 1):

Part one was a self-prepared questionnaire with questions about demographic information, with questions on working place, working tenure, training, workload, remuneration, job satisfaction, alcohol consumption, smoking, use of psychoactive medication, sick leave, etc.

Part two was the Maslach Burnout Inventory, Human Services Survey, a conceptualization of burnout as a syndrome characterized by three dimensions: emotional exhaustion, depersonalization and decreased sense of personal accomplishment (13), and Part three was a seven-point Likert type satisfaction questionnaire.

In those Countries where the use of an English-language instrument may have posed a barrier, the questionnaire was translated to the native language by the key co-ordinating FP/GP in that Country. The translation process was validated by cross translation.

## Data collection and Statistical Analysis

The country co-ordinators, one lead FD in each of 5 participating countries were responsible to send the questionnaire to a representative sample of their country's FDs. The original target was a sample size of 100 completed questionnaires from each country. Each country co-ordinator coded the data from the returned questionnaires into a custom-designed Microsoft Excel spreadsheet template, and these were then imported into SPSS version 17 by the coordinator of the study.

Scores were output in the three dimensions of burnout and were then transformed into dummy categorical variables for high, average and low burnout in the dimensions of emotional exhaustion (EE), depersonalization (DP), and Personal Accomplishment (PA) as recommended by Maslach using the cutoff values applicable for doctors (13). However, the burnout outcome variables were recoded into high and not-high (average or low burnout) for the statistical analyses.

EE: low burnout < 13, average burnout 14-26, high burnout > 27 (The scoring guide actually recommends that average scores for EE range from 19 to 26. Scores in the range from 14 to 18 are thus difficult to classify. For the purposes of the description of rates of burnout found in this

study, EE scores in the range of 14 to 18 were classified as average, to avoid unclassified cases. However, all the statistical analyses performed on the data set used the outcome variable of high as against not high burnout in the three dimensions.)

**DP:**

low burnout < 5, average burnout 6-9, high burnout > 10.

**PA:**

high burnout < 33, average burnout 34-39, low burnout > 40 (inverse scale).

## Results

A total of 500 completed questionnaires were returned from more than 700 sent giving a response rate of approximately 71%. Among the 500 respondents (270 males, 54 %) had a mean age of 47.4 years (SD 6.5 years) and had graduated 15 years previously to filling in the questionnaire (SD 7.5 years), worked 42 hours per week (SD 10 hours), saw 170 patients per week (SD 63 patients) and were roughly evenly distributed amongst the 5 countries

(See Table 2, page 9)

On the job satisfaction questions on Likert scale 6% of the sample have very low satisfaction and only 11% are highly satisfied with their jobs.

Table 3 (page 9) lists the frequency distributions of respondents by degree of burnout (high, average or low) in the three dimensions (EE, DP, PA). Table 4 gives the frequency distribution of respondents by presence of high burnout scores in none (0), one or more of the three dimensions (1, 2 or 3). In all, 44% of respondents scored high for EE (95% CI = 41.5-45.0%), 30 % for high DP (28.2-34.9%), 28.0% low for PA (26.6-32.3%). In Table 4 (page 9) 15% of respondents (13.3-17.1%) scored high for burnout in all three dimensions. Only 34.6 % of doctors (32.1-38.6 %) did not score high for burnout in any dimension.

Iraq and Lebanon scored the highest in term burnout score in each of the three dimensions followed by Iran, Saudi Arabia and Kuwait. Lebanese and Iranian respondents demonstrated high proportions of high EE burnout, Iraqi and Kuwaiti respondents demonstrated high proportions of high DP burnout, whilst Saudi respondents demonstrated high proportions of high PA burnout.

When looking at the factors associated with high burnout the strongest associations using both logistic regression and included job satisfaction and intention to change job, the (ab) use of tobacco, alcohol and psychotropic drugs, male sex, age, type of work and sick leave utilization.

Table 1

## PART 1

**Human services survey**

The information you record in this questionnaire will be treated with extreme confidentiality. Your identity will be unknown to us. Please answer all questions as truthfully as you can. Please only complete this questionnaire if you are a full-time general practitioner or family doctor, working either in state employment (including academic or educational work) or private practice, or both. Please do not return this questionnaire if you work 50% or more of your time in another specialty besides general practice or family medicine, or if you are presently retired.

*Thank you for your time.*

Age: \_\_\_\_\_

Sex: \_\_\_\_\_

Marital status: \_\_\_\_\_ (married, single, divorced/separated, widowed)

Number of children: \_\_\_\_\_ (number under 5 years of age: \_\_\_\_\_)

Years since qualification as M.D.: \_\_\_\_\_ Years in current position / workplace: \_\_\_\_\_

Further qualifications: \_\_\_\_\_

Type of work: (please tick all that apply)

State-employed  private practice  education/academic

currently in training

other (e.g. occupational health physician) – please specify \_\_\_\_\_

Do you work solo or in a group setting? \_\_\_\_\_ (solo/group)

Is your practice mainly rural or urban? \_\_\_\_\_ rural \_\_\_\_\_ urban \_\_\_\_\_ mixed

How much do you earn a month from all your GP/FM work, approximately?

Euro \_\_\_\_\_

How many patients do you see in one week, on average? \_\_\_\_\_

How many hours do you work in one week, on average? \_\_\_\_\_

How many hours a day do you sleep, on average?

\_\_\_\_\_ (> or = 8) \_\_\_\_\_ (> 4 but < 8) \_\_\_\_\_ (< or = 4)

Do you do night visits, or work night shifts (after 8 pm, before 6 am)? \_\_\_\_\_ (Y/N)

If you do work at night, how many nights a month you do work on average? \_\_\_\_\_

Do you work on the weekend, or work weekend shifts? \_\_\_\_\_ (Y/N)

If you do work on the weekend, how many weekends a year are you off? \_\_\_\_\_

How many days were you off work on sick leave last year? \_\_\_\_\_

Have you seriously considered changing your job at least once over the past months? \_\_\_\_\_ yes \_\_\_\_\_ no

\_\_\_\_\_ undecided

How satisfied are you with your current job? (0 = very little, to 6 = very much) \_\_\_\_\_

Do you smoke tobacco regularly? \_\_\_\_\_ (Y/N)

Has your consumption of tobacco increased during the last year? \_\_\_\_\_ (Y/N)

Do you drink alcohol regularly? \_\_\_\_\_ (Y/N)

Has your consumption of alcohol increased during the last year? \_\_\_\_\_ (Y/N)

Have you taken psychoactive medication in the last year? \_\_\_\_\_ (Y/N)

## PART 2

Please reply to each question below with a score from 0 to 6 (one choice only per question).

The meaning of the scores are explained below:

0 = never,

1 = a few times a year or less frequently,

2 = once a month or less frequently,

3 = a few times a month,

4 = once a week,

5 = a few times a week,

6 = every day

1. I feel emotionally drained from work

Score =

2. I feel used up at the end of the workday

Score =

3. I feel fatigued when I get up in the morning and have to face another day on the job

Score =

4. I can easily understand how my patients feel about things

Score =

5. I feel I treat some patients as if they were impersonal objects

Score =

6. Working with people all day is really a strain for me

Score =

7. I deal very effectively with the problems of my patients

Score =

8. I feel burned out from my work

Score =

9. I feel I am positively influencing other people's lives through my work

Score =

10. I have become more callous towards people since I took this job

Score =

11. I worry that this job is hardening me emotionally

Score =

12. I feel very energetic

Score =

13. I feel frustrated by my job

Score =

14. I feel that I am working too hard on my job

Score =

15. I do not really care what happens to some patients

Score =

16. Working with people directly puts too much stress on me

Score =

17. I can easily create a relaxed atmosphere with my patients

Score =

18. I feel exhilarated after working closely with my patients

Score =

19. I have accomplished many worthwhile things in this job

Score =

20. I feel like I am at the end of my rope

Score =

21. In my work I deal with emotional problems very calmly

Score =

22. I feel patients blame me for some of their problems

Score =

*Thank you for your time.*

Table 2: Job Satisfaction on Likert Scale

Job Satisfaction	Frequency	Percentage
1 (Low)	30	6
2	50	10
3	105	21
4	150	30
5	110	22
6 (High)	55	11

Table 3: Frequency and cumulative frequency distributions of respondents by degree of burnout (high, average and low) with 95% CI in each of the three dimensions

Burnout	EE (n = 500)	% (95% CI)	DP (n =500)	% (95% CI)	PA (n = 500)	% (95% CI)
High	220	44.0 (41.5–45.0)	150	30.0 (28.2–34.9)	144	28.0 (26.6–32.3)
Medium	200	40.0 (36.5–43.6)	160	32.0 (29.9–33.1)	156	31.0 (26.1–30.2)
Low	80	16.0 (14.1–18.0)	190	38.0 (35.0–40.0)	200	40.0 (37.0–42.0)

Table 4: Frequency and cumulative frequency distributions of respondents by high burnout score in none (0) or any one, any two or all three dimensions (1, 2 or 3) with 95% CI

High Burnout	N=500	% (95% CI)
No Dimension	173	34.6 (32.1-38.6)
One Dimension	162	32.4 (28.1-34.7)
Two Dimension	90	18.0 (17.1-20.2)
All Three Dimensions	75	15.0 (13.3-17.1)

## Discussion

In rundown, MEPCRN investigation of burnout among family doctors in 5 Middle Eastern Countries with an approved instrument to gauge burnout accomplished a response rate of 71%. Taking all things together, 44% of respondents scored high for EE burnout, 30% scored high for DP burnout and 28% scored high for PA burnout. Just 34.6% of respondents did not score high for burnout in any measurement, whilst 21% scored high for burnout in no less than two measurements and 15% scored high for each of the three. In the wake of controlling for nation, low occupation fulfillment, communicated goal to change work, abuse of liquor, tobacco and psychotropic medication, sick leave usage, more youthful age, male sex and kind of work were connected with high burnout, as beforehand reported.(1)

Some prior studies reported lower rates of burnout, yet a comparable number of late studies reported comparable information (14,15,16,17-21). Not surprisingly, high burnout was more probable with low occupation fulfillment and

goal to change job (1, 15,22). Additionally,(1,3,4,14,22) elevated amounts of burnout were observed to be more probable with certain organizational elements (nation of root, as surrogate for health services framework, and kind of work) and increased sick leave use, and less so with high workload (patients per week and hours per week) and other employment stressors (pulling all nighters and weekends). Individual variables, for example, more youthful age, sex, conjugal status and number of youngsters were likewise connected with burnout, yet male sex all the more unequivocally so (1,22).

Scholastic work sort was connected to lower EE, however higher PA burnout, as beforehand reported (1). Low self-regard has been already answered to be connected with burnout.(1) In this study, we watched that burnout was more probable with expanding smoking, expanded utilization of liquor and utilization of psychotropic drug, which might be indications of low self-regard (15). Different variables, for example, salary, were shockingly rather feebly connected with high burnout, whilst others (non-scholastic kind of work, years since graduation, not

having further capabilities, expanding smoking) appeared to be connected with high EE burnout, yet make high PA burnout more outlandish; be that as it may, such vague discoveries have been beforehand depicted in burnout research in specialists, for instance, by Deckard et al. (4) Generally, the example of related variables seems like that reported by Goehring et al.(8) for those variables which were incorporated into both studies.

This is the initially reported study exploring the pervasiveness of burnout among Family Physicians in the Middle East, planned to look at the variables connected with high burnout. The constraints of this study incorporate the way that it is cross-sectional, that it has not been led simultaneously in all nations, that the study included FDs in different nations and working in various social insurance and healthcare frameworks without measuring the multifaceted nature of this environment. The burnout scores discovered seemed practically identical or high concerning prior studies.

## Conclusion

Burnout is by all accounts a typical issue in FDs crosswise over the Middle East, with high levels obviously influencing 66% of respondents in this study. Taking all things together, 44% of respondents reported abnormal amounts of EE, 30% DP and 28% low sentiments of PA. There is extensive variation between nations. High burnout was observed to be more probable in relationship with a few of the variables under study, especially those in respect to respondents' nation of living, work fulfillment, intention to change work, sick leave usage, the misuse of liquor, tobacco and psychotropic prescription, younger age and male sex.

Future examination is expected to investigate the issue top to bottom, create models to portray the marvel and to recognize causative elements and compelling between intervention methodologies. Work fulfillment is an essential element in such research, and it ought to be prioritized by MEPCRN as a potential for further work and research.

Late research dealing with burnout expects to grow new hypothetical structures that expressly coordinate both individual and situational elements, utilizing a model of job-person fit. Maslach and Leiter (30) address the test by defining a model that spotlights on the degree of match or befuddle between the individual and six spaces of the employment environment, specifically workload, control, reward, community, fairness and values. Re-look has shown that the more noteworthy the confounder, the more noteworthy the potential for burnout.

Future studies ought to address these elements when examining burnout in FDs, and the attention ought to be on positive as opposed to negative states, managing work engagement and fulfillment and not simply work stress.(1) In such manner, the solid relationships found in this study between low employment satisfaction and burnout support the thought of centering future examination on enhancing work fulfillment instead of tending to burnout straightforwardly.

Shockingly, little research has been led into mediations for burnout. In spite of the fact that examination demonstrates that it is the organizational attributes that appear to have more grounded relationship with burnout; generally intercessions have in the past incidentally been fixated on changing individuals (1). Various mediation methodologies have been concentrated, some concentrating on aversion of burnout and others on treatment when it has as of now happened, and results have been varied (1). This is another essential area where our knowledge is lacking.

## References

1. Deckard GJ, Hicks LL & Hamory BH (1992). The occurrence and distribution of burnout among infectious disease physicians. *JID*. 165:224-8.
2. Fawzy IF, Fawzy NW & Pasnau R (1991). Burnout in the health professions. In: *Handbook of studies on general hospital psychiatry*. Judd, Burrows, Lipsitt (Ed). NewYork. Elsevier Science Publishers. pp.119-130.
3. Deckard G, Meterko M & Field D (1994). Physician Burnout: An examination of personal, professional, and organisational relationship. *Med Care*. 32:745-754.
4. Thommasen HV, Lavanchy M, Connelly I, Berkowitz J. Mental health, job satisfaction, and intention to relocate-opinions of physicians in rural British Columbia. *Can Fam Physician* 2001;47:737-744.
5. Shanafelt TD, Boone S, Tan L, et al. Burnout and satisfaction with work-life balance among US physicians relative to the general US population. *Arch Intern Med*. 2012;172:1377-1385. <http://archinte.jamanetwork.com/article.aspx?articleid=1351351> Accessed December 1, 2014
6. Ludwig DS, Kabat-Zinn J. Mindfulness in medicine. *JAMA*. 2008;300:1350-1352. Abstract
7. Houkes I, Winants Y, Twellaar M, Verdonk P. Development of burnout over time and the causal order of the three dimensions of burnout among male and female GPs. A three-wave panel study. *BMC Public Health*. 2011;11:240. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3101180/> Accessed December 3, 2014.
8. West CP, Dyrbye LN, Satele DV, Sloan JA, Shanafelt TD. Concurrent validity of single-item measures of emotional exhaustion and depersonalization in burnout assessment. *J Gen Intern Med*. 2012;27:1445-1452. <http://link.springer.com/article/10.1007%2Fs11606-012-2015-7> Accessed December 10, 2014.
9. Dolan ED1, Mohr D, Lempa M, Joos S, Fihn SD, Nelson KM, Helfrich CD. Using a single item to measure burnout in primary care staff: a psychometric evaluation. *J Gen Intern Med*. 2014 Dec 2. [Epub ahead of print]
10. Linzer M, Levine R, Meltzer D, Poplau S, Warde C, West CP. 10 bold steps to prevent burnout in general internal medicine. *J Gen Intern Med*. 2014;29:18-20. <http://link.springer.com/article/10.1007/s11606-013-2597-8/fulltext.html> Accessed December 1, 2014.
11. Twellaar M, Winants Y, Houkes I. How healthy are Dutch general practitioners? Self-reported (mental) health among Dutch general practitioners. *Eur J Gen Pract*. 2008;14:4-9. Abstract

12. Yaman H, Soler JK. The job related burnout questionnaire. A multinational pilot study. *Australian Family Physician* 2002. 31: 1055-6.
13. Maslach C., & Jackson S.E. (1986). *Maslach Burnout Inventory*. 2nd ed. Pal Alto: Consulting Psychologists Press.
14. Goehring C, Bouvier Gallacchi M, Ku" nzi B, Bovier P. Psychological and professional characteristics of burnout in Swiss primary care practitioners: a cross-sectional survey. *Swiss Med Wkly*. 2005; 135: 101-108.
15. Thommasen HV, Lavanchy M, Connelly I, Berkowitz J, Grzybowski S. Mental health, job satisfaction and intention to relocate. *Can Fam Physician* 2001; B47: 737-744.
16. Yaman H, Soler JK. The job-related burnout questionnaire in family practice: a multinational pilot study. *Aust Fam Physician*. 2002; 31: 1055-1056.
17. Cathebras P, Begon A, Laporte S, Bois C, Truchot D. Burn out among French general practitioners. *Presse Med*. 2004; 33:1569-1574.
18. Prieto Albino L, Robles Aguero E, Salazar Martinez LM, Daniel Vega E. Burnout in primary care doctors of the province of Ca- ceres. *Aten Primaria*. 2002; 29: 294-302.
19. Esteva M, Larraz C, Jimenez F. La salud mental en los me` dicos de familia: efectos de la satisfaccio` n y el estre`s en el trabajo. *Rev Clin Esp*. 2006; 206: 77-83.
20. Grassi L, Magnani K. Psychiatric morbidity and burnout in the medical profession: an Italian study of general practitioners and hospital physicians. *Psychother Psychosom*. 2000; 69:329-334.
21. Kirwan M, Armstrong D. Investigation of burnout in a sample of British general practitioners. *Br J Gen Pract*. 1995; 45: 259-260.
22. Linzer M, Visser MRM, Oort FJ, et al. Predicting and preventing physician burnout: results from the United States and the Neth- erlands. *Am J Med*. 2001; 111: 170-175.

# Effect of Ginger and its Extract on Blood Sugar and on Kidney Function of Type I Diabetic Rats

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## Abstract

Diabetes is one of the high-risk diseases; one of its complications is nephropathy. This can be reduced by eating some foods. The goal of this study was to study the effect of different concentrations of ginger and its extracts on kidney functions and glucose in rats (2010-2011) at King Saud University in Riyadh. Six weeks Wister Albino rats were divided into six groups each of ten rats: control group (C), diabetic group (DC), while other groups were fed by addition of ginger Freeze-dried or extract concentration (0.5% - 2%) respectively (DGL, DGH, DGEL, DGEH). Diabetes was induced by an intraperitoneal injection of streptozotocin (50 mg/kg of body weight). The results showed that DGH, DGEL and DGEH groups had less weight than the two control (C, DC) groups. The DGEL and DGEH group showed statistically lowered food intake compared with the C and DC group. Ginger and its extracts caused an increase in glucose level. With regard to nitrogen blood urea (NBU) and urea, the DGL, DGEL and DGEH groups had no significant differences when compared with the C and DC groups. With regard to creatinine and uric acid there were no significant differences among all groups. This study recommends intake of the low dose of ginger (0.5%) and the high dose of the ginger extract (2%) for improvement of the kidney tissue of diabetic patients.

**Key words:** diabetes, rats, ginger, ginger extract, glucose, kidney function, kidney tissue.

## Introduction

Diabetes causes many complications with the highest kidney failure caused by sorbitol accumulation in the kidney. The sorbitol is produced by enzyme aldose reductase and the sorbitol is converted to fructose by sorbitol dehydrogenase.

This enzyme is absent in the kidney tissue when the glucose level becomes high and aldose reductase sufficient so that the sorbitol becomes high and accumulates in kidney and causes kidney failure (5).

The high blood glucose in the blood leads to elevation of sorbitol which is one of the causes of kidney failure in the diabetic patient. We have to study some kinds of food like ginger which might affect kidney function and tissues. The research goals are: Study the effect of fresh ginger and its extract (zingeron) on the body weight and food intake. Study the effect of fresh ginger and its extract (zingeron) on the blood sugar in the diabetic rats type one; Study the effect of fresh ginger and its extract (zingeron) on the function of kidney and tissue in type one diabetic rats.

## Ingredients of diet (g/1000g for diet)

Ingredient	g/kg DGEH	g/kg DGEL	g/kg DGH	g/kg DGL	g/kg DC	g/kg C
Casein, High Nitrogen	200	200	200	200	200	200
L-Cystine	3	3	3	3	3	3
Sucrose	100	100	100	100	100	100
Cornstarch	377.486	392.486	377.486	392.486	397.486	397.486
Dyetrose	132	132	132	132	132	132
Soybean Oil	70	70	70	70	70	70
t-Butylhydroquinone	0.014	0.014	0.014	0.014	0.014	0.014
Cellulose	50	50	50	50	50	50
Mineral Mix #210025	35	35	35	35	35	35
Vitamin Mix #310025	10	10	10	10	10	10
Choline Bitartrate	2.5	2.5	2.5	2.5	2.5	2.5
Ginger	-	-	20	5	-	-
Ginger extracted	20	5	-	-	-	-
	1000	1000	1000	1000	1000	1000

## Materials and Research Methods

We used 60 adult rats type Wister albino, average weight  $185 \pm 30$  g, divided into two groups. One control group had ten rats the (C) the other one had fifty rats injected with streptozotocin to make them diabetic rat type one (magnitude 50mg/kg by body weight). All experimental procedures and protocols in this study including euthanasia were conducted in accordance with the National Institute of health guide for the care and use of laboratory animals, Institute for laboratory animal research (NIH publications No80-23; 1996) as well as the ethical guidelines of the experimental animal care center, college of Medicine, King Saud university, Riyadh, Saudi Arabia. The diabetic group was divided into five groups, each one had ten rats. The second diabetic group (DC), the third one diabetic and ate 0.5% ginger in diet (DGL), the fourth one diabetic and ate 2% ginger in diet (DGH), the fifth one diabetic and ate

0.5% ginger extract (zingeron) in diet (DGEL), the sixth one diabetic and ate 2% ginger extract(zingeron) in diet (DGEH). At the end of the six weeks of experiment the rats were fasted and anesthetized to pull the blood and the kidney was saved in formalin to study the tissues. The glucose was measured by fluorometric enzymatic analysis (15) and the kidney function urea by (7), creatinine (7), uric acid (4). We used spectrophotometer model Ultrospec 2100 pro from (Amersham Biosciences, San Francisco, CA, USA). For the kidney tissues we used Automated tissue processor by company Lecia model LEICA TP 1020 from Germany (6). We used statistical analysis average and standard deviation (means  $\pm$  SD). We analyzed the transactions to see the differences between the average measurements of the transactions and conducted analysis of variance (One Way ANOVA) and Duncan test using statistical analysis software(12).

## Results and Discussion

The result shown in Figure 1, the diabetic control group (DC) showed no significant effect on weight but in (DGH, DGEL, DGEH) showed decrease in comparison with the (C, DC) groups ( $P \leq 0.05$ ). Our study was inconsistent with the study (8) that showed lower weight in diabetic control rats and our study agreed with (13) which showed it caused lower weight in a group of rats that ate ginger compared with the diabetic group. Food intake in (figure 2) we see in a groups (DGEL, DGEH) low in statistical analyses compared to the (C, DC) groups and our study was inconsistent with this study (11) where there was no significant difference in the food intake in all groups. For this study, the reason for the low food intake may return to the diet because it contains fibre and gives feeling of fullness. The glucose in (figure 3) of the ginger and its extracts led to a rise in glucose results of this study is inconsistent to another study (14), that found very small amounts of ginger juice lowered blood sugar significantly in control and diabetic rats. Our results agree with this study (9), which explained that ginger leads to inhibition of the enzyme aldose reductase and reduces the level of sorbitol and raises the level of blood glucose. Ginger and extract did not affect all blood nitrogen urea, urea and Uric acid (figure 4, 5 and 7), but led to a rise in creatinine (figure 6). Inconsistent with our results was a study (1) that found giving ginger oil returned the kidney function to normal urea, uric acid and creatinine. In another study, the cause of creatinine rise was an increase in demolitions in both the liver and protein in blood giving glucose from non-carbohydrate sources(2).

Kidney section under the microscope showed tube and Glomeruli (Photo 8.B). Glomerulus contains intermediate cells (Photo 8.A). Group DGL and DGEH compared to control group in glomeruli tissue (Photo 10.A) and (Photo A.13) is healthy and there is no fibrosis or inflammatory activity in the renal tubules. Both groups showed some tubule atrophy and swelling in (Photo B.10) and (Photo B.13). There was found an increase in the size and number of intermediate cells in (CD, DGH, DGEL) in (Photo A.9), (Photo A.11) and (Photo B.12) and atrophy of the tubules and cellular fibrosis (Photo B.9), (Photo B.11) and (Photo A.12). Our result is contrary to the results of this study (3) that found a significant change among diabetic people in kidney tissues treated with ginger. Our result agrees with the study (10), where there has been a very simple change in all groups.

### Compare the Groups

Group	Food intake (g)	Ureic acid (mg/dl)	Urea (mg/dl)	Blood urea nitrogen (mg/dl)	Creatinine (mg/dl)	Glucose (mg/dl)	Body weight (g)
C	a 0.14±0.01	a 3.14±0.71	b 27.92±2.55	b 13.04±1.19	a 2.51±0.72	c 117.9±2.3	a 338.6±9.3
DC	b 0.05±0.02	a 4.05±0.96	b 31.53±3.89	b 14.72±1.82	a 1.40±0.59	b 370.8±68.9	b 227.0±24.9
DGL (0.5%)	bc 0.036±0.02	a 3.85±0.57	ab 36.3±4.48	ab 16.94±2.09	a 0.86±0.62	a 506.6±39.4	bc 186.6±24.5
DGH (2%)	bcd 0.016±0.01	a 2.30±0.56	a 51.02±8.85	a 23.86±4.12	a 2.34±0.73	a 573.5±16.6	c 140.1±11.5
DGEL (0.5%)	d -0.016±0.01	a 2.86±1.14	b 24.73±1.73	b 11.54±0.81	a 1.03±0.24	a 535.8±26.7	c 169.7±13.3
DGEH (2%)	cd -0.006±0.01	a 4.40±2.33	ab 36.89±6.66	ab 17.22±3.11	a 1.63±0.39	a 560.6±12.0	c 145.2±13.2

Different groups of rats during the experimental period. Data are mean ± SD values animals. Different letters are for those significantly different from the other groups of animals ( $P < 0.05$ ). C, control; DC, diabetic control; DGL, diabetic of low ginger dose; DGH, diabetic of high dose; DGEL, diabetic of low ginger extract dose; DGEH, diabetic of high ginger extract dose

Figure 1: Comparison of groups in terms of weight

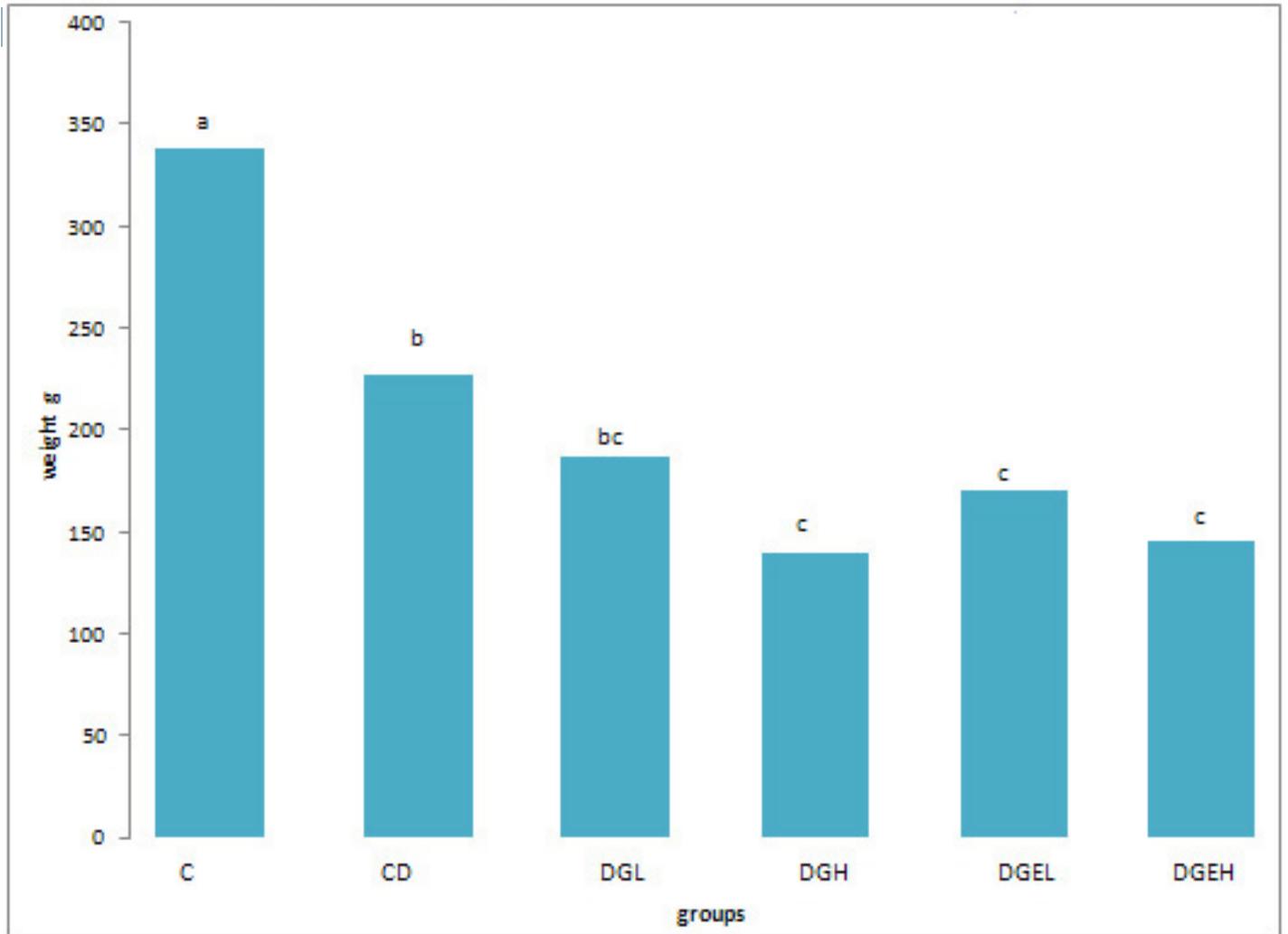


Figure 2: Comparison of groups in terms of glucose

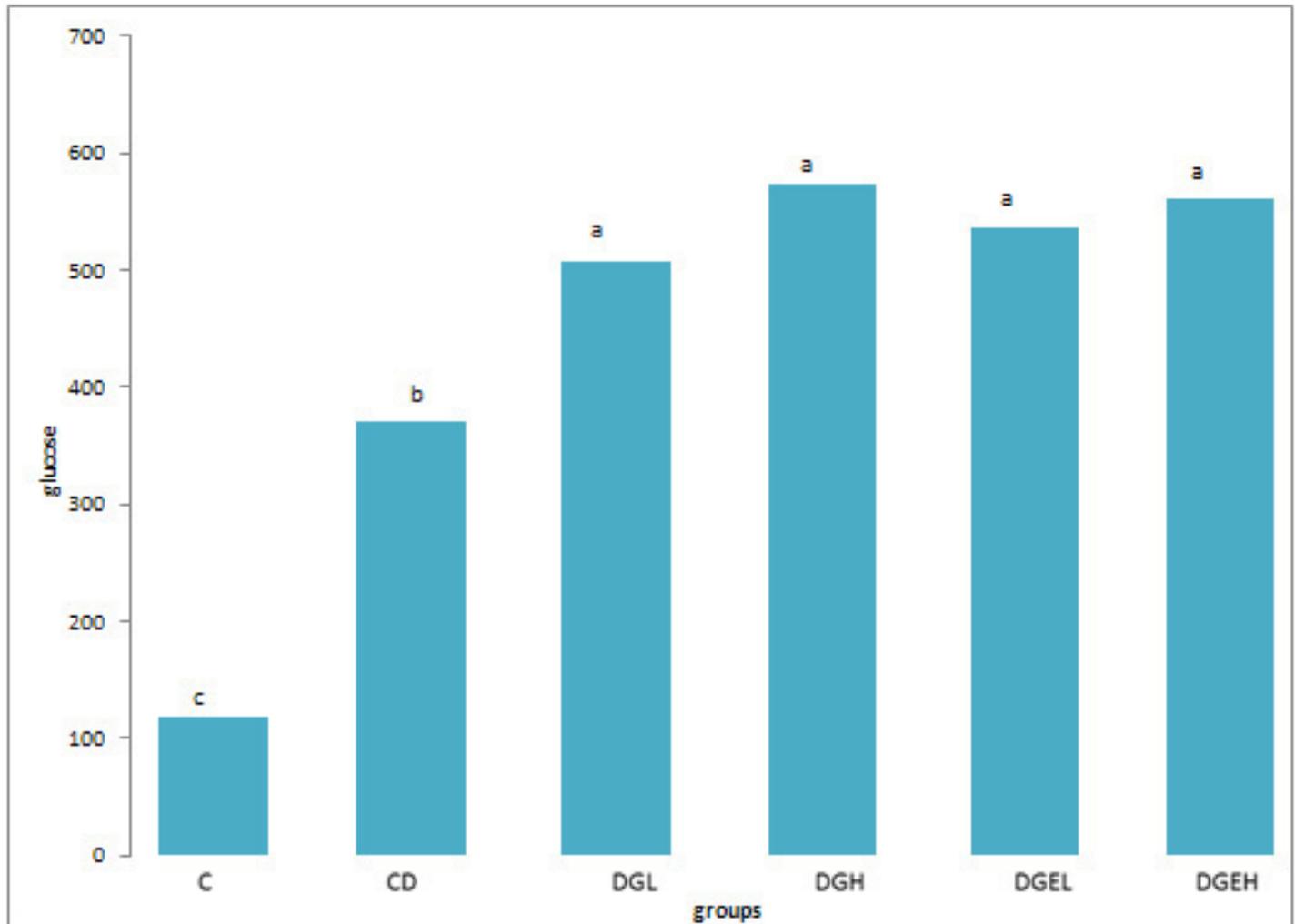


Figure 3: Comparison of groups in terms of creatinine

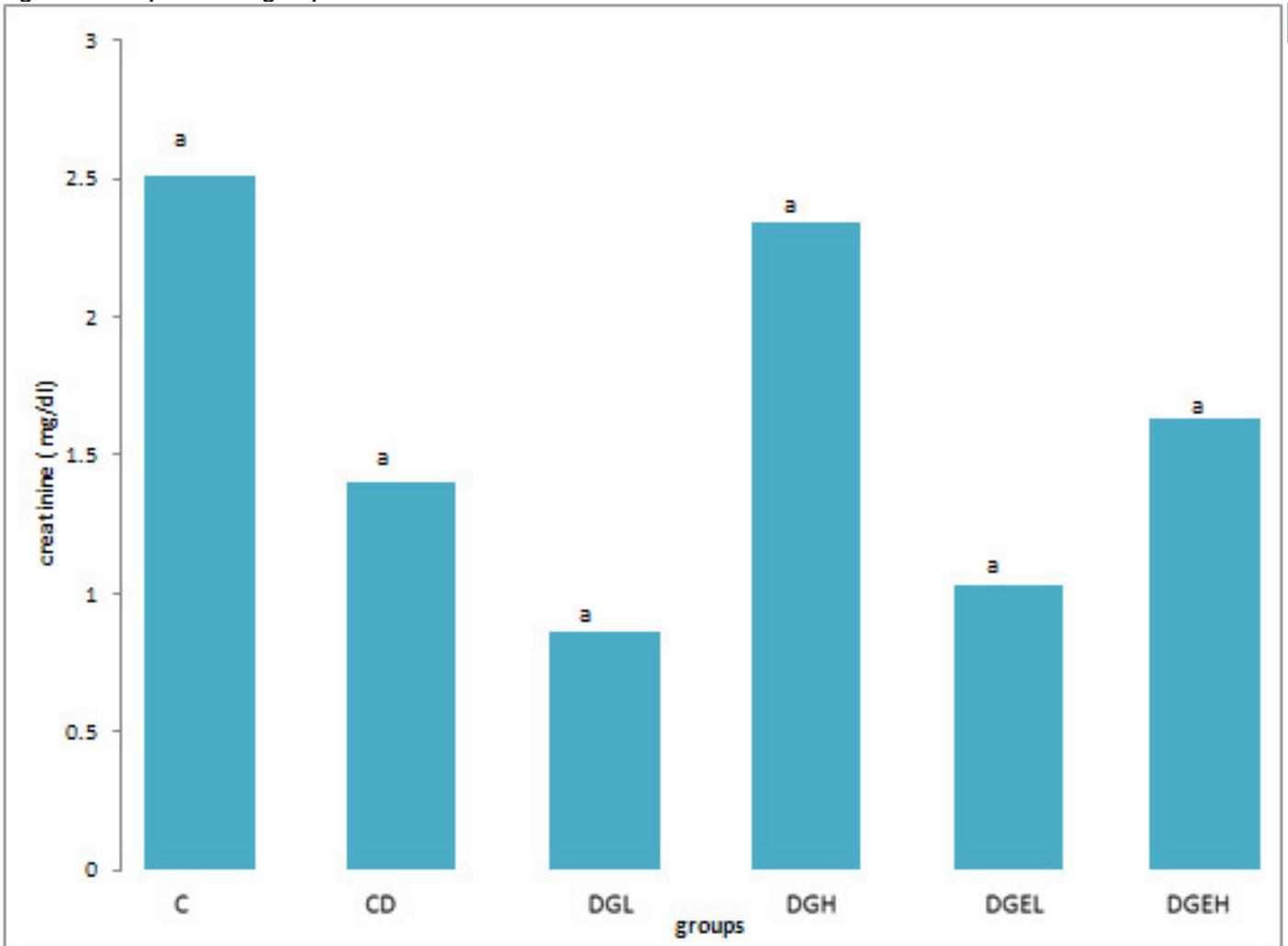


Figure 4: Comparison of groups in terms of blood urea nitrogen

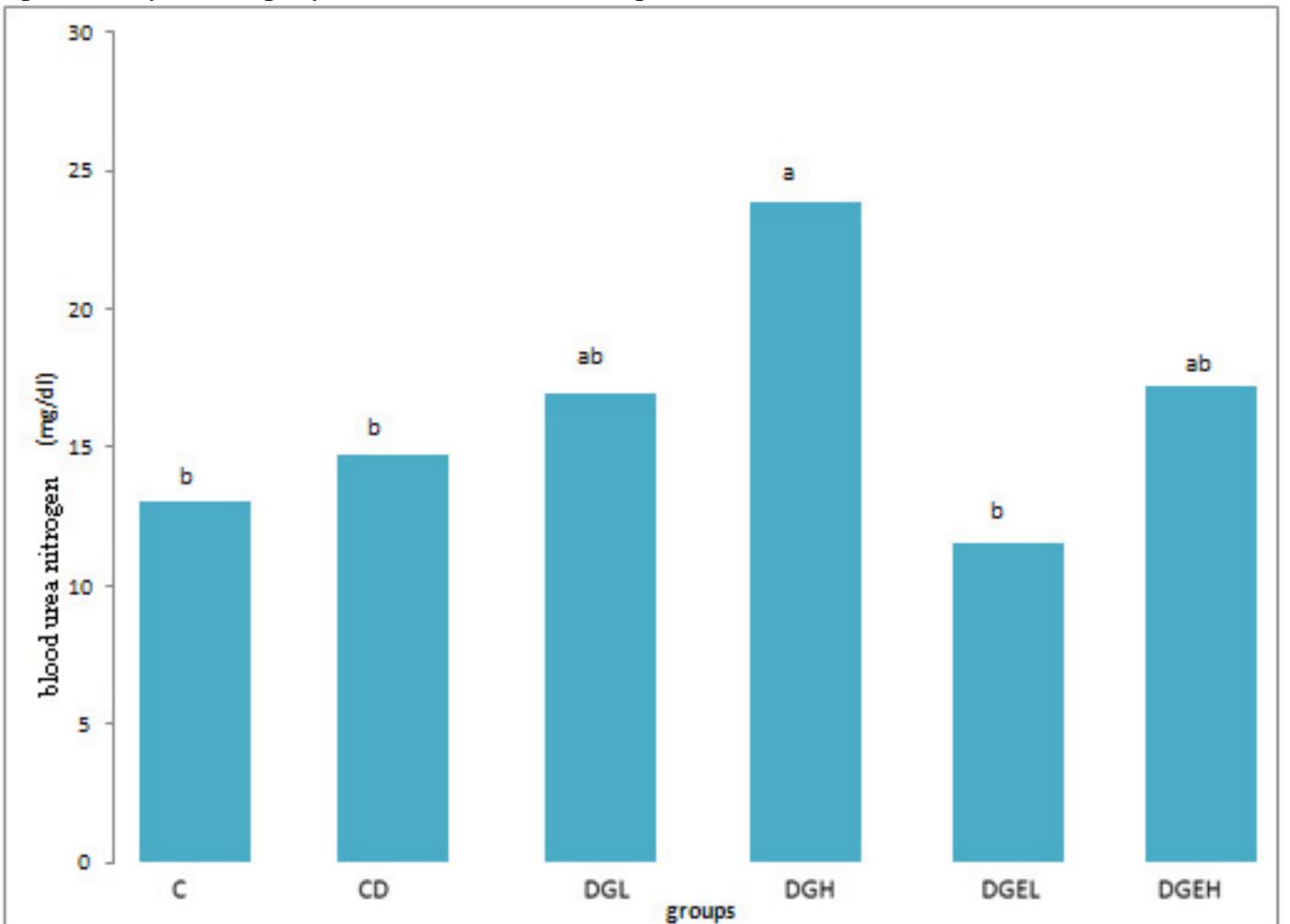


Figure 5: Comparison of groups in terms of urea

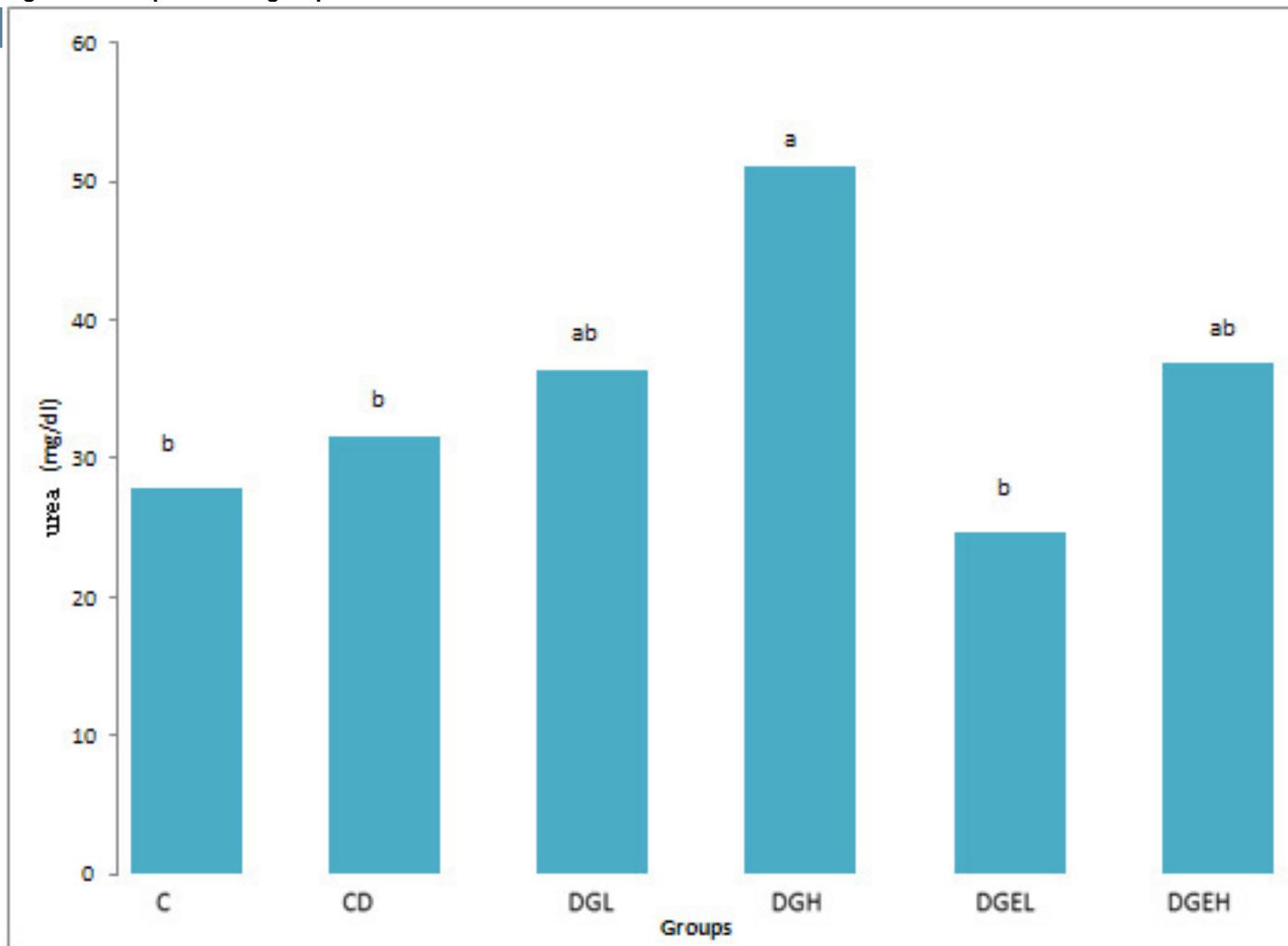
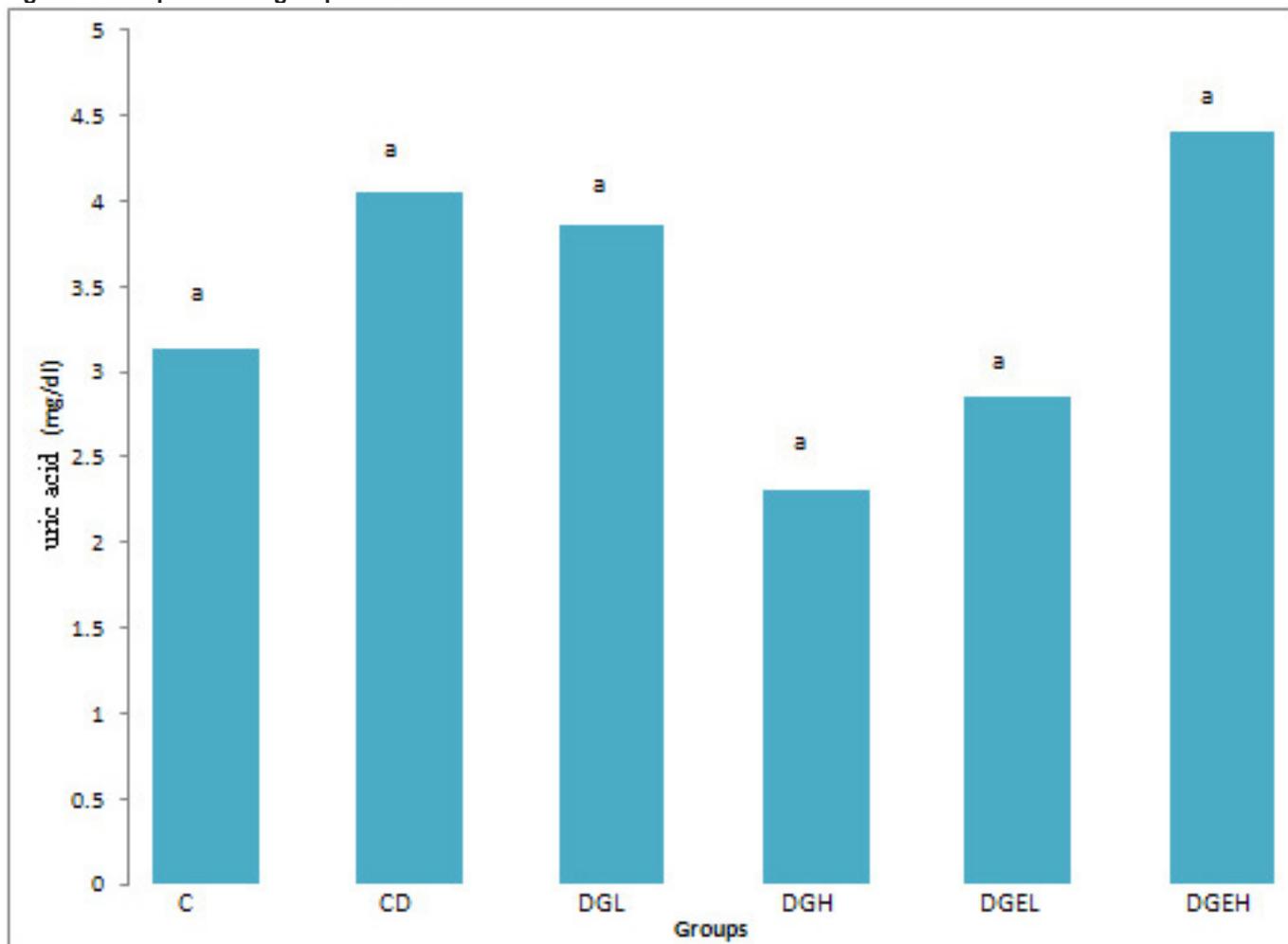
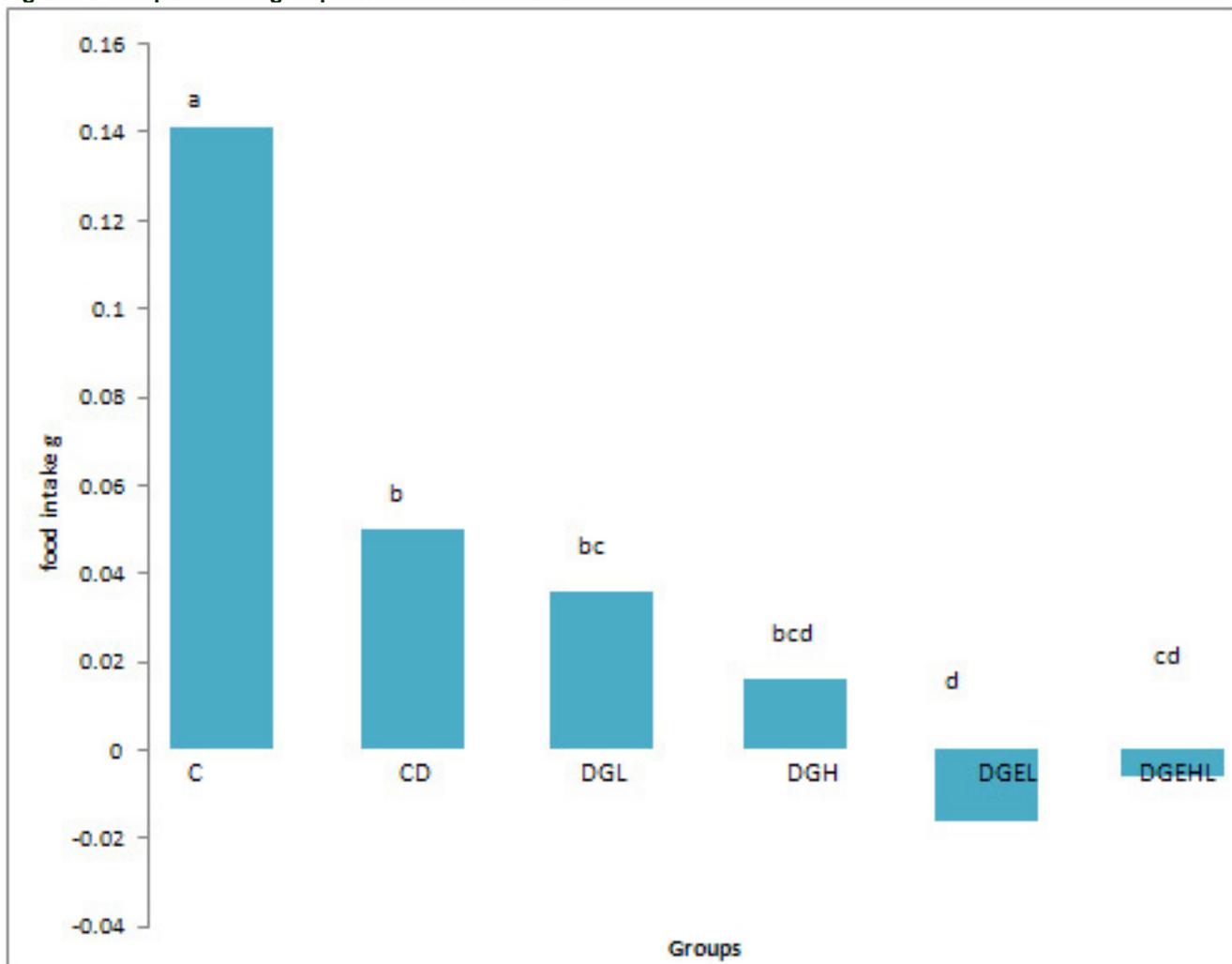


Figure 6: Comparison of groups in terms of uric acid



**Figure 7: Comparison of groups in terms of food intake**

## Recommendations

- 1) We recommend doing this study longer and in different concentrations in extracting: gingerol, shogaol, paradol and zingerone in human and rats.
- 2) We recommend to measure many things like sorbitol, enzyme aldose reductase, enzymes of kidney and urea protein.

## Conclusions

Ginger and its extract did not implement any change in blood glucose and kidney function but the low dose of ginger and the high dose of ginger extract caused improvement in the tissue of the kidney.

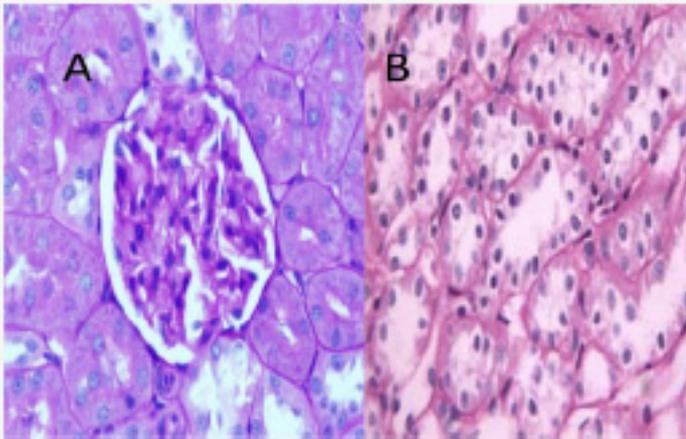
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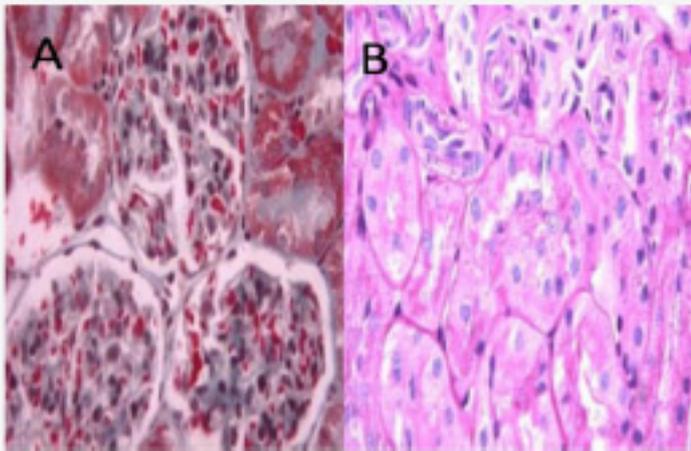
## References

- 1) Al-Attar, A.M.; Zari, T.A. (2007). Modulatory effect of ginger clove oils on physiological responses in streptozotocin-induced diabetic rats. *Int J pharmacology*. 3(1): 34-40
- 2) Almdal, T.P.; Vilstrup, H. (1987). Effects of streptozotocin-induced diabetes and diet on nitrogen loss from organs and on the capacity of urea synthesis in rats. *Diabetologia*. 30(12):952-6.
- 3) Al-Qattan, K.; Thmoson, M.; Ali, M. (2008). Garlic (*Allium sativum*) and ginger (*Ziniber officinal*) attenuate structural nephropathy progression in streptozotocin - induced diabetic rats. *e - SPEN. the European e- J. ClinNutrandMetabl*. 3:e62-e71
- 4) Barham, D.; Trinder, P. (1972). An improved colour reagent for the determination of blood glucose by the oxidase system. 97:142-145.
- 5) Champe, P. A.; Harvey, R. A.; Ferrier, D. R. (2008). *Biochemistry*. Lippincott's Williams and Wikins. 4th edition. United States of America. New York. Pp139-141.
- 6) Geoffrey, G.; John, M. (1974). *An introduction to histotechnology*. Printed in the United States of America. New York. Pp 65.
- 7) Henry, J. B.; Todd, S. D. (1974). *Clinical Diagnosis and Management by Laboratory Methods* 16th ed., W.B. Saunders & Co. Philadelphia, PA. Pp260,263.
- 8) Islam, M. S.; Choi, H. (2008). Comparative effects of dietary ginger (*Zingiberofficinale*) and garlic (*Allium sativum*) investigated in type 2 diabetes model of rats. *J Med Food*. 11(1):152-159.
- 9) Kato, A.; Higuchi, Y.; Goto, H.; Kizu, H.; Okamoto, T.; Asano, N.; Hollinshead, J.; Nash, R. J.; Adachi, I. (2006). Inhibitory effect of *Zingiberofficinale* Roscoe derived components on aldose reductase activity in vitro and in vivo. *J Agric Food Chem*.(54):18:6640-6644.

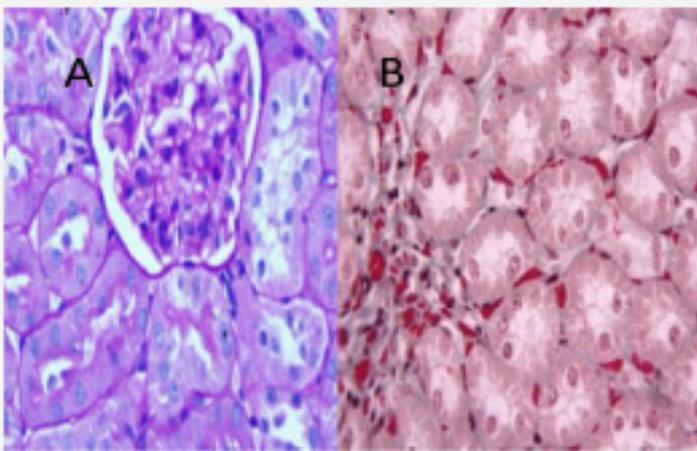
control group (C) photo 8



diabetic group (DC) photo 9



diabetic and eat 0.5% ginger in diet (DGL) photo 10



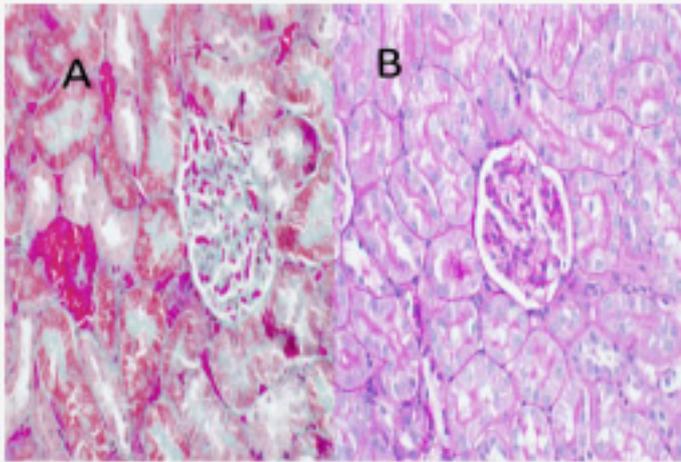
10) Lakshmi, B. V. S.; Sudhakar, M. (2010). Protective effect of Zingiber officinal on gentamicin- induced nephrotoxicity in rats. *Int J Pharmacol.* 1-5. 11) Saraswat, M.; Suryanarayana, P.; Reddy, P. Y.; Patil, M. A.; Balakrishna, N. ; Reddy, G. B. (2010). Antigliating potential of Zingiberofficinalis and delay of diabetic cataract in rats. *Molecular Vision.* 16:1531(1525-1537) 12) SAS.(2009). SAS user's guide: Statistics Version (8.1) (ed.) SAS Institute Inc., Cary, N. C., USA.

13) Shanmugam, K. R.; Ramakrishana, C. H.; Mallikarjuna, K.; Sathyavelu, K. R. (2009). The impact of ginger on kidney carbohydrate metabolic profiles in STZ induced diabetic rats. *Asian J Exp Sci.* 1:127-134.

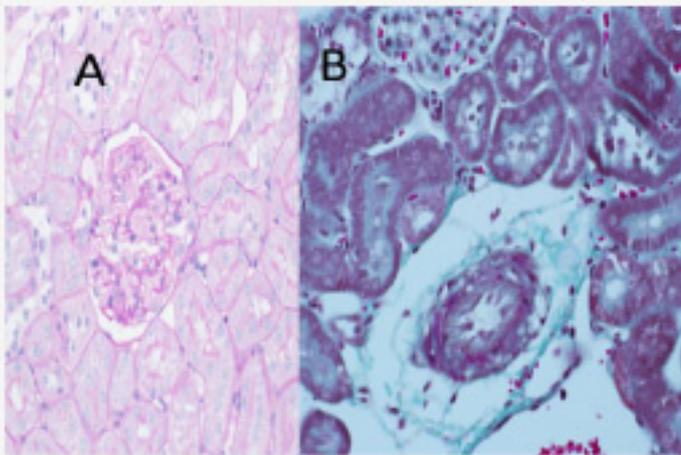
14) Sharma, M.; Shukla, S. (1977). Hypoglycemic effect of ginger. *J Res Ind Yoga Homeop.* 12:127-130.

15) Trinder, P. (1969). Determination of blood glucose using 4-Aminophenazone. *J Clin Path.* (22)246

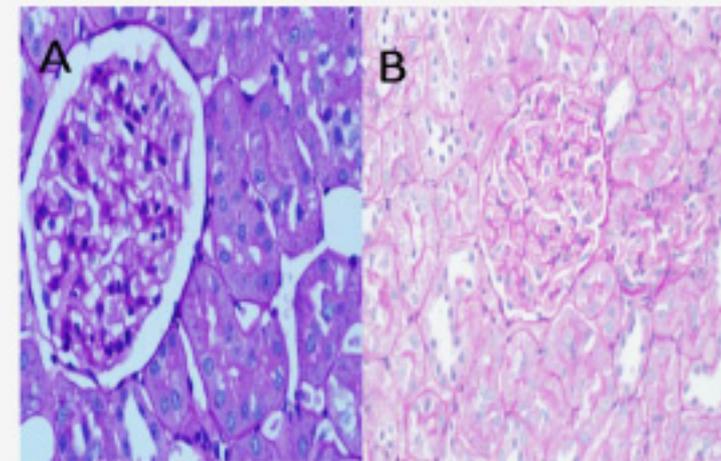
diabetic and eat 2% ginger in diet (DGH) photo 11



diabetic and eat 0.5% ginger extract (zingeron) in diet (DGEL) photo 12



diabetic and eat 2% ginger extract(zingeron) in diet (DGEH) photo13



# Prevalence of Diabetic Retinopathy among Newly Diagnosed Type 2 Diabetes Mellitus Patients in Abha City, Saudi Arabia

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## Abstract

**Objectives:** To estimate the prevalence of DR and to compare the difference in the prevalence rate according to different patient's characteristics among newly diagnosed type 2 diabetic patients in Abha, Kingdom of Saudi Arabia.

**Study design:** A cross sectional study

**Methods:** This study was conducted at the ophthalmology clinic in Abha General Hospital, Saudi Arabia. All newly diagnosed diabetic type 2 patients attending primary health care centers in Abha during the period of study (39 PHCCs) were referred to the ophthalmology department in Abha General Hospital for diabetic retinopathy screening until the required sample size was reached. After adequate mydriasis, the examination of the posterior segment was carried out using slit-lamp biomicroscope with 90-diopter lens. The intraocular pressure was measured using applanation tonometry. Diabetic retinopathy was classified using Friedman's standards.

**Results:** The study included 393 newly diagnosed type 2 diabetic patients. Their age ranged between 21 and 96 years with a mean of 52.9 years and standard deviation of 11.8 years. Female patients represented (242) 61.6% of them. The prevalence of diabetic retinopathy among newly diagnosed type 2 diabetic patients was (13) 3.3%. All DR cases were classified using Friedman's standards as background or non-proliferative diabetic retinopathy. The prevalence of DR among female newly diagnosed type 2 diabetic patients was (13) 5.4% compared to none among males. This difference was statistically significant,  $p=0.002$ . The prevalence of DR was (13) 4.3% among not working type 2 diabetic patients compared to none among working patients. This difference was statistically significant,  $p=0.027$ . Intra-ocular pressure was within normal values for all patients in both eyes.

**Conclusion:** The prevalence of retinopathy in newly diagnosed type 2 diabetes mellitus patients was found to be relatively low in this study compared to international studies.

**Key words:** Diabetic retinopathy; Diabetes mellitus; Prevalence; Diagnosis; Ophthalmology

## Introduction

Diabetic retinopathy (DR) is a complication of diabetes mellitus (DM) that affects the blood vessels of the retina and leads to blindness. The progression of retinopathy is gradual, advancing from mild abnormalities, characterized by increased vascular permeability, to moderate and severe non-proliferative diabetic retinopathy, characterized by the growth of new blood vessels on the retina and posterior surface of the vitreous.(1)

Individuals with diabetes are 25 times more likely to become blind than individuals without this disease.(2) In many developed countries, diabetic retinopathy is the leading cause of new cases of visual impairment and blindness among adults aged 20-74 years.(3) Among people who have type 2 diabetes, around 21% have retinopathy at diagnosis,(3) and more than 60% have diabetic retinopathy during the first two decades of the disease.(4)

The Wisconsin epidemiological study of diabetic retinopathy (WESDR) concluded that 1.6% of those diagnosed with type 2 DM were legally considered blind. For type 2 DM, blindness was related to retinopathy in 33% of the cases.(5) The prevalence of DR is probably around 30% in type 2 DM, but notably was above this level in five out of six studies reported from the Asian and Pacific island nations of the Western Pacific Region.(6) The annual incidence of retinopathy requiring ophthalmological follow up or treatment has been reported to average 1.5% after one year.(7) The same source estimates that 6-9% of patients with proliferative retinopathy or severe non-proliferative disease would become blind each year.(7) Moreover, growing evidence also suggests that after 15 years of diabetes, approximately 2% of patients develop blindness, while about 10% develop severe visual handicap.(7) Thus, the early detection of sight-threatening retinopathy and the timely intervention with laser photocoagulation has been shown to be effective in preventing severe visual loss.

Diabetes-related blindness is a personal catastrophe to the individual and costs the United States approximately \$500 million annually.(8) However, risk of vision loss due to diabetic retinopathy can be reduced by effective control of serum glucose and blood pressure and by its early detection and timely treatment.(9-11) The efficacy and cost-effectiveness of early detection and treatment of diabetic retinopathy is well established.(12, 13)

Several factors have been identified as determinants for the development of DR and its progression; including, type and duration of DM, age, gender, glycemic control, hypertension, body mass index (BMI), smoking, serum lipids and presence of microalbuminuria (MA)(14-18).

## Methodology

**Study design:** A cross-sectional method.

**Study setting:** This study was conducted at the ophthalmology clinic in Abha General Hospital, Aseer region, Saudi Arabia.

**Study population:** Newly diagnosed diabetic type 2 patients attending primary health care centers (39 PHCCs) in Abha during the period of study from September 2013 until April 2014. They were requested to participate in the study. They were referred to the ophthalmology department in Abha General Hospital for diabetic retinopathy screening.

**Sample size and sampling technique:** The sample size was estimated to determine the prevalence of diabetic retinopathy among newly diagnosed diabetic patients type 2 of 12% (according to average of previous regional studies in the literature), with a 3% absolute error (25% of prevalence) and finite population correction, at 95% level of confidence. The newly diagnosed type 2 diabetic patients in Abha in 2012 was 3059 patients.

Using the single proportion equation for dichotomous variables in Raosoft software package, and the previous information to answer the following questions: What margin of error can you accept? (3%); What confidence level do you need? (95%); What is the population size? (3059) and What is the response distribution? (12%). Accordingly, the required sample size is 393 patients.(19)

All newly diagnosed type 2 diabetic patients referred to the ophthalmology department in Abha General Hospital were invited to be included in the study until the required sample size was reached.

**Inclusion criteria:** Diabetic type 2 patients who were diagnosed within two years, All ages (more than 20 years old), Both genders.

**Exclusion criteria:** Those who refused to participate in the study, With chronic debilitating diseases (hypertension, asthma ...) and With serious eye problems (cataract, glaucoma...)

### Study tool and procedure:

All patients referred to ophthalmologists at the Abha General Hospital underwent detailed eye examination. After adequate mydriasis, the examination of the posterior segment was carried out using slit-lamp biomicroscope with 90-diopter lens. The intraocular pressure was measured using applanation tonometry.

Diabetic retinopathy was classified using Friedman's (2005) standards, and was as follows:

- i) Background or non-proliferative diabetic retinopathy: haemorrhages, exudates, cotton wool spots, microaneurysms, intraretinal microvascular abnormalities, venous beading;
- ii) Severe NPDR ("4-2-1 rule"): defined as any one of the following: 4 quadrants of hemorrhages/MAs, 2 quadrants of venous beading, 1 quadrant of IRMA;
- iii) Very Severe NPDR: defined as 2 or more of the above;
- iv) Proliferative (PDR): neovascularization (NV) of disc or elsewhere;

v) High-risk proliferative (HR-PDR): defined as any one of the following:

1. NVD  $\geq$  1/4 to 1/3 disc area,
2. Any NVD with vitreous haemorrhage,
3. NVE  $\geq$  1/2 disc area with vitreous haemorrhage.(20)

Then, a data collection sheet was filled in by the researcher including the following:

- Demographic variables including: age, gender, marital status, job and educational level;
- Medical history including diabetic complications other than DR, diabetic coma, treatment and treatment satisfaction;
- Ophthalmological examination regarding DR and its grade was done by the ophthalmologist.

#### Data management and statistical analysis:

SPSS package, version 20 was used for data entry and analysis. Descriptive statistics were applied as follows: Frequency and percentage were used to describe categorical variables while mean and standard deviation were used to describe continuous variables. Chi-square test was applied to test for the association and/or difference between categorical variables. Fisher exact test was applied instead of chi-square test in case of small frequencies. Differences were considered statistically significant when the p-value was less than 0.05.

## Results

The study included 393 newly diagnosed type 2 diabetic patients. Their age ranged between 21 and 96 years with a mean of 52.9 and standard deviation of 11.8 years. More than half of them 213 (56%) were over 50 years. Female patients represented 242 (61.6%) of them. The majority of them 256 (90.6%) were married. Most of them 299 (76.1%) were not working. Among working patients 94 (23.9%), governmental employees 28 (29.8%) and teachers 27 (28.7%) were the most common reported jobs. Slightly less than half of them 186 (47.3%) were illiterate and 49 (12%) finished university and postgraduate studies (Table 1).

**Table 1: Personal characteristics of newly diagnosed type 2 diabetic patients who participated in the study (n=393)**

Personal Characteristics	Categories	Frequency	Percentage
Age in years	20-30	18	4.5
	31-40	36	9.2
	41-50	119	30.3
	51-60	158	40.2
	>60	62	15.8
Gender	Males	151	38.4
	Females	242	61.6
Marital status	Single	18	4.6
	Married	356	90.6
	Divorced	4	1.0
	Widowed	15	3.8
Job status	Not working	299	76.1
	Working	94	23.9
	-Teacher	27	28.7
	-Military	11	11.7
	-Governmental Employee	28	29.8
	-Retired	22	23.4
	-Others	6	6.4
Education	Illiterate	186	47.3
	Primary	89	22.6
	Intermediate	22	5.6
	Secondary	49	12.5
	University	45	11.5
	Postgraduate	2	0.5

The prevalence of diabetic complications (other than diabetic retinopathy) among newly diagnosed type 2 diabetic patients was 7(1.8%). This complication was diabetic neuropathy.

Newly diagnosed type 2 diabetic patients had history of diabetic coma which accounted for 12 (3.1%). Regarding treatment among newly diagnosed type 2 diabetic patients, oral hypoglycemic drugs were the most commonly reported 270 (76.6%), followed by diet regimen 76 (27.2%). Insulin was the line of treatment among 12 (3.1%) of them while a combination of oral hypoglycemic drugs and insulin was the type of treatment for 4 (1%) of them.

Almost two-thirds 272 (69.2%) of type 2 diabetic patients were very satisfied with their disease therapy while 97 (24.7%) were somewhat satisfied with it.

#### Diabetic Retinopathy

The prevalence of diabetic retinopathy among newly diagnosed type 2 diabetic patients was 13 (3.3%). All DR cases were classified using Friedman's standards as background or non-proliferative diabetic retinopathy.

The prevalence of DR was 4 (6.5%) among newly diagnosed type 2 diabetic patients over 60 years compared to none among those aged between 20 and 40 years. However, the difference was not statistically significant,  $p=0.210$  (Table 2).

**Table 2: Prevalence of diabetic retinopathy according to personal characteristics, diabetes therapy and satisfaction therapy**

Characteristics	Diabetic Retinopathy		Chi-square	p-value
	No N (%)	Yes N (%)		
<b>Age (years)</b>				
20-30 (n=18)	18 (100)	0 (0.0)		
31-40 (n=36)	36 (100)	0 (0.0)		
41-50 (n=119)	113 (95.0)	6 (5.0)		
51-60 (n=158)	155 (98.1)	3 (1.9)		
>60 (n=62)	58 (93.5)	4 (6.5)	<b>5.86</b>	<b>0.210</b>
<b>Marital status</b>				
Single (n=18)	18 (100)	0 (0.0)		
Married (n=356)	343 (96.3)	13 (3.7)		
Divorced (n=4)	4 (100)	0 (0.0)		
Widowed (n=15)	15 (100)	0 (0.0)	<b>1.40</b>	<b>0.706</b>
<b>Educational level</b>				
Illiterate (n=186)	177 (95.2)	9 (4.8)		
Primary (n=89)	85 (95.5)	4 (4.5)		
Intermediate (n=22)	22 (100)	0 (0.0)		
Secondary (n=49)	49 (100)	0 (0.0)		
University+ (n=47)	47 (100)	0 (0.0)	<b>5.79</b>	<b>0.215</b>
<b>Diabetes therapy</b>				
Diet regimen (n=76)	76 (100)	0 (0.0)		
Oral hypoglycemics (n=270)	257 (95.2)	13 (4.8)		
Insulin (n=12)	12 (100)	0 (0.0)		
Oral hypoglycemics and insulin (n=4)	4 (100)	0 (0.0)	<b>6.13</b>	<b>0.190</b>
<b>Satisfaction with therapy</b>				
Very satisfied (n=272)	259 (95.2)	13 (4.8)		
Somewhat satisfied (n=97)	97 (100)	0 (0.0)		
Neutral (n=22)	22 (100)	0 (0.0)		
Somewhat dissatisfied (n=2)	2 (100)	0 (0.0)	<b>5.98</b>	<b>0.113</b>

**Table 3: Prevalence of diabetic retinopathy according to patient's gender, job status, diabetic complications**

Characteristics	Diabetic Retinopathy		p-value of Fisher exact test
	No N (%)	Yes N (%)	
<b>Gender</b>			
Male (n=151)	151 (100)	0 (0.0)	<b>0.002</b>
Female (n=242)	229 (94.6)	13 (5.4)	
<b>Job Status</b>			
Not working (n=299)	286 (95.7)	13 (4.3)	<b>0.027</b>
Working (n=94)	94 (100)	0 (0.0)	
<b>Diabetic complications</b>			
No (n=386)	373 (96.6)	13 (3.4)	<b>0.789</b>
Yes (n=7)	7 (100)	0 (0.0)	
<b>Diabetic coma</b>			
No (n=381)	368 (96.6)	13 (3.4)	<b>0.664</b>
Yes (n=12)	12 (100)	0 (0.0)	

The prevalence of DR was 13 (3.7%) among married newly type 2 diabetic patients compared to none among singles, divorced and widowed patients. However, the difference was not statistically significant,  $p=0.706$  (Table 2).

DR was more reported among lower educated diabetic type 2 patients 9 (4.8%) and 4 (4.5%) among illiterate and primary educated patients compared to none of higher educated patients. However, this difference was not statistically significant,  $p=0.215$  (Table 2).

The prevalence of DR among female newly diagnosed type 2 diabetic patients was 13 (5.4%) compared to none among males. This difference was statistically significant,  $p=0.002$  (Table 3).

The prevalence of DR was 13 (4.3%) among not working type 2 diabetic patients compared to none among working patients. This difference was statistically significant,  $p=0.027$  (Table 3).

There was no statistically significant association between DR and other diabetic complications among newly diagnosed type 2 diabetic patients,  $p=0.789$ . Also, there was no statistically significant association between DR and history of diabetic coma among newly diagnosed type 2 diabetic patients,  $p=0.664$ . DR was more reported among diabetic type 2 patients treated by oral hypoglycemic drugs (4.8%) compared to none among patients treated by diet regimen, insulin and a combination of insulin and oral hypoglycaemic drugs. However, this difference was not statistically significant,  $p=0.190$ . There was no statistically significant association between DR and satisfaction of diabetic patients with their therapy,  $p=0.113$  (Table 3).

#### Intra-ocular Pressure

Intra-ocular pressure was within normal values for all patients in both eyes (10 mmHg and 21 mmHg).

#### Discussion

The prevalence of retinopathy in patients with newly diagnosed Type 2 diabetes mellitus was found to be relatively lower in this study (3.3%) compared to international data.

Diabetes Prevention Program Research Group(21) reported 12.6% prevalence of retinopathy in recent onset diabetes in the diabetes prevention programme. Wahab et al in Pakistan reported that 15% (95% CI 14.7, 15.3) of patients were found to have diabetic retinopathy within two months of diagnosis of type 2 diabetes mellitus.(22)

Multiple clinic-based studies conducted on newly diagnosed diabetes patients have shown varied prevalence; Abdollahi et al.(23) from Iran reported 13.8%, Agarwal et al.(24) reported 11.7%, while Rema and associates reported 5.1% and 7.3% respectively.(25,26) Klein et al.(27) reported the prevalence of 10.2% in newly discovered type 2 diabetic patients in Beaver Dam Eye Study. Kohar and associates(28) have reported 39% and 35% prevalence of retinopathy in men and women respectively in the United Kingdom Prospective Diabetes Study.

In a study on 1640 Pima Indians of 15 years and older, 18% of those with two-hour post-load plasma glucose levels of equal to or greater than 200 mg/dl had some evidence of retinopathy.(29)

Two studies performed in Australia showed the prevalence of diabetic retinopathy in newly diagnosed type 2 non-treated diabetic patients to be 14%-20%.(30, 31)

In Kenya, overall, the prevalence of diabetic retinopathy and clinically significant macular oedema was 30.4% and 8.7% respectively among newly diagnosed black African patients.(32)

The differences in the reported prevalence of retinopathy in people with newly discovered type 2 diabetes might be due to variation in the time between onset and detection of diabetes. This could be a result of socioeconomic factors, which determine the access to and availability of medical care, the health care seeking behaviour of the specific group studied, as well as variation in the definitions used to define the presence of diabetes.

The low prevalence in the current study could be attributed to the fact that the Saudi health system is free of charge and results in early diagnosis of diabetic patients. Similarly, in a population-based study in Denmark, the prevalence of DR was reported to be 5%-8%. They suggested that the low prevalence is due to the Danish health system which is free of charge and results in early diagnosis of diabetic patients.(33)

In accordance with others,(22,34) DR was more prevalent among older diabetic patients in the present survey although it is not statistically significant. This could be due to the small number of patients (n=13) who developed DR in the present study. In addition, the present study reports a significant association between prevalence of DR and female gender and not working status. This could be due to the confounding effect of age with these two factors. Again, due to the small number of patients who developed DR, we could not perform Logistic regression analysis to control for the effect of age on the development of DR.

Evaluation of diabetic patients who sought ophthalmologic consult for the first time in Farabi Hospital in Iran showed that 48.4% of patients were diagnosed as non-PDR and 45.4% of them were PDR.<sup>23</sup> In the present study, all DR cases were classified using Friedman's standards as background or non-proliferative diabetic retinopathy.

In addition, the average time to seek ophthalmologic consult after diagnosis of diabetes mellitus was 11.5± 5.5 years in Farabi Hospital's study. All the data revealed that those patients designated as newly diagnosed diabetes mellitus have had the disease for a significant duration of time and after diagnosis of their disease their ophthalmologic examination was postponed until it was too late for effective treatment of diabetic retinopathy. It is believed that undiagnosed type 2 diabetes mellitus may occur 4-12 years before its clinical diagnosis and that diabetes may be present for five years before the onset of retinopathy.(35,36) Undiagnosed type 2 diabetes is thus not a benign condition. The unknown duration (years) of undiagnosed diabetes in our patients is likely to be a more important contributory factor to retinopathy than the known (weeks) duration of diagnosis. This is further supported in the present study by the fact that patients with diabetic retinopathy were older than those without.

This existence of DR among newly diagnosed diabetic type 2 patients may be also due to the fact that patients are more likely to consult a medical doctor than eye care professionals in dealing with signs and symptoms of medical conditions such as DM. Optometrists are also more likely perceived by patients as professionals who deal more with refractive conditions rather than medical problems, especially amongst the elderly population. However, the role of optometrists as part of primary health care in the screening and management of diabetic retinopathy has been recognized and documented in the National Service Framework in Britain and the Strategy Implementation plan in Australia.(37,38)

Among important limitations of the present study, we did not include other factors that could be associated with the development of DR in newly diagnosed diabetic patients such as glycemic control, hypertension, body mass index (BMI), smoking, serum lipids and presence of microalbuminuria (MA) due to lack of sufficient time and resources. Due to the cross-sectional nature of the survey, we cannot draw definitive causal conclusions about the observed relationships between demographic and disease characteristics and DR.

## Conclusion

The prevalence of retinopathy in newly diagnosed type 2 diabetes mellitus patients was found to be relatively low in this study. The prevalence was significantly higher among female and not working patients. All DR cases were classified using Friedman's standards as background or non-proliferative diabetic retinopathy. Intra-ocular pressure was within normal values for all patients.

## Recommendations

Although, we reported a relatively low prevalence rate of diabetic retinopathy, there is a need for intensified efforts for early diagnosis of type 2 diabetes mellitus and careful fundus biomicroscopic examination of all newly diagnosed type 2 diabetics in our community where diabetes type 2 is highly prevalent.

1. Population-based studies are suggested with larger sample sizes to determine a better estimation of DR prevalence among Saudi newly diagnosed diabetic patients and study its associated risk factors.
2. There should be emphasis for all optometrists to become competent in the diagnosis and management of ocular manifestations of systemic conditions such as diabetes.
3. Further prospective longitudinal studies are recommended for diabetic patients free from DR at the onset to confirm the causal association between DR and possible associated factors as well as to enable a more precise determination of the onset of diabetic retinopathy.
4. Screening program for early diagnosis of type 2 diabetes mellitus, and consequently diminishing its complications including retinopathy, should be encouraged.

**Ethical and administrative considerations:** All the necessary official permissions were fully obtained before study conduction. The collected data were kept strictly confidential and used only for research purposes. Verbal informed consent was obtained from all participants.

## References

1. Diabetes Care. Diabetic Retinopathy. American Diabetes Association Journals, 2000; 73-6.
2. U-Din J, Qureshi M, Khan A, Khan M, Ahmad K. Prevalence of diabetic retinopathy among individuals screened positive for diabetes in five community-based eye camps in Northern Karachi, Pakistan. *Journals of Ayub Medical College: Abbottabad*, 2006; 40-3
3. Diabetes Care. Standards of medical care for patients with Diabetes mellitus. American Diabetes Association Journals, 2003; 49.
4. Fong D, Aiello L, Gardner T, Ferris F, Klein R, et al. Diabetic retinopathy. American Diabetes Association Journals, 2004; 27(10): 2540-53.
5. Klein R, Klein B, Moss S. The Wisconsin epidemiological study of diabetic retinopathy: a review. *Diabetes Metabolism Review*, 1989; 5(7): 559-70.
6. Diabetes Atlas - International Diabetes Federation (IDF). Retrieved from International Diabetes Federation: 2012; <http://www.idf.org/diabetesatlas/5e/middle-east-and-north-africa>
7. Amos A, McCarty D, Zimmet P. The rising global burden of diabetes and its complications: estimates and projections to the year 2010. *Diabetic Medicine; a Journal of the British Diabetic Association*, 1997; 14 (Supp3): S1-85.
8. Javitt J, Aiello L, Chiang Y, Ferris F, Canner J, Greenfield S. Preventive eye care in people with diabetes is cost-saving to the federal government: implications for health-care reform. *Diabetes Care*, 1994; 17(8): 909-17.
9. National Diabetes Data Group. *Diabetes in America*. 1995; (Vol. 2nd ed). Bethesda, MD, Maryland: NIH Publications.
10. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *The New England Journal of Medicine*, 1993; 329(14): 977-86.
11. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *British Medical Journal* 1998; 703-13.
12. Vijan S, Hofer T, Hayward R. Cost-utility analysis of screening intervals for diabetic retinopathy in patients with type 2 diabetes mellitus. *JAMA*, 2000; 283(7): 889-96.
13. Javitt J, Aiello L. Cost-effectiveness of detecting and treating diabetic retinopathy. *Annals of Internal Medicine Journals*, 1996; 124(1PT2): 164-9.
14. Cai X, Wang F, Ji L. Risk Factors of Diabetic retinopathy in type 2 diabetic patients. *Chinese Medical Journal (English Edition)*, 2006;119(10): 822-6.
15. Waked N, Nacouzi R, Haddad N, Zain R. Epidemiology of diabetic retinopathy in Lebanon. *Journal Francais D Ophthalmologie (J Fr Ophthalmol)*, 2006; 29(3): 289-95.
16. Mwendwa F, Otieno C, Kayima J, Amayo E, Otieno P. Risk factor profile and the occurrence of microvascular complications in short-term type 2 diabetes mellitus at Kenyatta National Hospital, Nairobi. *East African Medical Journal*, 2005; 82(12 Suppl): S163-72.
17. Herrera-Bombo J, Aguilar-Diosdado M, Hawkins F, Campos M, Moreno A, et al. Is increasing urinary albumin a better marker for microvascular than for macrovascular complication of type 2 diabetes mellitus? *Nephron Clinical Practice - Karger Publisher*, 2005; 116-21.
18. Parving H, Lewis J, Rayid M, Remuzzi G. Demand investigators. Prevalence and risk factors for microalbuminuria in a referred cohort of type II diabetic patients: a global perspective. *Kidney Int*, 2006; 69(11): 2057-63.
19. Raosoft ® Sample Size Calculator. Retrieved from Raosoft ®: <http://www.raosoft.com/samplesize.html>. 2013
20. Freidman NJ, Kaiser PK, Trattler WB. Review of Ophthalmology 2005; (Vol 1st edition). Pennsylvania, Philadelphia: Elsevier. Inc.
21. Diabetes Prevention Program Research Group. The prevalence of retinopathy in impaired glucose tolerance and recent-onset diabetes in the Diabetes Prevention Program. *Diabetic Med* 2007; 24: 137-44.
22. Wahab S, Mahmood N, Shaikh Z, Kazmi WH. Frequency of retinopathy in newly diagnosed type 2 diabetes patients. *JPMA* 2008; 58: 557-61.
23. Abdollahi A, Malekmadani M H, Mansoori M R, Bostak A, Abbaszadeh M R, Mirshahi A. Prevalence of diabetic retinopathy in patients with newly diagnosed type II diabetes mellitus. *Acta Medica Iranica* 2006; 44: 415-9.
24. Agarwal S, Raman R, Kumari RP, Deshmukh H, Paul PG, Gnanamoorthy P, et al. Diabetic retinopathy in type II diabetics detected by targeted screening versus newly diagnosed in general practice. *Ann Acad Med Singapore* 2006; 35: 531-5.
25. Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V. Prevalence of diabetic retinopathy in urban India: the Chennai Urban Rural Epidemiology Study (CURES) eye study, I. *Invest Ophthalmol Vis Sci* 2005; 46: 2328-33.
26. Rema M, Deepa R, Mohan V. Prevalence of retinopathy at diagnosis among type 2 diabetic patients attending a diabetic center in South India. *Br J Ophthalmol* 2000; 84: 1058-60.
27. Klein R, Klein BE, Moss SE, Linton KL. The Beaver Dam Eye Study. Retinopathy in adults with newly discovered and previously diagnosed diabetes mellitus. *Ophthalmology* 1992; 99: 58-62.
28. Kohner EM, Aldington SJ, Stratton IM, Manley SE, Holman RR, Mathews DR, et al. United Kingdom Prospective Diabetes Study, 30: diabetic retinopathy at diagnosis of non-insulin-dependent diabetes mellitus and associated risk factors. *Arch Ophthalmol* 1998; 116: 297-303.
29. Dorf A, Ballantine EJ, Bennett PH, Miller M. Retinopathy in Pima Indians. Relationships to glucose level, duration of diabetes, age at diagnosis of diabetes, and age at examination in a population with a high prevalence of diabetes mellitus. *Diabetes*. 1976; 25(7): 554-60.

30. Owens DR, Volund A, Jones D, Shannon AG, Jones IR, Birtwell AJ, et al. Retinopathy in newly presenting non-insulin-dependent (type 2) diabetic patients. *Diabetes Res.* 1988; 9(2): 59-65.
31. Nguyen HT, Luzio SD, Dolben J, West J, Beck L, Coates PA, Owens DR. Dominant risk factors for retinopathy at clinical diagnosis in patients with type II diabetes mellitus. *J Diabetes Complications.* 1996; 10(4): 211-19.
32. Nkumbe HE, Kollmann KH, Gaeckle HC. Assessment of diabetic retinopathy in newly diagnosed black Kenyan type 2 diabetics. *East Afr Med J.* 2010; 87(3): 109-14.
33. de Fine Olivarius N, Nielsen NV, Andreasen AH. Diabetic retinopathy in newly diagnosed middle-aged and elderly diabetic patients. Prevalence and interrelationship with microalbuminuria and triglycerides. *Graefes Arch Clin Exp Ophthalmol.* 2001; 239(9): 664-72.
34. Talu S, Kaucsar E, Soreanu A. Diabetic retinopathy in newly diagnosed patients with type II diabetes mellitus. *Oftalmologia.* 2002; 54(3): 27-30.
35. Ramachandran A, Snehalatha C, Vijay V, Viswanathan M. Diabetic retinopathy at the time of diagnosis of NIDDM in south Indian subjects. *Diabetes Res. Clin. Pract.* 1996; 32: 111-14.
36. Harris, MI, Klein R, Welborn TA, Knudman MW. Onset of NIDDM occurs at least 4-7 years before clinical diagnosis. *Diabetes Care.* 1992; 15: 815-19.
37. Layland B. National diabetes visual impairment program. *Clin Exp Optom* 2001; 84: 1-3.
38. Verma L, Gunjan P, Terwari HK, Gupta SK, Murthy GVS, Sharma N. Screening for diabetic retinopathy by non-ophthalmologist: an effective public health tool. *Acta Ophthalmologica Scandinavica* 2003; 81: 373-7.

# The prevalence of metabolic syndrome in Yemeni patients with hypothyroidism

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## Abstract

**Background:** Yemen faces major challenges in improving the health status of its population as it is entering an epidemiological transition with rising non-communicable diseases e.g. obesity, diabetes and cardiovascular diseases (CVDs). We designed this study to find out the prevalence of Metabolic Syndrome (MS) and its components among Yemeni patients with hypothyroidism.

**Methods:** 350 patients with past history or newly diagnosed hypothyroidism (diagnosed as having high TSH, and or low FT4 and FT3) (patients group) and 100 healthy euthyroid volunteers as (control group) attending the outpatients medical clinics at Al-Kuwait University hospital in Sana'a city. The patients and control groups underwent complete history and clinical examination including measurement of blood pressure and waist circumference. The laboratory parameters that were analyzed included fasting samples of plasma glucose, triglycerides, and HDL cholesterol. The diagnosis of MS was based on the Adult Treatment Panel III criteria as the presence of at least 3 of the following: systolic BP >130 mm Hg and/or diastolic BP >85 mm Hg or on treatment for high BP, waist circumference >102 cm for men and >88 cm for women, fasting glucose >110 mg/dl or on diabetes treatment, triglycerides ?150 mg/dl, and HDL cholesterol <40 mg/dl in men and <50 mg/dl in women.

**Results:** from 350 hypothyroid patients and 100 euthyroid volunteers included in this study 233 (66.6%) of hypothyroid patients had subclinical and 117 (33.4%) had overt hypothyroidism. MS was significantly higher in hypothyroid (37.4% ), (76.3%) in patients with subclinical and 31 (23.6%) in patients with overt hypothyroidism, than in the euthyroid group (17%). The commonest occurring metabolic syndrome defined criterion in hypothyroid patients was central obesity 89 (67.9%), high blood pressure 88 (67.1%), reduced high density lipoprotein (61%), high serum triglyceride (59.5%) and raised fasting blood glucose (54.9%).

**Conclusion:** Prevalence of MS is high among Yemeni patients with hypothyroidism and central obesity was the commonest co-morbidity. These findings highlight an urgent need to develop strategies for prevention, detection, and treatment of MS that could contribute to decreasing the prevalence of cardiovascular morbidity and mortality in hypothyroid patients.

**Key words:** hypothyroidism, metabolic syndrome , dyslipidemia

## Introduction

Worldwide prevalence of Metabolic syndrome (MS) ranges from <10% to as much as 84%, depending on the region, urban or rural environment, composition (sex, age, race, and ethnicity) of the population studied, and the definition of the syndrome used (1,2). In general, the IDF estimates that one-quarter of the world's adult population has the MS (3). Higher socioeconomic status, sedentary lifestyle, and high body mass index (BMI) were significantly associated with MS. Cameron et al. have concluded that the differences in genetic background, diet, levels of physical activity, smoking, family history of diabetes, and education all influence the prevalence of the MS and its components (4). The observed prevalence of the MS in National Health and Nutrition Examination Survey (NHANES) was 5% among the subjects of normal weight, 22% among the overweight, and 60% among the obese (6). It further increases with age (10% in individuals aged 20-29, 20% in individuals aged 40-49, and 45% in individuals aged 60-69) (6). The prevalence of MS (based on NCEP-ATP III criteria, 2001) varied from 8% to 43% in men and from 7% to 56% in women around the world (4). Park et al. (5) noticed that there is an increase in the prevalence of MS from 20 years old through to the sixth and seventh decade of life for males and females, respectively. Ponholzer et al. reported that there is high prevalence of MS among postmenopausal women, which varies from 32.6% to 41.5% (7). A Framingham Heart Study report indicated that a weight increase of >2.25kg over a period of 16 years was associated with an up to 45% increased risk of developing the MS (8), and it has been shown by Palaniappan et al. that each 11cm increase in waist circumference (WC) is associated with an adjusted 80% increased risk of developing the syndrome within 5 years (9). The metabolic alterations occur simultaneously more frequently than would be expected by chance and the concurrence of several factors increases cardiovascular risk over and above the risk associated with the individual factors alone (10).

MS is defined by a constellation of an interconnected physiological, biochemical, clinical, and metabolic factors that directly increases the risk of atherosclerotic cardiovascular disease (ASCVD), type 2 diabetes mellitus (T2DM), and all-cause mortality (11,12). This collection of unhealthy body measurements and abnormal laboratory test results include atherogenic dyslipidemia, hypertension, glucose intolerance, pro inflammatory state, and a pro thrombotic state. There have been several definitions of MS, but the most commonly used criteria for definition at present are from the World Health Organization (WHO) (13), the European Group for the study of Insulin Resistance (EGIR) (14), the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) (15), American Association of Clinical Endocrinologists (AACE) (16), and the International Diabetes Federation (IDF) (3). Under current guidelines, revised in 2005 by the National Heart, Lung and Blood Institute (NHLBI) and the American Heart Association (AHA) (16) metabolic syndrome is diagnosed when a patient has at least 3 of the following 5 conditions

- Fasting glucose  $\geq 100$  mg/dL (or receiving drug therapy for hyperglycemia)
- Blood pressure  $\geq 130/85$  mm Hg (or receiving drug therapy for hypertension)
- Triglycerides  $>150$  mg/dL (or receiving drug therapy for hypertriglyceridemia)
- HDL-C  $< 40$  mg/dL in men or  $< 50$  mg/dL in women (or receiving drug therapy for reduced HDL-C)
- Waist circumference  $\geq 102$  cm (40 in) in men or  $\geq 88$  cm (35 in) in women; if Asian American,  $\geq 90$  cm (35 in) in men or  $\geq 80$  cm (32 in) in women (The international diabetes federation [IDF] criteria allow the use of a body mass index [BMI]  $>30$  kg/m<sup>2</sup> in lieu of the waist circumference criterion.)

Abundant data suggest that patients meeting these diagnostic criteria have a greater risk of significant clinical consequences, the 2 most prominent of which are the development of diabetes mellitus (17) and of coronary heart disease. Pooled data from 37 studies involving more than 170,000 patients have shown that metabolic syndrome doubles the risk of coronary artery disease(18). It also increases risk of stroke, fatty liver disease, and cancer.(19)

In recent times there has been an increasing global prevalence of two endocrine disorders, thyroid disorders and type 2 DM, with frequency of thyroid disorders being second to type 2DM. About three percent of the general population has hypothyroidism (20). In community surveys, the prevalence of overt hypothyroidism varies from 0.1 to 2 percent (20-22). The prevalence of subclinical hypothyroidism is higher, ranging from 4 to 10 percent of adults, with possibly a higher frequency in older women (23,24,25,26). However, there is an age-related shift towards higher thyroid-stimulating hormone (TSH) concentrations in older patients and, therefore, if age-adjusted normal ranges are used, the prevalence may not increase with old age. Hypothyroidism is five to eight times more common in women than men, and more common in women with small body size at birth and during childhood (24,27)

Almost one-third of the world's population lives in areas of iodine deficiency(28). In areas where the daily iodine intake is  $<50$   $\mu$ g, goitre is usually endemic, and when the daily intake falls  $<25$   $\mu$ g, congenital hypothyroidism is seen. The prevalence of goitre in areas of severe iodine deficiency can be as high as 80%. Populations at particular risk tend to be remote and live in mountainous areas in South-East Asia, Latin America and Central Africa. Iodization programs are of proven value in reducing goitre size and in preventing goitre development and cretinism in children. Autonomy can develop in nodular goitres leading occasionally to thyrotoxicosis and iodization programmes can also induce thyrotoxicosis, especially in those aged  $>40$  years with nodular goiters (29). In iodine-replete communities, the prevalence of spontaneous hypothyroidism is between 1 and 2%, and it is more common in older women and 10 times more common in women than in men.(30,31).

Hypothyroidism is a well known cause of hypertension, dyslipidemia, endothelial dysfunction and cardiovascular diseases (32,33). Considerable overlap occurs in the pathogenic mechanism of atherosclerotic cardiovascular diseases by metabolic syndrome and hypothyroidism. Insulin resistance has been studied as a basic mechanism in metabolic syndrome (34,35). Role of insulin resistance in development of dyslipidemia in hypothyroidism has been suggested in recent studies (36). Recent data have suggested that there may be some association between serum thyroid function and MS (36). Sub-clinical hypothyroidism (SCH) and overt hypothyroidism (OH) are established risk factors for insulin resistance, hyperlipidemia, hypercoagulability and low grade inflammation (37, 38). Several studies have proved the association between insulin resistance and hypothyroidism for overt hypothyroidism, but there is controversy as to whether this association is also present in sub clinical hypothyroidism. In a recent study it was found that insulin resistance was comparable in both SCH and OH (39, 40). It is known that overt hypothyroidism leads to an increase in plasma cholesterol levels (39, 41). Most studies in sub clinical hypothyroidism show comparable but less pronounced associations (42, 43). The prevalence of thyroid disease in patients with diabetes is significantly higher than that in the general population (44). This indicates a possible interplay between thyroid status and insulin sensitivity.

Insulin resistance leads to an increased production of hepatic cholesterol and very low density lipoproteins (VLDL) (45) and an increased HDL cholesterol (HDL-C) clearance (46). Insulin resistance augments the deleterious effect of hypothyroidism on the lipid profile as suggested by Bakker et al (46). Complex interplay between thyroid function and insulin resistance has been implicated in diabetic dyslipidemia (47).

## Methods

This case control study was conducted in the outpatient department of AL-Kuwait University Hospital Medical Department (Sana'a University, Yemen) in the period between 21st September 2014 to 11 January 2016. 312 patients with hypothyroidism (both subclinical and overt) (case group) and 100 healthy volunteers with normal thyroid function test (control group) were included. The hypothyroid patients who were selected in this study are those who are newly diagnosed by laboratory tests or who are known to have hypothyroidism on hormonal replacement therapy. A high serum TSH level (range between 4.2 uIU/ml to 10 uIU/ml) and normal free thyroxine (FT4) level were required for the diagnosis of sub-clinical hypothyroidism (SCH) (44). Patients with high TSH (> 10 uIU/ml) and low FT4 levels (< 0.93 ng/dl) were classified as having overt hypothyroidism. Patients with normal TSH and FT4 were considered euthyroid.

### Exclusion criteria

- 1- Patients with hyperthyroidism
- 2- Patients who are taking any medication that could affect the thyroid function or lipid level
- 3- Pregnant females
- 4- Patients with renal or liver disorders and congestive

cardiac failure

5- Patients with secondary hypothyroidism or surgically removed thyroid gland

Metabolic syndrome was diagnosed by the presence of three or more of the following criteria (16).

- Fasting glucose  $\geq 100$  mg/dL (or receiving drug therapy for hyperglycemia)
- Blood pressure  $\geq 130/85$  mm Hg (or receiving drug therapy for hypertension)
- Triglycerides  $\geq 150$  mg/dL (or receiving drug therapy for hypertriglyceridemia)
- HDL-C < 40 mg/dL in men or < 50 mg/dL in women (or receiving drug therapy for reduced HDL-C)
- Waist circumference >102 cm (40 in) in men or  $\geq 88$  cm (35 in) in women; if Asian American,  $\geq 90$  cm (35 in) in men or  $\geq 80$  cm (32 in) in women (The international diabetes federation [IDF] criteria allow the use of a body mass index [BMI] >30 kg/m<sup>2</sup> in lieu of the waist circumference criterion.)

All subjects were interviewed about their age, habits, occupation, and past history of diabetes, hypertension, dyslipidemia and hypothyroidism as well as their drug intake. Subjects underwent a physical examination consisting of the determination of waist circumference and systolic and diastolic blood pressure. Waist circumference was measured with a tape measure mid-way between the lower rib margin and the iliac crest. Blood pressure was recorded with the same mercury manometer in the sitting position after 10 - 15 minutes rest. Each subject had two measurements of blood pressure at 5 minutes intervals. Venous blood sampling was performed in the morning after an overnight fast for determination of plasma glucose, triglyceride, and High Density Lipoprotein (HDL) cholesterol. Laboratory techniques for biochemical analysis were glucose oxides for blood glucose, and the enzymatic method for triglyceride and HDL cholesterol.

Serum TSH and FT4 measurements were made using Roche Elecsys modular analytics E 170 using electrochemiluminescence immunoassay (ECLIA method). The analytical sensitivity of TSH was 0.005 uIU/ml and for FT4 was 0.023 ng/dl. Normal range for TSH was (0.27-4.2) uIU/ml and for FT4 was (0.93-1.7) ng/dl.

The research protocol was reviewed and approved by the Ethical Community of the Faculty of Medicine and Health Sciences, Sana'a University. All participants provided informed consent after explaining the study objectives and that the data will be used only for purpose of the research. Health education both verbally and using educational materials was provided to all participants and those who were found to have any medical problem were referred to the specialized clinic for proper management and follow up.

Statistical analysis was undertaken using the Statistical Package for the Social Sciences (Windows version 13.0; SPSS, Chicago IL USA).

Differences between groups were tested statistically using the chi square test for categorical and T test for numerical variables. Data were considered statistically significant when the p-value was  $\leq 0.05$ .

Results

**Table 1: Clinical and laboratory characteristics of hypothyroid and euthyroid group**

Factor	Total=450	Hypothyroid group=350	Euthyroid group=100	p-value
Female gender	341	279(79.7%)	62(62%)	0.002
WS ≥88cm in female ≥102cm in male	148	137(39.1)	11 (11%)	0.008
BP ≥130 85mmg	138	120(34.2)	18(18%)	0.0018
FBS ≥100mg   dl	89	81(23.1%)	8(8%)	0.0008
TG ≥ mg   dl	111	99(28.2%)	12(12%)	0.0008
HDL ≤40 mg   dl in men ≤50 mg   dl in women	120	107(30.5%)	13(13%)	0.0004
<b>MS</b>	<b>127</b>	<b>110 (39.4%)</b>	<b>17(17%)</b>	<b>0.004</b>

WS=waist circumference, BP= blood pressure, FBS = fasting blood sugar, TG = triglyceride, HDL = high density lipoprotein, MS = metabolic syndrome

The overall prevalence of the MS in the hypothyroid group was 37.4%, while the prevalence of MS in the euthyroid group was 17% (P-value > 0.005). In the hypothyroid group subclinical hypothyroidism was more prevalent than overt hypothyroidism (28.5% vs 8.8 %). Patients with hypothyroidism are more frequently female , centrally obese and have high BP than those with normal thyroid function test ( 79.7%, 39.1%, 34.2% vs 62%, 11%, 27% respectively ) also the prevalence of high FBS ,TG, and low HDL was significantly higher in the hypothyroid group than in the euthyroid group (23.1%, 28.2%, 30.5% vs 8%, 12%, 13% respectively ) ( P-value > 0.005 ).

The physical and metabolic characteristics of the hypothyroid patients with and without MS are shown in Table 2.

**Table 2. The physical and metabolic characteristics of the study population by Metabolic Syndrome**

Factors	Total =350	With MS=131 -subcli.100 -clinical=31	Without MS =219 -subcli.114 -clinical=113	P-value
Male gender	64(18.2%)	15 (11.4%)	49 (22.3%)	0.0103
Central obesity	137 (39.1%)	89 (67.9%)	48 (21.9%)	0.005
BP  mmHg	120 (34.2%)	88 (67.1%)	32 (14.6%)	0.005
FBS≥ 100md   dl	81 (23.1%)	60 (45.8%)	21 (9.5%)	0.005
SerumTG≥150mg   dl	99 (28.2%)	75 (57.2%)	24 (10.9%)	0.005
Serum HDL ≤40mg in males , ≤50mg in females	107 (30.5%)	81 (61.8%)	26 (11.8%)	0.005

The prevalence of MS was statistically significantly higher in female patients with hypothyroidism and MS than in those without MS. Also central obesity was higher in patients with hypothyroidism and MS than in those without MS (P-value =0.005). BP was higher in patients with hypothyroidism and MS than in those without MS.

Regarding laboratory parameters patients with hypothyroidism and MS had higher prevalence of FBS, serum TG and serum HDL than those without MS (P- value ≤ 0.05). The highest prevalent comorbidity in hypothyroid patients with MS was central obesity (67.9%) followed by high BP (67.1%), low serum HDL (61.8%), high TG (57.2%) and raised fasting blood glucose (45.8%).

## Discussion

This study analyzed the prevalence of the MS in hypothyroid patients who attended the medical clinics in Al-Kuwait University Hospital (Sanaa City, Yemen) using the NCEP - ATP III criteria for definition of the metabolic syndrome. There are a few international comparable studies of the MS among adult hypothyroid patients but we could not find similar studies from nearby Arabic countries among such high risk groups. The several definitions of the syndrome that are in use (i.e. the International Diabetes Federation criteria, the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III definition, the WHO criteria), makes it difficult to compare prevalence and impact. Furthermore, since our study is a hospital-based study, the findings could not be generalized to the whole population. Nevertheless, as this is the first study about the MS from Yemen among hypothyroid patients, its results provide invaluable information on the MS in such a high risk group and should encourage researchers to investigate more on such an emerging health problem.

Metabolic syndrome (MS) and hypothyroidism are well-established forerunners of atherogenic cardiovascular disease. MS includes a cluster of risk factors characterized by hypertension, dyslipidemia, hyperglycemia, and prothrombotic and proinflammatory conditions which accelerate the atherogenic process in the body. (51,52). Hypothyroidism is well known to cause hyperlipidemia, diastolic hypertension, endothelial dysfunction, and cardiovascular disease.(53,54). Considerable overlap occurs in the pathogenic mechanisms of atherosclerotic cardiovascular disease by MS and hypothyroidism. Insulin resistance has been studied as the basic pathogenic mechanism in MS (55,56). Role of insulin resistance in development of dyslipidemia in hypothyroidism has been suggested in recent studies(57). This relationship with insulin resistance can lead to a considerable overlap between the population subsets of MS and hypothyroidism as well.

The prevalence of MS in the hypothyroid group was 37.4% which is significantly higher than in the euthyroid group 17% ( P-value =0.005 ), also the prevalence of different MS comorbidities was higher in the hypothyroid than in the euthyroid group (Table 1) (58, 59,62).

The overall prevalence of the MS among hypothyroid patients in the present study was found to be 37.4% while the prevalence of MS in patients with subclinical hypothyroidism was 28.5% which is comparable to that found among hypothyroid patients in Nigeria (40%) in all hypothyroid and 35% in patients with subclinical hypothyroidism (59) and Bulgaria (34.9%) (60), and in Turkey (44%) in hypothyroid group and 35% in subclinical hypothyroid group (61), but still lower than what was found in Dhaka hypothyroid patients (82.5%) (62).

The prevalence of different MS comorbid conditions ( central obesity, Hypertension , FBS, high serum TG and low HDL) was statistically significantly higher in hypothyroid

patients with MS than in hypothyroid patients without MS. These findings are in concurrence with other studies which reported that both overt and subclinical hypothyroidism well effect each component of MS including blood pressure and metabolism of carbohydrate and lipids (54, 55,62).

Of the components of MS, central obesity was the prevalent MS defining criteria followed by high BP, low serum HDL, high serum TG and high FBS (56,57 ). Thyroid hormones play essential roles in regulating energy balance, metabolism of glucose and lipids and thus effects metabolic syndrome parameters including HDL-C, triglycerides, blood pressure and plasma glucose (63). Hypothyroidism is associated with obesity, dyslipidemia and increased risk of atherogenic cardiovascular diseases (64).

Obesity, a key component of metabolic syndrome, occurs due to increased energy intake, decreased energy expenditure, or a combination of both, thus leading to a positive energy balance. Thyroid hormones up-regulate metabolic pathways relevant to resting energy expenditure, hence, obesity and thyroid functions are often correlated. On one hand, obesity per se causes alterations in thyroid hormones, i.e., increased thyroid hormone levels,( 65), increased thyroid stimulating hormone (TSH) with no effect on T 3 and T 4 ,(66) or increased TSH and T 3 with no effect on T 4, (67) while on the other hand, subclinical hypothyroidism as a result of slow metabolism can also lead to obesity,(68, 69). The mechanism of normal levels of T 3, T 4 with increased TSH in metabolic syndrome is not defined, but it has been hypothesized that metabolic syndrome is associated with insulin resistance due to the defect in post-receptor signal transduction in target tissue; a similar mechanism of thyroid receptor resistance might be operating in these obese persons.

In a study done by Kumar et al., T 3 showed positive correlation with triglycerides, low density lipoprotein cholesterol (LDL-C), total cholesterol, insulin, HOMA-IR (insulin resistance) and negative correlation with body fat. TSH correlated positively with BMI, insulin, HOMA-IR, LDL-C and negatively with high density lipoprotein cholesterol (HDL-C) (P < 0.05). Free triiodothyronine (FT 3) correlated positively with waist circumference and T 4 did not show correlation with metabolic syndrome parameters(69). In a large Chinese case control study, all components of the metabolic syndrome were associated with systematically higher TSH levels (Lai et al.)(70). In a study done by Chugh et al.,(2012) evaluating the thyroid function tests in individuals with metabolic syndrome to explore the possibility of thyroid receptor resistance, a significant increase was found in TSH levels in patients as compared to controls, while T 3 and T 4 levels were comparable in patients and controls concluding that raised TSH in patients with metabolic syndrome independent of lowered T 3 and T 4 suggests it to be a part and parcel of this syndrome(71). Another study done by Meher et al., (2013) found that body mass index, waist circumference, mean systolic pressure, diastolic pressure, fasting blood sugar, total cholesterol, LDL-C, triglycerides, and TSH were significantly higher, and FT3, free thyroxine (FT4)

and HDL-C were significantly lower in the metabolic syndrome patients compared to the control group concluding that there is a significant association between subclinical hypothyroidism and metabolic syndrome, and it highlights the importance of thyroid function tests in patients with metabolic syndrome.(64,72). It is still not clear whether alterations in thyroid hormones are a cause or an effect of obesity (metabolic syndrome) suggesting need for further evaluation on a large scale with inclusion of various hormones elaborated by adipose tissue (like leptin, resistin, adiponectin, etc.).

## Conclusion

We conclude that metabolic syndrome was common in hypothyroid patients which could be explained by the metabolic syndrome per se or be due to different metabolic co-morbidities that are associated with it.

## References

- 1- Desroches S, Lamarche B; "The evolving definitions and increasing prevalence of the metabolic syndrome," *Applied Physiology, Nutrition and Metabolism*, vol. 32, no. 1, pp. 23-32, 2007.
- 2- "The prevalence of metabolic syndrome in various populations," *The American Journal of the Medical Sciences*, vol. 333, no. 6, pp. 362-371, 2007.
- 3- International Diabetes Federation: The IDF consensus worldwide definition of the metabolic syndrome
- 4- Cameron A. J., Shaw J. E, and Zimmet P. Z., "The metabolic syndrome prevalence in worldwide populations," *Endocrinology and Metabolism Clinics of North America*, vol. 33, no. 2, pp. 351-375, 2004.
- 5- Park Y.-W, Zhu S, Palaniappan L, Heshka S, Carnethon M.R, and S. B. Heymsfield, "The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988-1994," *Archives of Internal Medicine*, vol. 163, no. 4, pp. 427-436, 2003.
- 6- Ford E.S, Giles W.H, and Dietz W.H, "Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey," *Journal of the American Medical Association*, vol. 287, no. 3, pp. 356-359, 2002
- 7- Ponholzer A, Temml C, Rauchenwald M, Marszalek M, and Madersbacher S, "Is the metabolic syndrome a risk factor for female sexual dysfunction in sexually active women?" *International Journal of Impotence Research*, vol. 20, no. 1, pp. 100-104, 2008
- 8- Wilson P.W.F, Kannel W.B, Silbershatz H, and D'Agostino R.B, "Clustering of metabolic factors and coronary heart disease," *Archives of Internal Medicine*, vol. 159, no. 10, pp. 1104-1109, 1999
- 9- Palaniappan L, Carnethon M.R, Wang Y et al., "Predictors of the incident metabolic syndrome in adults: The Insulin Resistance Atherosclerosis Study," *Diabetes Care*, vol. 27, no. 3, pp. 788-793, 2004.
- 10- Reilly M. P. and Rader D. J., "The metabolic syndrome: more than the sum of its parts?" *Circulation*, vol. 108, no. 13, pp. 1546-1551, 2003
- 11- Grundy S. M., Cleeman J. I., Daniels S. R. et al., "Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement," *Circulation*, vol. 112, no. 17, pp. 2735-2752, 2005
- 12- Wilson P. W. F., D'Agostino R. B., Parise H., Sullivan. S, and Meigs J. B., "Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus," *Circulation*, vol. 112, no. 20, pp. 3066-3072, 2005
- 13- Alberti K. G. and Zimmet P. Z., "Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation," *Diabetic Medicine*, vol. 15, no. 7, pp. 539-553, 1998.
- 14- Balkau B and Charles M.A, "Comment on the provisional report from the WHO consultation: European Group for the Study of Insulin Resistance (EGIR)," *Diabetic Medicine*, vol. 16, no. 5, pp. 442-443, 1999
- 15- Cleeman J.I, "Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III)," *Journal of the American Medical Association*, vol. 285, no. 19, pp. 2486-2497, 2001.
- 16- Einhorn D, Reaven. G.M, Cobin R.H et al., "American College of Endocrinology position statement on the insulin resistance syndrome," *Endocrine Practice*, vol. 9, no. 3, pp. 237-252, 2003
- 17- Hanley AJ, Karter AJ, Williams K, et al. Prediction of type 2 diabetes mellitus with alternative definitions of the metabolic syndrome: the Insulin Resistance Atherosclerosis Study. *Circulation*. Dec 13 2005;112(24):3713-21.
- 18- Gami AS, Witt BJ, Howard DE, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol*. Jan 30 2007;49(4):403-14.
- 19- Giovannucci E. Metabolic syndrome, hyperinsulinemia, and colon cancer: a review. *Am J Clin Nutr*. Sep 2007;86(3): s836-42.
- 20- Tunbridge WM, Evered DC, Hall R, et al. The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinol (Oxf)* 1977; 7:481.
- 21- Vanderpump MP, Tunbridge WM, French JM, et al. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. *Clin Endocrinol (Oxf)* 1995; 43:55.
- 22- Vanderpump MP, Tunbridge WM. The epidemiology of thyroid diseases. In: *The thyroid: A fundamental and clinical text*, 8th, Braverman LE, Utiger RD (Eds), Lippincott Williams and Wilkins, Philadelphia 2000. p.467.
- 23- Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. *Arch Intern Med* 2000; 160:526.
- 24- Aoki Y, Belin RM, Clickner R, et al. Serum TSH and total T4 in the United States population and their association with participant characteristics: National Health and Nutrition Examination Survey (NHANES 1999-2002). *Thyroid* 2007; 17:1211
- 25- Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition

- Examination Survey (NHANES III). *J Clin Endocrinol Metab* 2002; 87:489.
- 26- Walsh JP, Bremner AP, Feddema P, et al. Thyrotropin and thyroid antibodies as predictors of hypothyroidism: a 13-year, longitudinal study of a community-based cohort using current immunoassay techniques. *J Clin Endocrinol Metab* 2010; 95:1095.
- 27- Kajantie E, Phillips DI, Osmond C, et al. Spontaneous hypothyroidism in adult women is predicted by small body size at birth and during childhood. *J Clin Endocrinol Metab* 2006; 91:4953.
- 28- DeRuiter J.(2002). "Thyroid pathology" (PDF). *Endocrine Module (PYPP 5260)*. Auburn University School of Pharmacy. p. 30.
- 29- Vanderpump MP; Tunbridge WM; French JM; Appleton D; Bates D; Clark F; Grimley Evans, J; Hasan DM et al. (1995). "The incidence of thyroid disorders in the community: a twenty-year follow-up of Whickham Survey". *Clinicalendocrinology* 43 (1): 55-68.
- 30- Fatourech V. (2009). "Subclinical Hypothyroidism: An Update for Primary Care Physicians". *Mayo Clinic Proceedings* 84 (1): 65-71.
- 31- Hak AF, Pols HF, Visser T. Subclinical hypothyroidism is an independent risk factor of atherosclerosis and myocardial infarction in elderly women .*The Rotterdam study. Study Ann.Intern.Med,200,132 ; 270-278*
- 32- Fernandez Real JM. Lopez-Bermejo A. Castro A, Casamitjana R. thyroid function is intrinsically linked to insulin sensitivity and endothelial dependent vasodilation in healthy euthyroid subject .*J.Clin.Endocrinol Meteb.2006;91;3337-43*
- 33- Reaven GM . Banting lecture , 1`988, rule of insulin resistance in human diseases , *Diabetes* 1988,37,1595-607
- 34- DeFronzo RA , Ferrannini F. Insulin resistance a multi faceted syndrome responsible for NIDDM, hypertension , dyslipidemia , and atherosclerotic cardiovascular diseases , *Diabetes care* , 1991, 14; 173-94
- 35- Singh BM, Goswami B, Maliko V. Association between insulin resistance and hypothyroidism in females attending a tertiary care hospital .*Indian J.Clin.Biochem.2010,25;141-5*
- 36- Serter R, Demirbas B, Culha C, Cakal E. The effect of L-thyroxine replacement therapy on lipid based cardiovascular risk in sub clinical hypothyroidism. *Invest J Endocrinol* 2004; 27:897-903.
- 37- American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. *Endocr Pract.* 2002; 8:457-69.
- 38- Fommei E, Iervasi G. The role of thyroid hormone in blood pressure homeostasis: evidence from short-term hypothyroidism in humans. *J Clin Endocrinol Metab* 2002; 87: 1996-2000.
- 39- Maratou E, Hadjidakis D, Kollias A, Tsegka K, Peppas M, Alevizaki M, et al. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. *Eur J Endocrinol* 2009 (In press)
- 40- Duntas LH. Thyroid disease and lipids. *Thyroid* 2002; 12:287-93.
- 41- Biondi B, Klein I. Hypothyroidism as a risk factor for cardiovascular disease. *Endocrine* 2004; 24: 1-13.
- 42- Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. *Arch Intern Med* 2000; 160: 526-34.
- 43- Reaven GM. Banting lecture. Role of insulin resistance in human disease. *Diabetes* 1988; 37: 1595-607.
- 44- Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA* 2001; 285: 2486-97.
- 45- Alberti KG, Zimmet P, Shaw J. The metabolic syndrome- a new worldwide definition. *Lancet* 2005; 366: 1059-62.
- 46- Bakker SJL, Ter Maaten JC, Popp-Snijders C, Slaets JPJ, Heine RJ, Gans ROB. The relationship between thyrotropin and low density lipoprotein cholesterol is modified by insulin sensitivity in healthy euthyroid subjects. *J Clin Endocrinol Metab* 2001; 86: 1206-11.
- 47- Chubb SAP, Davis WA, Inman Z, Davis TME. Prevalence and progression of subclinical hypothyroidism in women with type 2 diabetes: the Fremantle Diabetes Study. *Clin Endocrinol (Oxf)* 2005
- 48- Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2005;365:1415
- 49- Grundy SM. Metabolic syndrome: Connecting and reconciling cardiovascular and diabetes worlds. *J Am Coll Cardiol* 2006;47:1093-100.3.
- 50- Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: The Rotterdam Study. *Ann Intern Med* 2000;132:270-8.4.
- 51- Fernández-Real JM, López-Bermejo A, Castro A, Casamitjana R, Ricart W. Thyroidfunctionis intrinsically linked to insulin sensitivity and endothelium-dependent vasodilation in healthy euthyroid subjects. *J Clin Endocrinol Metab* 2006;91:3337-43.5.
- 52- Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes* 1988;37:1595-607.6.
- 53- DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care* 1991;14:173-94.7.
- 54- Singh BM, Goswami B, Maliko V. Association between insulin resistance and hypothyroidism in females attending a tertiary care hospital. *Indian J Clin Biochem* 2010;25:141-5
- 55- Pangaluri R,William E,A; The prevalence of metabolic syndrome and its components in women with subclinical hypothyroidism; *Asian journal of pharmaceutical and clinical research* ; 6;4; 2013
- 56- Duntas LH. Thyroid diseases and lipids. *Thyroid* 2002 , 12; 287-293
- 57- Jee-Young Oh, Yeon-Ah Sung, Hye Jin Lee Elevated thyroid stimulating hormone levels are associated with metabolic syndrome in euthyroid young women *J Endocrinol Metab.* 2012 May-Jun; 16(3): 417-422.
- 58- Anthonia O. Ogbera, Sonny Kuku, and Olusola Dada. The metabolic syndrome in thyroid disease: A report from

Nigeria; *Indian J. Intern. Med* 2013; 28(2): 180-18

59- Shinkov A, Borissova M,A. Kovatcheva R. The prevalence of the metabolic syndrome increases through the quartiles of thyroid stimulating hormone in a population-based sample of euthyroid subjects; *Arq Bras Endocrinol Metab* vol.58 no.9 São Paulo Dec. 2011

60- Erdogan M, Canataroglu A, Ganidagli S, Kulaks?ozglu M. Metabolic syndrome prevalence in subclinic and overt hypothyroid patients and the relation among metabolic syndrome parameters; *J Endocrinol Invest.* 2011 Jul-Aug;34(7):488-92. doi: 10.3275/7202. Epub 2010 Jul 22

61- Haque R, Ferdousi, S. Rahman W, Uddin MN; metabolic syndrome in hypothyroid patients *Bangladesh J Med. Biochem.* 2014, 7(2) 57-6

62- Kumar HK, Yadav RK, Prajapati J, Reddy CV, Association between thyroid hormone , insulin resistance and metabolic syndrome .*Saudi Med. J.* 2009, 30 ,907-11

63- Cappola AR, Landenson PW. Hypothyroidism and atherosclerosis .*J.Clin. Endocrinol.Met.* 2004;88.2438-44

64- Michalaki MA, Vagenakis AG, Leonardou AS, Argentou MN, Habeos IG, Makri MG, et al. Thyroid function in humans with morbid obesity. *Thyroid* 2006;16:73-8.

65- Bastemir M, Akin F, Alkis E, Kaptanoglu B. Obesity is associated with increased serum TSH level, independent of thyroid function. *Swiss Med Wkly* 2007;137:431-4.

66- Reinehr T, de Sousa G, Andler W. Hyperthyrotropinemia in obese children is reversible after weight loss and is not related to lipids. *J Clin Endocrinol Metab* 2006;91:3088-91.

67- Bhowmick SK, Dasari G, Levens KL, Rettig KR. The prevalence of elevated serum thyroid-stimulating hormone in childhood/adolescent obesity and of autoimmune thyroid diseases in a subgroup. *J Natl Med Assoc* 2007;99:773-6

68- Jayakumar RV, Nisha B, Unnikrishnan AG, Nair V, Kumar H. Thyroid status in metabolic syndrome - a clinical study. *Thyroid Res Pract* 2010;366-70

69- Kumar HK, Yadav RK, Prajapati J, Reddy CV, Raghunath M, Modi KD. Association between thyroid hormones, insulin resistance and metabolic syndrome. *Saudi Med J* 2009;30:907-11.

70- Lai Y, Wang J, Jiang F, Wang B, Chen Y, Li M, et al. The relationship between serum thyrotropin and components of metabolic syndrome. *Endocr J* 2011;58:23-30.

71- Chugh K, Goyal S, Shankar V, Chugh SN. Thyroid function tests in metabolic syndrome. *Indian J Endocr Metab* 2012;16:958-61.

72- Meher LK, Raveendranathan SK, Kota SK, Sarangi J, Jali SN. Prevalence of hypothyroidism in patients with metabolic syndrome. *Thyroid Res Pract* 2013;10:60-4

# Prevalence and determinants of Unintended Pregnancy: Systematic Review

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## Abstract

**Background:** Unplanned pregnancy is one of the leading causes of maternal mortality and morbidity in the world. The objective of this systematic review was to synthesize the findings of various studies regarding prevalence and determinates of unintended pregnancy.

**Data sources:** A range of electronic databases was searched for studies conducted in developing countries and published between 1990 and 2015. English-language publications were searched using relevant keywords, and reference lists were hand searched.

**Review methods:** A systematic review was carried out for all the quantitative studies which met the inclusion criteria. The quality of selected studies was assessed using Newcastle-Ottawa Scale.

**Results:** Twenty-two papers were included in the review. Average prevalence of unintended pregnancy was estimated to be 35% ranging from 13% to 82%. The predictors of unintended pregnancy were found to be, socio-demographic factors include women's age, women's education, parity, birth order and interval, previous pregnancy intention, age at the time of marriage, socioeconomic status, marital status, religion, caste, and ethnicity.

**Conclusion:** Main correlates were found to be age, parity, educational and economic status. This means that undertaking outreach in poor countries might be helpful in fulfilling the needs of Family planning for these women. Furthermore, community-based distribution of family planning methods or counseling should be targeted to the illiterate older aged women of reproductive age with poor socioeconomic status.

**Key words:** unintended pregnancy, developing countries, prevalence, predictors, systematic review

## Introduction

According to United Nations (UN) estimation, the world population is going to reach to 8.1 billion by the year 2025. Developing countries are attributing to 97% of this burden, which means 75-78 million people are added annually by developing countries(1). If this addition persists, the population of developing countries will increase from 5.9 billion (in 2013) to 8.2 billion (in 2050) and Asia and Africa countries will contribute 90% of the increase in population(2). The reason that developing countries will contribute more towards the world's population is because of their high birth rate, which in turn is due to low contraceptive use(2).

Worldwide use of the modern method of contraception has increased from 54% to 57%; however contraceptive usage rates vary widely across the world(3). In developed countries, more than 80% of women in reproductive age group (15-49 years) use contraceptives(2), while contraceptive use is much lower in African (21%) and Asian (67%) countries(2). The relatively high usage rates in Asia are driven to a large extent by near abundant usage in China (85%), Iran (79%), Sri Lanka (68%), Japan (54%), India (54%), Bhutan (66 %) and Indonesia (61%). While Pakistan (35%), Afghanistan (23%), Maldives (35%) and Nepal (48%) still lag behind(4, 5). Low contraceptive prevalence rates are directly related to a high number of unintended pregnancies(4).

Unintended pregnancies are reported to have been either unwanted (i.e. occurred when no more children, were desired) or mistimed (occurred earlier than desired)(6). Out of 210 million pregnant women, 75 to 80 million women experience unintended pregnancies, of which approximately 42 to 46 million pregnancies are terminated annually worldwide (2, 7, 8).

Currently, both developed and developing countries are facing the problem of unintended pregnancies (9, 10). Although worldwide, from 1995 to 2008 the rate of unintended pregnancy has declined by 20%, from 69 to 55 per 1000 women(9, 10). This decline in the rate of unintended pregnancy was greater in the developed world, where it fell by 29 percent (from 59 to 42 per 1000 women); while it declined by 20 percent, from 71 to 57 per 1000 women in the developing countries(9, 10). The highest rates of unintended pregnancies were in Africa (86 /1000 women) and the lowest were in Europe (38/1000 women) (9, 10).

Despite such decline in rates of unintended pregnancies, its proportion is still high i.e. about 4 out of 10 pregnancies (40%) were unintended worldwide in 2008, with a high proportion in South America and Southern Africa, where 6 out of 10 pregnancies were unintended(9, 10). It was even more in developing regions like Latin America and the Caribbean region (58%), South Africa (59%), South America (64%) and North America (48%)(9, 10).

Unplanned pregnancy is one of the leading causes of maternal mortality and morbidity in South Asia(6). It is estimated that every year about one-third of pregnancies are declared unintended in South and South-East Asia. In 2008, the proportion of unintended pregnancies in Bangladesh was 30%, while it was 21% in India and 35% in both Iran(10) and Nepal(1), 46 % both in Yamagata (Japan) and Pakistan(11, 12). Various reasons for unintended pregnancies have been identified, which include non-use of contraceptive methods and contraceptive method failure(13). Non- use of contraceptive methods is one of the important reasons for unintended pregnancy, which is mainly due to the high unmet need for contraceptives. Contraceptive method failure incorporates both users and technological faults(13).

In addition to this, different factors may predict or determine unintended pregnancy and numerous studies have reported different predictors of unintended pregnancies. Although the prevalence and determinants of unintended pregnancy are reported from multiple countries through various studies, however these studies are not compiled and synthesized particularly both from developed and developing countries. Thus, the objective of this systematic review was to synthesize the findings of various studies regarding prevalence and determinates of unintended pregnancy.

## Methods

### Eligibility criteria

Eligible studies were those that were cohort or demographic health surveys, conducted in low-, middle or high-income countries, reported the prevalence and risk factors of unintended pregnancy and reported estimates of the odds ratio, risk ratio, or relative risk.

### Search strategy

Under guidance of the librarian, we searched a range of electronic bibliographic databases: Medline and Embase through Ovid (1990 to 2015), Cochrane Library through Wiley Interscience, Cumulative Index to Nursing and Allied Health Literature (CINAHL) through EBSCO Host, PubMed through the National Center for Biotechnology Information (NCBI), and SCOPUS through Elsevier. We used a combination of Medical Subject Headings keywords, and text words for "unintended AND pregnancy", "prevalence", "mistimed", "unwanted", "risk factors", "predictors", "determinants" and "correlates" that appeared in abstracts and titles.

### Search outcome

#### **Data abstraction and quality assessment**

Two reviewers (Medical doctors) independently abstracted data from all of the included studies. Abstracted data included study design; type of database used for analysis (population-based or hospital-based); characteristics of the study subjects, unintended pregnancy definition; potential confounders or effect modifiers considered; and risk ratio or odds ratio for unintended pregnancy. We assessed the quality of each study using the Newcastle-Ottawa

Scale(14) for all studies. Differences in data abstraction were resolved by consensus between two reviewers.

## Results

### Search outcome

Of 4598 research papers initially identified using the search criteria, 4430 articles were found to be irrelevant after reviewing the titles. The abstracts of the remaining 168 papers with relevant articles were then examined. Of these, 130 abstracts were found to be irrelevant. Thus, full papers of the remaining 38 abstracts were accessed and 6 were found to be duplicates. Finally, 32 full papers were assessed for quality and eligibility. Thus, 22 unique citations were identified which met the inclusion criteria (Figure 1). The characteristics of the individual studies are summarized in Table 1.

Those studies which were conducted from 1990 to 2015 were retrieved for this review. Studies varied with regard to criteria for defining unintended pregnancy. Some of the studies had assessed the intention through binary outcome (intended or unintended) while others had assessed the intention under three categories (mistimed, wanted and unwanted). All studies were quantitative and among the selected studies, 8 analyzed secondary data from demographic health surveys or other national health surveys, while 14 were primary studies including 12 cross-sectional studies and 2 cohort studies.

Of the 22 studies, 18 had measured the prevalence of unintended pregnancy and 22 had measured the determinants of unintended pregnancy. Of these 22 studies, 11 were from Africa, 9 from Asia, 1 each from Europe and North America. All the determinants were categorized into three themes i.e. Socio-demographic factors, Affordability and women's knowledge, attitudes, beliefs and culture.

### Prevalence of Unintended pregnancy

Of the 18 studies which had measured the prevalence of unintended pregnancy, it was found that average prevalence was estimated to be 35% ranging from 13% to 82%.

### Factors determining the unintended pregnancy

#### Socio-demographic factors

Socio-demographic factors included women's age, women's education, parity, birth order and interval, previous pregnancy intention, age at the time of marriage, socioeconomic status, marital status, religion, caste, and ethnicity. Thirteen studies found that women's age was the best predictor of pregnancy intention (Table 1). Of these, 8 studies showed that older women were more likely to experience unintended pregnancy (15-21) while five studies had shown that younger women were at risk of unintended pregnancy (17, 21-24). Seven studies found that women's education was the best predictor of pregnancy intention (Table 1). Of these, 5 studies showed that women with primary or less education were more likely to experience unintended pregnancy (17, 19, 25-27) while two studies had shown contradictory findings(20, 26).

Ten studies found strong associations between parity and pregnancy intention (Table 1). Among all the studies, higher parity was generally found to be the positive predictor of unintended pregnancy. In addition to this, four studies found strong associations between age at the time of marriage and pregnancy intention (Table 1). All the studies had shown the inverse relation between age at the time of marriage and pregnancy intention, as the age at the time of marriage increased, the likelihood of unintended pregnancy reduced (20, 28-30). Likewise, five studies showed that religion played a significant role for the pregnancy intention. Around 60% of these studies found that non-Muslims were less likely to experience unintended pregnancy as compared to Muslims while 40% had shown the opposite findings(17, 31).

Seven studies found strong associations between marital status and pregnancy intention (Table 1). Of these, four studies found that married women were less likely to experience unintended pregnancy as compared to unmarried women. Three studies found that married women were more at risk of experiencing unintended pregnancy (Table 1).

#### Affordability

Eight studies found significant relationships between economic factors (socio-economic status or income of the household, working status of woman and woman's employment) and pregnancy intention (20, 28-30). The financial constraint was the most important factor determining the intention of pregnancy. Generally, women with high economic status were less likely to experience unintended pregnancy except the one study, which contradicted the above findings.

#### Women's knowledge, attitudes, beliefs, and culture

Different variables were included under this category like access to media, knowledge and practice of Family planning methods. Only one study from Nepal showed that exposure to mass media (radio) significantly predicted pregnancy intention (Table 1). Women with high levels of exposure were less likely to experience unintended pregnancy(28).

Four studies had found the strong association between pregnancy intention and knowledge of Family planning methods (Table 1). Of these 4 studies, 50% had shown that knowledge was positively associated with pregnancy intention and 50% of these had shown the negative association between two variables(28, 32). Additionally, eight studies had shown that contraceptive usage had also shown significant association with unintended pregnancy, 6 studies found the positive association with unintended pregnancy while 2 studies found the negative association.

**Table 1: Prevalence and determinants of unintended pregnancy (Part 1)**

Study	Year	Country	Study design	Prevalence of Unintended pregnancy	Important Statistically significant factors
Kamal Mustafa et al.	2011	Bangladesh	Bangladesh Demographic & Health Survey	30%	<ul style="list-style-type: none"> <li>Higher Socioeconomic status: OR 0.74 (95% CI 0.59-0.93) and 0.63 (95% CI 0.47-0.84) respectively</li> <li>Ever use of contraceptive methods: OR 1.81 (95% CI 1.20-2.72) and 1.92 (95% CI 1.54-2.39)</li> </ul>
Ikamari L et al.	2013	Kenya	Cross sectional survey	24%	<ul style="list-style-type: none"> <li>Age 20-34: OR 0.20 &amp; 35-49: OR 0.19</li> <li>Currently married women: OR 0.09 (p&lt;0.001) &amp; formerly married: 0.15 (p&lt;0.001)</li> <li>Parity 3+: 2.45 (p&lt;0.001)</li> </ul>
Ma. Q et al.	2013	China	Cross sectional study	43%	<ul style="list-style-type: none"> <li>Married women: OR 2.99 (95% CI 1.12-7.96)</li> </ul>
Kassa N et al.	2012	Ethiopia	Kersa Demographic Surveillance and Health Survey	27%	<ul style="list-style-type: none"> <li>Age &gt;40 years: OR 4.08 (95% CI 1.14-14.21)</li> <li>Parity 5-6 births: OR 6.12 (95% CI 2.41-15.57) &amp; 7+ births: OR 14.34 (95% CI 5.72-35.98)</li> <li>Poor wealth quintile: OR 1.68 (95% CI 1.26-2.25)</li> </ul>
Youseef RM et al.	2003	Egypt	Cross sectional survey	24%	<ul style="list-style-type: none"> <li>Age of women &lt;30 years: OR 2.1 (95% CI 1.28-3.44)</li> <li>Never used contraceptives: OR 2.31 (95% CI 1.52-3.45)</li> <li>&gt;2 living children: 1.91 (95% CI 1.16-3.15)</li> </ul>
Habte D et al.	2013	Ethiopia	Ethiopian Demographic and Health Survey	Not calculated	<ul style="list-style-type: none"> <li>Age 25-29 years: OR 0.46 (95% CI 0.25-0.83) &amp; 30-34 years: OR 0.40 (95% CI .20-.78)</li> <li>Primary education: OR 2.38 (1.73-3.26)</li> <li>Ever use of family planning: OR 1.79 (95% CI 1.31-2.45)</li> <li>&gt;5 ever born children: OR 2.36 (95% CI 1.01-5.49)</li> </ul>
Tebekaw et al.	2014	Ethiopia	Ethiopian Demographic and Health Survey	32%	<ul style="list-style-type: none"> <li>Age 15-19: OR 1.68 (95% CI 1.25-2.25)</li> <li>Secondary education: OR 0.5 (0.33-0.76)</li> <li>Rich women: OR 3.11 (95% CI 1.32-7.32)</li> <li>Parity 6+: OR 2.56 (1.43-4.57)</li> <li>Married women: OR 0.18 (95% CI 0.12-0.53)</li> <li>Knows at least one contraceptive method: OR 1.78 (95% CI 1.21-2.62)</li> </ul>

Table 1: Prevalence and determinants of unintended pregnancy (Part 2)

Eliason S et al.	2014	Ghana	Cross sectional survey	70%	<ul style="list-style-type: none"> <li>Parity 5+: OR 6.06 (95% CI 3.24-11.38)</li> <li>Marital status (engaged) OR 1.58 (95% CI 1.10-2.28); cohabitation OR 2.91 (1.96-4.31); Single OR 7.32 (95% CI 4.21-12.75)</li> <li>Awareness of traditional family planning method: OR 0.66 (95% CI 0.49-0.89)</li> </ul>
Takahashi S. et al	2012	Japan	The Hamamatsu Birth Cohort (HBC) Study	Not calculated	<ul style="list-style-type: none"> <li>≤ 12 years of education: OR 1.7 (95% CI 1.0-2.9) &amp; ≥ 17 years of education: OR 3.3 (1.1-9.9)</li> <li>Household income ≥8 million JPY: OR 0.4 (95% CI 0.2-0.9)</li> </ul>
Dixit P et al.	2012	India	National Family Health surveys	Not calculated	<ul style="list-style-type: none"> <li>Muslim women: OR 1.27 (95% CI 1.02-1.60)</li> <li>Ever used contraceptives: OR 1.85 (95% CI 1.64-2.09)</li> </ul>
Adhikari R et al.	2009	Nepal	Nepal Demographic and Health Survey	41%	<ul style="list-style-type: none"> <li>Age of women (OR 1.105),</li> <li>Ideal number of children (OR 0.725),</li> <li>Knowledge of family planning methods (OR 0.60)</li> </ul>
Faye CM et al.	2013	Senegal	Cross sectional survey	14.3%	<ul style="list-style-type: none"> <li>Medium wealth group: RRR 0.6 (95%CI 0.45-0.80) &amp; rich wealth group: RRR 0.6 (0.43-0.84)</li> <li>Married women: RRR 0.33 (95% CI 0.21-0.51)</li> <li>Age 40+: RRR 0.21 (95%CI 0.21-0.73)</li> <li>4+ living children: RRR 4.85 (95% CI 2.62-8.99)</li> <li>Ever used contraceptive: RRR 0.65 (95% CI 0.46-0.9)</li> </ul>
Che Y et al.	2004	China	Cohort study	21%	<ul style="list-style-type: none"> <li>Wife's age at marriage between 20-23 years: OR 2.21 (95%CI 1.62-3.01)</li> </ul>
Font-Ribera L et al.	2007	Spain	Cross sectional study	41%	<ul style="list-style-type: none"> <li>Age between 15-24: OR 4.37 (95%CI 3.21-5.95)</li> <li>&lt;Primary education: OR 7.22 (95% CI 4.82-10.81)</li> </ul>
Exavery A et al.	2014	Tanzania	Cross sectional survey	13.4%	<ul style="list-style-type: none"> <li>Parity &gt;4: OR 2.65 (1.54-4.54)</li> </ul>
Besculides M et al.	2004	USA	Cross sectional survey	82%	<ul style="list-style-type: none"> <li>Age between 10-19 years: OR 2.03 (95%CI 1.66-2.47) &amp; age between 30-39 years: OR 0.67 (0.54-0.84)</li> <li>Unmarried women: OR 2.52 (95% CI 2.19-2.87)</li> <li>Never used contraceptives: OR 0.36 (95% CI 0.29-0.45)</li> </ul>

**Table 1: Prevalence and determinants of unintended pregnancy (Part 3)**

Goto A et al.	2002	Japan	Cross sectional survey	46.20%	<ul style="list-style-type: none"> <li>Marriage during teens OR 11.14</li> </ul>
Islam MM et al.	2004	Bangladesh	Bangladesh Demographic and health Survey	13% unwanted and 19% mistimed	<ul style="list-style-type: none"> <li>Age 30+: OR 3.44</li> <li>Primary education: OR 1.16</li> <li>Parity: OR 1.56</li> <li>High socioeconomic status: OR 0.78</li> <li>Use of modern contraceptive methods: OR 2.42</li> </ul>
Le CL et al.	2004	Vietnam	Demographic and health survey	40%	<ul style="list-style-type: none"> <li>Age of women 40+: OR 8.97 (p&lt;0.001)</li> <li>Use of traditional method of contraceptive: OR 4.14 (p&lt;0.001) &amp; modern method OR 4.24 (p&lt;0.001)</li> </ul>
Okonofua FE et al.	1999	Nigeria	Cross sectional Survey	20%	<ul style="list-style-type: none"> <li>Age 45+: OR 3.4</li> <li>Secondary education: 1.9 &amp; University level education: 3.4</li> <li>Knowledge of FP methods: OR 2.0 &amp; knows</li> </ul>
Sedgh G et al.	2006	Nigeria	Community based survey	Not calculated	<ul style="list-style-type: none"> <li>Women age 40+: OR 0.3</li> <li>Married women: 2.5</li> </ul>
Hamdela B et al.	2012	Ethiopia	Cross sectional study	Not calculated	<ul style="list-style-type: none"> <li>Number of pregnancy ≥5: OR 5.6 (95% CI 1.62-19.41)</li> </ul>

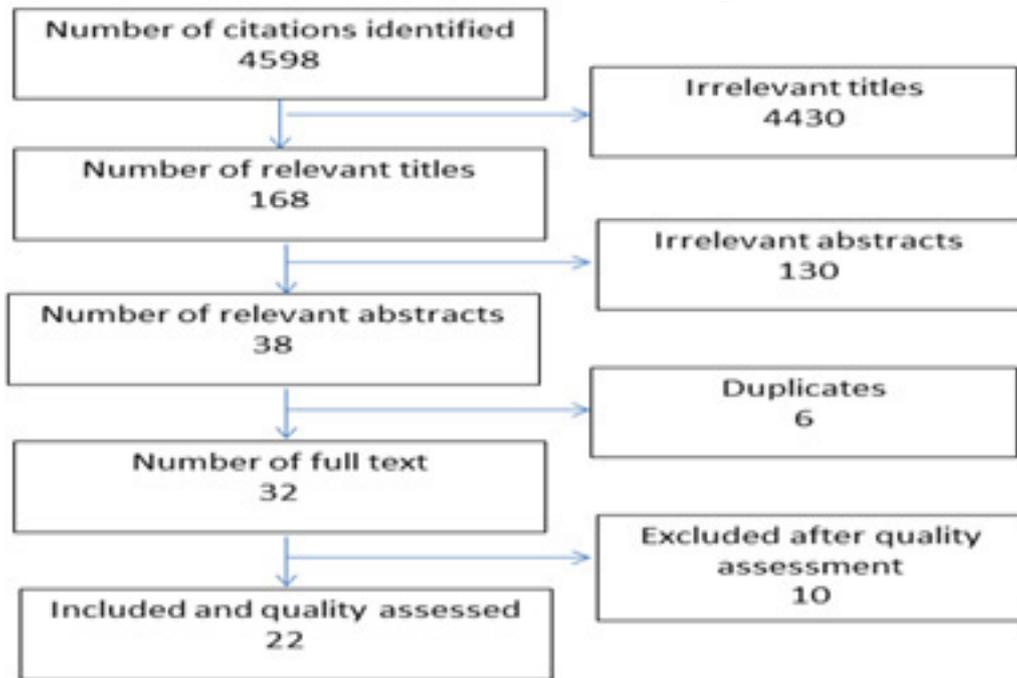
**Legend to Table 2 (opposite page)**

\*According to the Newcastle-Ottawa Scale for cross sectional and case-control studies in Systematic review. Maximum score for selection = 4 stars, maximum score for comparability = 2 stars, maximum score for outcome or exposure (for case-control studies) = 3 stars, maximum total score = 9.

Table 2: Quality assessment\* of individual studies included in the systematic review

Eliason S et al.	2014	Ghana	Cross sectional survey	70%	<ul style="list-style-type: none"> <li>Parity 5+: OR 6.06 (95% CI 3.24-11.38)</li> <li>Marital status (engaged) OR 1.58 (95% CI 1.10-2.28); cohabitation OR 2.91 (1.96-4.31); Single OR 7.32 (95% CI 4.21-12.75)</li> <li>Awareness of traditional family planning method: OR 0.66 (95% CI 0.49-0.89)</li> </ul>
Takahashi S. et al	2012	Japan	The Hamamatsu Birth Cohort (HBC) Study	Not calculated	<ul style="list-style-type: none"> <li>≤ 12 years of education: OR 1.7 (95% CI 1.0-2.9) &amp; ≥ 17 years of education: OR 3.3 (1.1-9.9)</li> <li>Household income ≥8 million JPY: OR 0.4 (95% CI 0.2-0.9)</li> </ul>
Dixit P et al.	2012	India	National Family Health surveys	Not calculated	<ul style="list-style-type: none"> <li>Muslim women: OR 1.27 (95% CI 1.02-1.60)</li> <li>Ever used contraceptives: OR 1.85 (95% CI 1.64-2.09)</li> </ul>
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Exavery A et al.	2014	Tanzania	Cross sectional survey	13.4%	<ul style="list-style-type: none"> <li>Parity &gt;4: OR 2.65 (1.54-4.54)</li> </ul>
Besculides M et al.	2004	USA	Cross sectional survey	82%	<ul style="list-style-type: none"> <li>Age between 10-19 years: OR 2.03 (95%CI 1.66-2.47) &amp; age between 30-39 years: OR 0.67 (0.54-0.84)</li> <li>Unmarried women: OR 2.52 (95% CI 2.19-2.87)</li> <li>Never used contraceptives: OR 0.36 (95% CI 0.29-0.45)</li> </ul>

**Figure 1: Flow diagram showing the process of retrieving the articles**



## Discussion

This review has evaluated all the peer-reviewed studies, published in English language from 1990-2015. It was found that the prevalence of unintended pregnancy ranged from 13-82%. Common predictors identified were age, parity, socioeconomic status, religion and use of family planning methods. Age was found to be positively associated with unintended pregnancy in most of the studies. Studies from Bangladesh, Ethiopia, Egypt, Nepal, Spain, Vietnam and Nigeria reported the positive association of age with an unintended pregnancy (16, 21, 23, 27, 28, 33, 34). Consistent with definitions of mistimed and unwanted pregnancies, this review showed that mistimed pregnancies occurred to younger women and were seen more often in the first and second pregnancies, while unwanted pregnancies occurred to older women and in the third or later pregnancies. Furthermore, this analysis showed that many mistimed and unwanted pregnancies occurred either as a result of no contraceptive use, or due to method failure. Although we could not explore the types of methods used by the women or reasons for method failure, the increased likelihood of unintended pregnancy among users of contraceptive methods could be due to inappropriate usage of short term methods, which has been highlighted through prior research(35).

Studies from Kenya, Ethiopia, Ghana, Tanzania and Bangladesh reported that high parity was significantly associated with unintended pregnancy (22, 23, 31-33). These findings can be explained by the fact that couples from rural areas prefer to have more sons and they may end up having more children. Furthermore, women in the Asian region usually prefer to have enough sons who can become their source of income for the family(34). Moreover, these couples want to balance the sex of their children, and will continue to give birth if all the children are of the same sex.

In this review, it was found that wealth quintile and educational status was associated with unintended pregnancy in the same direction. Studies from Ethiopia, Japan, Spain, Bangladesh and Nigeria reported that illiterate women or women with primary education are at risk of unintended pregnancy (17, 23, 26, 27, 33). This finding can be explained by the fact that women may not even realize that they are pregnant until it has become too late, and they may not be able to negotiate with their spouses with regards to safe sex.

Knowledge about contraceptives was reported to be negatively associated with unintended pregnancy(17, 28). Various studies found that women who have more knowledge about contraceptives are less likely to experience an unintended pregnancy, as compared to those who do not have adequate knowledge about these methods. Moreover, the use of contraceptive methods is positively associated with unintended pregnancy. Studies have also found a strong positive association between users of modern contraceptives and unintended pregnancy, which can be explained by the fact that users of these methods might fail. Since this review did not focus on method failure, therefore, it can be assumed that method failure might have increased the chances of unintended pregnancy among these women.

With respect to women's autonomy, men are usually considered as the main decision-makers in developing countries, and they decide when and where a woman should seek healthcare. Hence, women are often given less power in the male-dominant societies to decide for themselves, and they have to depend on the male partners/relatives for their survival and other life matters. Besides, social norms limit women's freedom to make important decisions(36). In some regions of South Asia, women have substantially lower social status and autonomy than men(37). It has been found that low social status and autonomy seems to be associated with low fertility control(38). Such women

are more likely to experience an unintended pregnancy, as compared to those who have some autonomy(36).

### Strengths and Limitations of the Study

We believe that this is first systematic review on prevalence and predictors of unintended pregnancy, which has synthesized the data both from developing and developed countries. Despite the extensive literature review, there are some limitations to this study. Firstly, we had reviewed all the cross-sectional studies except one cohort study, therefore causal association between various determinants and unintended pregnancy cannot be determined to establish a relationship between unintended pregnancy and various studied correlates. Secondly, different countries have different predictors for unintended pregnancy, depending upon the epidemiologic and demographic variations in those particular countries, so results might not be generalized to all settings. Thirdly, this review included papers only in the English language and we might have missed the important information published in language other than English. The decision to exclude non-English language studies was made for practical reasons based on the increased time, expense and complexity of translating and synthesizing these studies. However, much research in developing countries may not be published in peer-reviewed journals, but might be available as gray literature in local languages. These limitations should have a minor impact on the scope of the study in view of the large size of the sample and that the main variables of interest are demographic factors associated with unintended pregnancy.

### Conclusion and Recommendations

This review demonstrates that unintended pregnancy is common both in developing and developed countries and age, parity, educational and economic status can be considered as important determinants of the unintended pregnancy. This means undertaking outreach in poor and inaccessible settings and providing community-based distribution of family planning methods including counseling and referral for women with unmet need. In addition to this, programs can be undertaken to target youth through youth corners in existing health facilities or training providers in offering youth friendly services. Implementation of targeted programs will guarantee access to family planning for all categories of women in need. These types of targeted approaches can help women to meet their fertility desires and reduce unintended pregnancies with the overall objective of reducing maternal mortality and morbidity.

### References

1. Haub C, Gribble J, Jacobsen L. World Population Data Sheet 2011. Population Reference Bureau, Washington. 2011.
2. Hossain SMI, Khan M, Rahman M, Sebastian MP. South east Asia regional training manual. New Delhi, India: Population Council. 2005.
3. Press B. Round Up. Reproductive Health Matters. 2010;18(35):211-8.
4. Ali SA, Ali SA. Unmet need for contraception and

- unintended pregnancies among women of reproductive age group: A situation analysis. *Elective Medicine Journal*. 2014;2(3):259.
5. Tsui AO, McDonald-Mosley R, Burke AE. Family planning and the burden of unintended pregnancies. *Epidemiologic reviews*. 2010:mxq012.
6. Smith R, Ashford L, Gribble J, Clifton D. Family planning saves lives. 2009.
7. Glasier A, Gülmezoglu AM, Schmid GP, Moreno CG, Van Look PF. Sexual and reproductive health: a matter of life and death. *The Lancet*. 2006;368(9547):1595-607.
8. Kott A. Rates of unintended pregnancy remain high in developing regions. *International perspectives on sexual and Reproductive Health*. 2011;37(1):46-7.
9. Singh S, Sedgh G, Hussain R. Unintended pregnancy: worldwide levels, trends, and outcomes. *Studies in family planning*. 2010;41(4):241-50.
10. Abbasi-Shavazi MJ, Hosseini-Chavoshi M. Unintended pregnancies in the Islamic Republic of Iran: levels and correlates. *Asia-Pacific population journal*. 2004;19(1):27-38.
11. Collumbien M, Gerressu M, Cleland J. Non-use and use of ineffective methods of contraception. 2004.
12. Sathar Z, Singh S, Rashida G, Shah Z, Niazi R. Induced abortions and unintended pregnancies in Pakistan. *Studies in family planning*. 2014;45(4):471-91.
13. Kost K, Singh S, Vaughan B, Trussell J, Bankole A. Estimates of contraceptive failure from the 2002 National Survey of Family Growth. *Contraception*. 2008;77(1):10-21.
14. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *European journal of epidemiology*. 2010;25(9):603-5.
15. Ma Q, Pan X, Cai G, Yan J, Xu Y, Ono-Kihara M, et al. Unintended Pregnancy and Its Correlates among Female Attendees of Sexually Transmitted Disease Clinics in Eastern China. *BioMed research international*. 2013;2013.
16. Youssef R, Moubarak I, Gaffar Y, Atta H. Correlates of unintended pregnancy in Beheira governorate, Egypt. 2002.
17. Tebekaw Y, Aemro B, Teller C. Prevalence and determinants of unintended childbirth in Ethiopia. *BMC pregnancy and childbirth*. 2014;14(1):1.
18. Faye CM, Speizer IS, Fotso JC, Corroon M, Koumtingue D. Unintended pregnancy: magnitude and correlates in six urban sites in Senegal. *Reproductive health*. 2013;10(1):59.
19. Islam MM, Rashid M. Determinants of unintended pregnancy among ever-married women in Bangladesh. *Journal of Family Welfare*. 2005;50(2):40.
20. Okonofua FE, Odimegwu C, Ajobor H, Daru PH, Johnson A. Assessing the prevalence and determinants of unwanted pregnancy and induced abortion in Nigeria. *Studies in family planning*. 1999;30(1):67-77.
21. Sedgh G, Bankole A, Oye-Adeniran B, Adewole IF, Singh S, Hussain R. Unwanted pregnancy and associated factors among Nigerian women. *International family planning perspectives*. 2006:175-84.
22. Ikamari L, Izugbara C, Ochako R. Prevalence and

determinants of unintended pregnancy among women in Nairobi, Kenya. *BMC pregnancy and childbirth*. 2013;13(1):1.

23. Kamal M, Islam A. Prevalence and socioeconomic correlates of unintended pregnancy among women in rural Bangladesh. *salud pública de méxico*. 2011;53(2):108-15.

24. Besculides M, Laraque F. Unintended pregnancy among the urban poor. *Journal of Urban Health*. 2004;81(3):340-8.

25. Habte D, Teklu S, Melese T, Magafu MG. Correlates of unintended pregnancy in Ethiopia: results from a national survey. *PLoS One*. 2013;8(12):e82987.

26. Takahashi S, Tsuchiya KJ, Matsumoto K, Suzuki K, Mori N, Takei N, et al. Psychosocial determinants of mistimed and unwanted pregnancy: the Hamamatsu Birth Cohort (HBC) study. *Maternal and child health journal*. 2012;16(5):947-55.

27. Font-Ribera L, Pérez G, Salvador J, Borrell C. Socioeconomic inequalities in unintended pregnancy and abortion decision. *Journal of Urban Health*. 2008;85(1):125-35.

28. Adhikari R, Soonthorndhada K, Prasartkul P. Correlates of unintended pregnancy among currently pregnant married women in Nepal. *BMC International Health and Human Rights*. 2009;9(1):1.

29. Che Y, Cleland J. Unintended pregnancy among newly married couples in Shanghai. *International family planning perspectives*. 2004:6-11.

30. Goto A, Yasumura S, Reich MR, Fukao A. Factors associated with unintended pregnancy in Yamagata, Japan. *Social Science & Medicine*. 2002;54(7):1065-79.

31. Exavery A, Kanté AM, Njozi M, Tani K, Doctor HV, Hingora A, et al. Predictors of mistimed, and unwanted pregnancies among women of childbearing age in Rufiji, Kilombero, and Ulanga districts of Tanzania. *Reproductive health*. 2014;11(1):63.

32. Eliason S, Baiden F, Yankey BA, Awusabo-Asare K. Determinants of unintended pregnancies in rural Ghana. *BMC pregnancy and childbirth*. 2014;14(1):1.

33. Kassa N, Berhane Y, Worku A. Predictors of unintended pregnancy in Kersa, Eastern Ethiopia, 2010. *Reprod Health*. 2012;9(1):2-7.

34. Le LC, Magnani R, Rice J, Speizer I, Bertrand W. Reassessing the level of unintended pregnancy and its correlates in Vietnam. *Studies in family planning*. 2004:15-26.

35. Keshtkaran A. The survey of effective factors on different practical failure methods of family planning in women referred to health centers. *Middle East Journal of Family Medicine*. 2005;3(2).

36. Ali A, Ali SA, Aziz Ali S, Khuwaja NS. Determinants of Unintended Pregnancy among Women of Reproductive Age in Developing Countries: A Narrative Review. *Journal of Midwifery and Reproductive Health*. 2016;4(1):513-21.

37. Weiner M. *Sons of the soil: Migration and ethnic conflict in India*. Princeton University Press; 2015.

38. Singh KK, Singh K, Singh BP, Pathak AK. Impact of education and autonomy on fertility of women in eastern Uttar Pradesh. *Demography India*. 2015;31(2):223-33.



