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Self-monitoring of Blood Glucose Among Type-2 Diabetic Patients: An Analytical Cross-Sectional Study

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This is the third issue this year with papers from the region and strong collaborative papers across the region.

Alzahrani AS et al; explored the effect of using SMBG on glycemic control among type 2 diabetic patients attending the primary health care centers in Abha city in the Kingdom of Saudi Arabia by comparing those who are monitoring themselves and others who are not. The study design was analytical cross-sectional and conducted through an interviewing questionnaire. The age of participants was 30-82 years old, with a mean age distribution of 57.4 years old. The percentages of groups doing and not doing SMBG were 43% and 57% respectively. The relationship between glycemic control and compliances according to SMBG shows there is a statistically significant relationship with appointment compliance among the group doing SMBG, and with drug compliance among the other group. The authors concluded that there is no sufficient evidence to show that the self-monitoring of blood glucose is associated with an improvement in glycemic control among type2 diabetics and it is shown that glycemic control for both groups that are using and not using SMBG is above the target .It is recommended that more well conducted randomized controlled trials should be undertaken to evaluate the relationship between SMBG and glycemic control in type 2 diabetes ,at the same time the current guidelines for the use of SMBG among patients with well controlled non-insulin treated type 2 diabetes need to be reviewed.

Helvaci MR et al, tried to understand significance of white coat hypertension (WCH), clinically. Consecutive patients with underweight were taken in the first phase, and age-matched consecutive patients with normal weight, overweight, and obesity were taken in the second phase into the study. Although we were able to detect 50 cases in the underweight group with a mean age of 24.7 years, we were only able to detect nine age-matched cases in the obesity group, thus the obesity group was not taken for comparison. There were gradual and statistically significant increases in the prevalence of WCH beside the gradual and significant decreases in the sustained normotension (NT) from the underweight towards the normal weight and overweight groups. Eventually, only 31.8% of the overweight cases have sustained NT although the very young mean age of them. The authors concluded that due to the gradually increased prevalence of WCH from the underweight towards the normal weight and overweight groups and the very low prevalence of sustained NT in the overweight group although the very young mean age of them and the already known increased prevalence of hypertension, impaired fasting glucose, impaired glucose tolerance, type 2 diabetes mellitus, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, coronary artery disease, chronic obstructive pulmonary disease, cirrhosis, chronic renal disease, and stroke and an increased all-cause mortality rate in the same direction, WCH may actually be an acute phase reactant mainly alarming overweight and obesity and many associated health problems in future.

Alqahtani Y.M et al, report an Unusual Persistent Mullerian Duct Syndrome in a child in Abha city: A Case Report. The authors stressed that Persistent Mullerian duct syndrome (PMDS) is a rare condition that is characterized by the presence of the Mullerian duct structures among phenotypically and genotypically male. It could result from insufficiency of Mullerian inhibiting factor (MIF) or its receptors. A 9 months-old Syrian boy was admitted to Abha Maternity and Children Hospital with a previous history of huge left inguinal swelling since 8 hours, vomiting 4 times, yellowish discharge. Routine examinations and investigations were done and the boy was diagnosed with left unilateral inguinal hernia with obstruction and during surgery left ovotestes with fallopian tubes and rudimentary uterus were detected. The histopathology showed no signs of malignancy. After two weeks from left inguinal hernia repair, the boy was presented with right incarcerated hernia. The boy undergone right inguinal herniotomy and right gonadopexy. During the operation, right ovotestis, with vas and fallopian tube were detected. The tube was resected and the sac was dissected, vas and vessels were secured. The boy had no sexual dysfunction and chromosomal investigation showed normal male karyotype. The testosterone level was less than the normal range (0.087 nmol/l).

The authors concluded that The PMDS is a rare condition and during early stages can't be detected but the only diagnostic procedure is when the children are tested for other diseases as hernia or cryptorchidism. The correct and early diagnosis depend on genetic investigation and endocrinology. Surgery is the treatment of choice.

A paper from Yemen looked at the Prevalence of abdominal obesity and its associated comorbid condition in adult Yemeni people of Sana'a City. A sample of 118 adult Yemeni people aged equal or over 18 years was randomly chosen to represent the population living in Sana'a City during a period of two years from April 2016 to April 2018. All the study group undergo full clinical history and examination includes measurement of BP and waist circumference and the following laboratory investigation (FBS , serum TG , HDL , and LDL). the prevalence of abdominal obesity in this study was 24.5% (7.9% male and 44.2% female) .central obesity in this study was significantly correlated with age, sex , The highest prevalent comorbidity in patients with abdominal obesity was high BP (41.3%), followed by high serum TG (40 %), higher prevalence of MS (40%) , low serum HDL (37.8%) high LDL (20.1%) raised fasting blood glucose (22.1%) than those without abdominal obesity (5.5%, 31.3%, 16.6%, 8.5%, 12.5% and increased FBS 10% respectively .The authors concluded that hypertension, diabetes, dyslipidemia and MS are strongly correlated with abdominal obesity.

A paper from Turkey, Lebanon and Australia looked at the possibility of Smoking causing irritable bowel syndrome. The study included 647 patients with the IBS and 340 control cases. Mean age of the IBS patients was 41.4 years. Interestingly, 64.2% of the IBS patients were female. Prevalence of smoking was higher in the IBS cases (36.4% versus 20.5%, $p<0.001$). Similarly, prevalence of antidepressants use was higher in the IBS patients (48.0% versus 15.5%, $p<0.001$). Additionally, prevalence of urolithiasis was also higher in the IBS group (23.3% versus 9.4%, $p<0.001$). Mean body mass index values were similar in the IBS and control groups (27.5 versus 27.7 kg/m2, $p>0.05$, respectively). Prevalence of white coat hypertension were also similar in them (29.3% versus 31.4%, $p>0.05$, respectively). Although prevalence of hypertension and diabetes mellitus and mean values of total cholesterol, triglycerides, low density lipoproteins, and high density lipoproteins were all similar in them, mean value of fasting plasma glucose (FPG) was significantly higher in the IBS group (110.1 versus 105.6 mg/dL, $p= 0.013$). The authors concluded that IBS may be a low-grade inflammatory process being initiated with infection, inflammation, psychological disturbances-like stresses, and eventually terminated with dysfunctions of gastrointestinal and genitourinary tracts and other systems of the body. Although there may be several possible causes of IBS, smoking induced chronic vascular endothelial inflammation may even cause IBS. The higher FPG in the IBS patients should be researched with further studies.

A paper from Scotland provides a review of the literature on early onset dementia. The author finds there is increasing recognition that EOD (Early Onset Dementia) represents an important social problem affecting economic and social impacts

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Self-monitoring of Blood Glucose Among Type-2 Diabetic Patients: An Analytical Cross-Sectional Study

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Abstract

Background: Diabetes mellitus (DM) is a public health disease needing urgent consideration; it has a great impact on human life in addition to being costly to manage. According to the current recommendations, self-monitoring of blood glucose (SMBG) is important in order to achieve and maintain glycemic control, prevent and identify hypoglycemia, prevent severe hyperglycemia and support lifestyle changes.

Methods: The objective of this study is to explore the effect of using SMBG on glycemic control among type 2 diabetic patients attending the primary health care centers in Abha city in the Kingdom of Saudi Arabia, by comparing those who are monitoring themselves and others who are not. The study design was analytical cross-sectional and conducted through an interviewing questionnaire.

Results: The age of participants was 30-82 years old, with a mean age distribution of 57.4 years old. The percentages of groups doing and not doing SMBG were 43% and 57% respectively. Chi square tests show that the relationship between glycemic control and SMBG is statistically significant according to frequency and time of doing SMBG, since almost all of the results for the participants who do SMBG are above the target for glycemic control (>=7%). The relationship between glycemic control and compliance according to SMBG shows there is a statistically significant relationship with appointment compliance among the group doing SMBG, and with drug compliance among the other group.

In both groups, almost all the participants were above the target for control (>=7%), which means that there is no relationship between doing SMBG and better glycemic control.

Conclusion: There is not sufficient evidence to show that the self-monitoring of blood glucose is associated with an improvement in glycemic control among type 2 diabetics and it is shown that glycemic control for both groups that are using and not using SMBG is above the target. It is recommended that more well conducted randomized controlled trials should be undertaken to evaluate the relationship between SMBG and glycemic control in type 2 diabetes, at the same time the current guidelines for the use of SMBG among patients with well controlled non-insulin treated type 2 diabetes need to be reviewed.

Key words: Self-monitoring, blood glucose (SMBG), glycemic control, type 2 diabetes, comorbidities.

Introduction

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia that results from defects in insulin secretion, action or both(1).

Diabetes can be classified into type 1 diabetes (B-cell destruction usually leading to absolute insulin deficiency), type 2 diabetes (ranging from being characterized predominantly by insulin resistance with relative insulin deficiency to predominantly an insulin secretory defect with insulin resistance) and other specific types of diabetes (1).

Diabetes and its complications are major causes of death in many countries. Type 2 is the most prevalent type occurring in up to 91% of adults with diabetes in high-income countries. It is estimated that 193 million people with diabetes are undiagnosed and they are more at risk of developing complications (2).

The prevalence of type 2 diabetes in Saudi Arabia is about 32.8%; the predicted prevalence will be 35.37% in 2020; 40.37% in 2025 and 45.36% in the year 2030. The coefficient on time factor indicates that the prevalence rate has increased from 1982-2015 (3).

Saudi Arabia should include preventive measures against diabetes on a war footing basis in its national health policy to minimise the burden of the disease (3).

In patients with type 2 diabetes, SMBG can help to achieve better glycemic control, although there is not sufficient evidence to confirm that strict monitoring in these patients is associated with an improved outcome (4).

The outcome of several clinical studies, especially amongst diabetics on insulin therapy, has shown that SMBG plays a key role in preventing complications in the short, medium and long term.

According to the American Diabetes Association (ADA) and the National Academy of Clinical Biochemistry (NACB), patients and healthcare personnel should be trained on the appropriate use of the device, as well as on the correct interpretation of data (5).

In type 2 diabetes, the efficacy of frequent glucose measurements remains uncertain. The results of studies suggest that SMBG can play an important role in improving metabolic control if it is an integral part of a wider educational strategy (6).

Higher SMBG testing rates were associated with lower HbA1c, only when stratifying the analyses to control for treatment intensification (4).

A significant reduction in HbA1c levels was associated with Asian populations, in a small sample size, and telecare, and with those patients with baseline HbA1c greater than 8.0% (7).

There was no convincing evidence to support a recommendation for routine self- monitoring of all patients and no evidence of improved glycemic control in predefined subgroups of patients(8).

SMBG indications can be used as a measure for acute correction (“primary adjustment”), if blood glucose levels are increased or decreased during intensive insulin therapy, when correction may be made with rapid-acting insulin or administration of carbohydrate (9).

The OneTouch® Select Simple™ glucose meter meets current regulatory expectations for glucose meter performance (10) and consideration of personal aspects of daily living that impact on an individual’s ability to achieve their desired glycemic control(11).

Optimal glycemic control will improve long-term outcomes in many patients with diabetes. Tools such as new therapeutics and advanced technology, including highly accurate BGMSs, will help patients, working alongside their diabetes teams, to achieve the goal of improved glucose control (12).

The health burden due to DM in Saudi Arabia is predicted to rise to catastrophic levels, unless a wide-ranging epidemic control program is adopted, with great emphasis on healthy diet, including exercise and active lifestyles, and weight control. To properly manage DM in Saudi Arabia, a multidisciplinary approach is required (13).

SMBG is recommended as an essential part of daily DM management regardless of type and mode of treatment strategy of adjusting medication at monthly intervals based on intensified SMBG data can be adopted in conjunction with HbA1c results to achieve better glycemic control (14). According to one published study, 15.3% of people with type 2 diabetes practice SMBG (15).

Results of a Saudi study conclude that SMBG has a positive impact on glycemic control, expressed as decrease in HbA1c levels with time post referral(19). T2DM patients following SMBG have shown better lifestyle changes and compliance to drug therapy. It could be due to regular monitoring of blood glucose levels thereby patients became motivated and understood the importance of dietary changes, regular exercise and intake of antidiabetic pills in controlling the disease and its associated complications(19). Patients following SMBG have also shown a more positive attitude and awareness about diabetes and risk factors associated with it than patients without SMBG follow-up (19).

According to ADA, the glycemic targets are : HBA1c at target (defined as <7%) and not at target (defined as ≥7) (19). FBS at target (defined as 80-130mg/dl) and not at target (defined as >130mg/dl.) (20). RBG at target (defined as <180 mg/dl.) and not at target (defined as ≥180mg/dl) (20).

This study aimed to explore the effect of using SMBG on glycemic control among type 2 diabetic patients at Abha city’s PHCCs.

Materials and methods

This research had an analytical cross-sectional study design to explore the effect of SMBG on glycemic control among type 2 diabetics in Abha city's PHCCs by comparing those who are doing it and others who are not doing it.

Type 2 diabetic patients attending governmental primary health care centres (PHCCs), excluding those with type 1 and gestational diabetes, made up the study population. There are about 10 primary health care centres in Abha city according to Abha sector of Aseer health affairs, serving about 5,000 diabetic patients. The study used STATCALC EPI software and the sample size was 314 calculated. The sample was recruited using systematic random sampling of patients attending the PHC.

The data were collected using a validated questionnaire which was distributed and initiated through an interview with participants. The study was approved by the ethical committee (institutional review board), and permission was granted by Aseer health affairs. Consent was obtained from participants verbally. Data were cleaned, coded, entered and analyzed using SPSS version 21.

Results

Participants were aged between 30 and 82 years old with a mean age distribution of 57.4. Males constituted 47.8% of the sample and females made up 52.2%. The bio-demographic characteristics of type 2 diabetic patients according to their self-monitoring of blood glucose status are shown in Table 1.

Table 1: Bio-demographic characteristics of type 2 diabetic patients according to their self-monitoring of blood glucose status

Bio-demographic characteristics		Doing SMBG in last 6months						P
		Yes		No		Total		
		No	%	No	%	No	%	
Gender	male	65	48.1%	85	47.5%	150	47.8%	.907
	female	70	51.9%	94	52.5%	164	52.2%	
Age in years	30-49	26	19.3%	32	17.9%	58	18.5%	.016*
	50-59	66	48.9%	63	35.2%	129	41.1%	
	60-69	19	14.1%	50	27.9%	69	22.0%	
	70-89	24	17.8%	34	19.0%	58	18.5%	
Nationality	Saudi	135	100.0%	160	89.4%	295	93.9%	.001*
	Not Saudi	0	0.0%	19	10.6%	19	6.1%	
Marital status	Unmarried	10	7.4%	12	6.7%	22	7.0%	.809
	Married	125	92.6%	167	93.3%	292	93.0%	
Occupation	worker	31	23.0%	34	19.0%	65	20.7%	.001*
	retired	44	32.6%	31	17.3%	75	23.9%	
	housewife	37	27.4%	100	55.9%	137	43.6%	
	other	23	17.0%	14	7.8%	37	11.8%	
Educational status	illiterate	38	28.1%	113	63.1%	151	48.1%	.001*
	educated	97	71.9%	66	36.9%	163	51.9%	
Smoking status	ex-smoker	26	19.3%	0	0.0%	26	8.3%	.001*
	non-smoker	86	63.7%	145	81.0%	231	73.6%	
	current smoker	23	17.0%	34	19.0%	57	18.2%	

* P < 0.05 (significant)

Table 2 reveals complications of diabetes were present in about 43.9% of the participants (46.7% among the group doing SMBG) with 25.4% Retinopathy (14.3% were doing SMBG and 34.7 were not), Neuropathy is about 51.4% (23.8% were doing SMBG and about 74% were not). About 78.3 % of participants had diabetes for five years or more (87.4% among those doing SMBG), the majority of treatment received was by metformin in about 82.2% of participants: 69.6% were doing SMBG and 91.6% were not; the lowest is glimepiride by 5.1%. Comorbidities of diabetes were present in 51.3% of all participants: hypertension 50%, lipid disorders 26%, obesity 4% and others 20%.

In the group doing SMBG: 46% had comorbidities and 54% had no comorbidities, while in the other group: 55% had comorbidities and 45% had no comorbidities.

Our result shows, causes of not doing SMBG were mainly because of unavailability of strips (36%) and no desire (about 24%).

Table 2: Diabetes data for patients according to their self-monitoring of blood glucose status

Diabetes data		Doing SMBG in last 6months						
		Yes		No		Total		P
		No	%	No	%	No	%	
Duration of DM	0-6 months	0	0.0%	12	6.7%	12	3.8%	.001*
	1-3 years	10	7.4%	7	3.9%	17	5.4%	
	3-5 years	7	5.2%	32	17.9%	39	12.4%	
	5 years or more	118	87.4%	128	71.5%	246	78.3%	
Treatment received #	Glibenclamide	34	25.2%	45	25.1%	79	25.2%	.993
	Gliclazide	22	16.3%	47	26.3%	69	22.0%	.035*
	Metformin	94	69.6%	164	91.6%	258	82.2%	.001*
	Metformin XR	29	21.5%	10	5.6%	39	12.4%	.001*
	Glimepiride	0	0.0%	16	8.9%	16	5.1%	.001*
	Insulin	67	49.6%	52	29.1%	119	37.9%	.001*
	Other Medications	37	27.4%	82	45.8%	119	37.9%	.001*
Complications of diabetes	No	72	53.3%	104	58.1%	176	56.1%	.399
	Yes	63	46.7%	75	41.9%	138	43.9%	
If yes, mention # (n=138)	Retinopathy	9	14.3%	26	34.7%	35	25.4%	.006*
	Nephropathy	9	14.3%	5	6.7%	14	10.1%	.140
	Cardiovascular	37	58.7%	41	54.7%	78	56.5%	.631
	Neuropathy	15	23.8%	56	74.7%	71	51.4%	.001*

#: more than one answer was allowed
* P < 0.05 (significant)

Table 3 shows the number of people doing SMBG three times a day was lowest at 5.2%, and twice a day was highest at 45.9%, and moderately more than once a week by about 25%. Time of doing SMBG was before meals in 59.3%, feeling of hypoglycemic episode 35.6% and during episode of illness 5.2%.

The scale of was SMBG helpful shows extremely helpful in 28.9%, somewhat helpful in 40.7%, slightly helpful in 11.9% and not at all helpful in 0.7%. For reason for SMBG being helpful if scale was 7 or more it indicated the following: improved diabetes control (70.0%), help during episode of illness (12.7%), better to do physical activity (9.1%) and avoid hypoglycemia (8. Reason for SMBG being helpful if scale is 4 or less is because it is painful 100%. Good diet compliance constitutes about 28 %, fair 55% and poor 18 percent .

Good drug compliance constitutes about 54 percent, fair 45% and poor about 0.64%. Diet compliance among the group doing SMBG was fair (54.1%), good (40%) and poor (10%). Drug compliance among them was fair (29%), good (70%) and poor (1.5%), Physical activity compliance: fair in 63%, good in 24% and poor in 13% appointment compliance: fair in 38%, good in 61% and poor in 0.7%.

Table 3: Relationship between glycemic control and SMBG among type 2 diabetic patients

SMBG		HBA1C				p
		<7%		>=7%		
		No	%	No	%	
Frequency of SMBG	once a day	5	26.3%	14	73.7%	.001*
	twice a day	0	0.0%	62	100.0%	
	three times a day	0	0.0%	7	100.0%	
	once a week	6	46.2%	7	53.8%	
	more than once a week	0	0.0%	34	100.0%	
Time of doing SMBG	before meals	11	13.8%	69	86.3%	.016*
	during episode of illness	0	0.0%	7	100.0%	
	feeling of hypoglycemic episode	0	0.0%	48	100.0%	
Scale of SMBG being helpful	somewhat unhelpful	0	0.0%	3	100.0%	.377
	slightly unhelpful	0	0.0%	7	100.0%	
	not at all unhelpful	0	0.0%	14	100.0%	
	not at all helpful	0	0.0%	1	100.0%	
	slightly helpful	0	0.0%	16	100.0%	
	somewhat helpful	5	9.1%	50	90.9%	
	extremely helpful	6	15.4%	33	84.6%	

* P < 0.05 (significant)

Table 4 shows the relationship between glycemic control and SMBG:

In relation to glycemic control the frequency of SMBG once daily was in 26% at target, once a week in 46% while twice a day, three times a day and more than once a week all were not at target 100%. Time of doing before meals was at target in 14% while during episode of illness and feeling of hypoglycemic episode was not at target 100%. Not all scales of 'helpful' were at target except extremely helpful 15% and somewhat helpful 9% were at target.

Findings elicit the relationship between glycemic control and compliance according to SMBG:

Among the group doing SMBG: diet compliance was good and at target in 9%, fair and at target in 8% and poor and at target 0% drug compliance: good and at target in 12%, fair, poor and at target in 0%. Physical activity compliance: good and at target in 16%, fair and at target in 7% and 0 in poor, Appointment compliance: good and at target 13%, fair, poor and at target 0%.

Findings show that about 57% were not doing SMBG in last 6 months and only 43% were not doing SMBG in last 6 months and only 43% are doing it.

Table 4: Relation between glycemic control and compliance according to SMBG among type II diabetic patients

SMBG	Compliance		HBA1C laboratory results				P
			<7%		>=7%		
			No	%	No	%	
Yes	diet compliance	good	5	9.3%	49	90.7%	.671
		fair	6	8.2%	67	91.8%	
		poor	0	0.0%	8	100.0%	
	drug compliance	good	11	11.7%	83	88.3%	.073
		fair	0	0.0%	39	100.0%	
		poor	0	0.0%	2	100.0%	
	physical activity compliance	good	5	15.6%	27	84.4%	.127
		fair	6	7.1%	79	92.9%	
		poor	0	0.0%	18	100.0%	
	appointment compliance	good	11	13.3%	72	86.7%	.023*
		fair	0	0.0%	51	100.0%	
		poor	0	0.0%	1	100.0%	
No	diet compliance	good	0	0.0%	33	100.0%	.336
		fair	5	5.0%	95	95.0%	
		poor	1	2.2%	45	97.8%	
	drug compliance	good	0	0.0%	75	100.0%	.034*
		fair	6	5.8%	98	94.2%	
	physical activity compliance	good	0	0.0%	33	100.0%	.063
		fair	5	7.4%	63	92.6%	
		poor	1	1.3%	77	98.7%	
	appointment compliance	good	4	7.5%	49	92.5%	.066
		fair	1	.9%	110	99.1%	
		poor	1	6.7%	14	93.3%	

* P < 0.05 (significant)

Discussion

The age of participants was from 30-82 years old with a mean age distribution of 57.4. Males constituted 47.8% of participants and females made up 52.2%, which is similar to some extent to the results of the Fremantle diabetes study (16).

There was a statistically significant difference ($p < 0.05$) in all bio demographic characteristics according to SMBG, and only gender and marital status were insignificant ($p > 0.050$), and these findings are in accordance with the Fremantle diabetes study(16). In terms of diabetic data, the duration of diabetes shows significant differences between the groups doing SMBG and those who were not ($p<0.001$) also in concordance with Fremantle diabetes study(16); all types of treatment received show significant differences except glibenclamide ($p>0.05$). The complications in general show an insignificant difference in terms of who had complications or those who were free of them, but among those who had complications, there is a significant difference with retinopathy and neuropathy groups rather than with nephropathy and cardiovascular complications.

Comorbidities with diabetes were present in 51.3% of all the participants; half of them had hypertension and of the other half, one third had a lipid disorder and one quarter had obesity.

Out of our participants, there were 43% self-monitoring blood glucose, and most of the remaining 57% were not doing this because of unavailability of strips and because they had no motivation to.

In terms of the frequency of doing SMBG, approximately half the participants (46%) did it twice a day, mostly before meals (about 60%), followed by more than once a week (25%) and least frequently three times a day and this is similar to results of the Barnard et al study (17).

About 40% of participants who indicated how helpful SMBG was chose 'somewhat helpful', 30% chose 'extremely helpful' and 10% chose 'not at all helpful'. Among those choosing that SMBG is helpful, 70% of them stated that it was because it improved diabetes control, while of the other group not doing SMBG who chose that it was unhelpful, two thirds of them because it reminded them of their illness and discouraged them from making any changes in their lifestyles, and these findings are in accordance with results from the Barnard et al study(17).

All participants who did SMBG and who chose the option stating it was unhelpful indicated that this was because it is painful, also in accordance with previous study (17).

The diet, drug, physical activity and appointment compliance among both groups show significant differences ($p<0.001$), with good compliance being more prevalent amongst the group doing SMBG while there was more poor compliance among the other group.

The laboratory results show significant differences between both groups in terms of their FBS and RBS results ($p<0.05$), but not HBA1C results ($p>0.05$) and these findings are in accordance with impact of self-monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomized trial (18).

In the group doing SMBG, 89% were above the target of control for FBS and 70% for RBS. The relationship between glycemic control and SMBG is statistically significant according to frequency of and time of doing SMBG, demonstrating that all of the results of the participants who did SMBG were above the target for glycemic control (>=7%). This means that doing SMBG is not currently associated with better glycemic control. The relationship between glycemic control and compliance according to SMBG shows there is a statistically significant relationship with appointment compliance among the group doing SMBG, and with drug compliance among the other group.

In both groups, almost all of them were above the target of control (>=7%), again meaning that, there is no relation between doing SMBG and better glycemic control.

The relevance of these findings will add information similar to that of most of the previous studies that concluded the routine using of SMBG among type 2 diabetic patients may be not recommended or if it is done should be highly individualized.

Conclusion

According to the results of this study, there is not sufficient evidence to show that the self-monitoring of blood glucose is associated with an improvement in glycemic control among type 2 diabetics and it is shown that glycemic control for both groups that are using and not using SMBG is above the target.

It is recommended that more well conducted randomized controlled trials should be undertaken to evaluate the relationship between SMBG and glycemic control in type 2 diabetes; at the same time the current guidelines for the use of SMBG among patients with well controlled non-insulin treated type 2 diabetes need to be reviewed.

References

1. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2004; 27 (Supplement 1): S5–10.
2. Tobergte D.R., Curtis S. IDF 2015. J Chem Inf Model. 2013; 53 (9):1689–99.
3. Meo S.A. Prevalence and future prediction of type 2 diabetes mellitus in the Kingdom of Saudi Arabia: A systematic review of published studies. 2016; (April 2015): 2014–7.

4. Murata G.H., Duckworth W.C., Shah J.H., Wendel C.S., Mohler M.J., Hoffman R.M. Blood glucose monitoring is associated with better glycemic control in type 2 diabetes: A database study. J Gen Intern Med. 2009; 24(1): 48–52.
5. Montagnana M., Caputo M., Giavarina D., Lippi G. Overview on self-monitoring of blood glucose. Clin Chim Acta. 2009; 402(1–2): 7–13.
6. Szymborska-Kajanek A., Psurek A., Hese R., Strojek K. Self-monitoring of blood glucose in treatment of type 2 diabetes. Diabetes Res Clin Pract. 2009; 86 (SUPLL.1).
7. Garg S.K., Hirsch I.B. Self-Monitoring of Blood Glucose. Diabetes Technol Ther. 2016; 18 (S1): S-3-S-9.
8. Clarke S.F., Foster J.R. A history of blood glucose meters and their role in self-monitoring of diabetes mellitus. Br J Biomed Sci. 2012; 69(2): 83–93.
9. Nauck M.A., El-Ouaghlidi A., Vardarli I. Self-monitoring of blood glucose in diabetes mellitus: arguments for an individualized approach. Dtsch Arzteblatt Int. 2009; 106 (37): 587–94.
10. Krouwer J.S. Analysis of the Performance of the OneTouch SelectSimple Blood Glucose Monitoring System: Why Ease of Use Studies Need to Be Part of Accuracy Studies. 2011; 5 (6): 1610–1.
11. Kerr D., Messing R., Resch A. Actionable self-monitoring of blood glucose: redefining the role for patients using multiple daily injection therapy. J Diabetes Sci Technol. 2011; 5 (6): 1584–90.
12. Bernstein R., Parkes J.L., Goldy A., Brown D., Harrison B., Chu A., et al. A new test strip technology platform for self-monitoring of blood glucose. J Diabetes Sci Technol. 2013; 7 (5): 1386–99.
13. Al Dawish M.A., Robert A.A., Braham R., Al Hayek A.A., Al Saeed A., Ahmed R.A., et al. Diabetes Mellitus in Saudi Arabia: A Review of the Recent Literature. Curr Diabetes Rev. 2015;
14. Ba-Essa E.M., Mobarak E.I., Alghamdi A., Al-Daghri N.M. Intensified glucose self-monitoring with education in Saudi DM patients. Int J Clin Exp Med. 2015; 8 (10): 19374–80.
15. Ong W.M., Chua S.S., Ng C.J. Barriers and facilitators to self-monitoring of blood glucose in people with type 2 diabetes using insulin: A qualitative study. Patient Prefer Adherence. 2014; 8: 237–46.
16. Davis WA, Bruce DG, Davis TM. Is self-monitoring of blood glucose appropriate for all type 2 diabetic patients? The Fremantle diabetes study. Diabetes Care. 2006;29 (8):1764–70.
17. Barnard KD, Young AJ, Waugh NR. Self-monitoring of blood glucose - A survey of diabetes UK members with type 2 diabetes who use SMBG. BMC Res Notes. 2010.
18. Farmer A, Wade A, Goyder E, Yudkin P, French D, Craven A, et al. Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomised trial. BMJ. 2007.
19. Vijayaraghavalu S et al. / Pharmacie Globale (IJCP) 2015, 03 (01).
20. American Diabetes Association. 6. Glycemic targets: Standards of Medical Care in Diabetes-2018. Diabetes Care 2018; 41(Suppl. 1):S55–S64.

White coat hypertension may actually be an acute phase reactant in the body

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Abstract

Background: We tried to understand the significance of white coat hypertension (WCH), clinically.

Methods: We took consecutive underweight patients in the first phase, and age-matched consecutive patients with normal weight, overweight, and obesity in the second phase of the study.

Results: Although we were able to detect 50 cases in the underweight group with a mean age of 24.7 years, we were only able to detect nine age-matched cases in the obesity group, thus the obesity group was not taken for comparison. There were gradual and statistically significant increases in the prevalence of WCH beside the gradual and significant decreases in the sustained normotension (NT) from the underweight towards the normal weight and overweight groups. Eventually, only 31.8% of the overweight cases had sustained NT although they had very young mean age.

Conclusions: Due to the gradually increased prevalence of WCH from the underweight towards the normal weight and overweight groups and the very low prevalence of sustained NT in the overweight group despite their very young mean age and the already known increased prevalence of hypertension, impaired fasting glucose, impaired glucose tolerance, type 2 diabetes mellitus, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, coronary artery disease, chronic obstructive pulmonary disease, cirrhosis, chronic renal disease, and stroke and an increased all-cause mortality rate in the same direction, WCH may actually be an acute phase reactant, mainly alarming overweight and obesity and many associated health problems in future.

Key words: White coat hypertension, acute phase reactant, overweight, obesity

Introduction

In recent years, overweight and obesity have become major health problems particularly in developed countries. For example, 30% of adults in the United States can be classified as obese (1). Overweight and obesity are characterized by increased mass of adipose cells that result from a systemic imbalance between food intake and energy expenditure, and they are associated with increased levels of inflammatory parameters and many systemic disorders including white coat hypertension (WCH), hypertension (HT), impaired fasting glucose (IFG), impaired glucose tolerance (IGT), type 2 diabetes mellitus (DM), hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), cirrhosis, chronic renal disease (CRD), stroke, and an increased all-cause mortality rate (2-5). Additionally, obesity is highly correlated with dietary intake of increased calories and fat, both of which were linked to several types of cancers (6). For example, in a recent study performed among 900,000 people it was found that obese individuals were more likely to die from a number of cancers including breast, colon, and prostate (7). On the other hand, cardiovascular death, myocardial infarction, and stroke are the most common causes of deaths particularly in the developed countries again, and most of them are related with increased blood pressure (BP) (8). Therefore BP control is the mainstay for prevention of cardiovascular deaths. But diagnosis and management of HT is difficult due to the fact that BP varies greatly depending on physical and mental stresses. WCH is a well-known clinical entity defined as a persistently elevated BP in the doctor's office whereas normal in other conditions, and prognostic significance of it remains controversial (9, 10). For instance, it was reported in an Ohasama study that WCH is a risk factor for development of home HT (11). Similarly, 46.9% of cases with WCH versus 22.2% of cases with sustained normotension (NT) progressed to home HT in an eight-year follow up study (12). So the results demonstrated that WCH is a transitional condition eventually terminating with home HT. Additionally, intima-media thickness and cross-sectional area of carotid artery were found as similar in patients with WCH and HT, which were significantly higher than the sustained NT cases so authors concluded that there is target organ damage in WCH therefore it should not be considered as an innocent trait, clinically (13). Similarly, complication risks of WCH were different from subjects with sustained NT in another study (14). On the other hand, there was not any proof that WCH exhibits a clearly higher risk for cardiovascular events in the above 7.4-year follow up study (10). So most of the already performed studies about WCH have just focused on the progression to home HT in time or whether WCH causes any target organ damage or not. We therefore tried to understand some other possible clinical consequences of WCH in the present study.

Material and methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and August 2006 in two phases. In the first phase, we took consecutive underweight patients between the ages of 15 and 70 years to be able to see the possible consequences of weight on BP and to avoid debility induced weight loss in elders. In the second phase, age-matched consecutive cases with normal weight, overweight, and obesity were detected. Their medical histories including smoking habit and medications were learnt, and a routine check up procedure was performed. Current regular smokers at least for the last 6 months and cases with a previous smoking history of at least five pack-years were accepted as smokers, and cigar or pipe smokers were excluded. Insulin using diabetics and patients with devastating illnesses including malignancies, acute or chronic renal failure, chronic liver diseases, hyper- or hypothyroidism, and heart failure were excluded to avoid their possible effects on weight. Body mass index (BMI) of each case was calculated by the measurements of the Same Physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared, and underweight is defined as a BMI of lower than 18.5, normal weight between 18.5-24.9, overweight between 25–29.9, and obesity as a BMI of 30.0 kg/m(2) or higher (15). Office blood pressure (OBP) was checked after a 5-minute rest in seated position with the mercury sphygmomanometer on three visits, and no smoking was permitted during the previous 2 hours. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases even in normotensives in the office due to the risk of masked HT after a 10-minute education session about proper BP measurement techniques (16). The education included recommendation of upper arm while discouraging wrist and finger devices, using a standard adult cuff with bladder sizes of 12 x 26 cm for arm circumferences up to 33 cm in length and a large adult cuff with bladder sizes of 12 x 40 cm for arm circumferences up to 50 cm in length, and taking a rest at least for a period of 5 minutes in the seated position before measurement. An additional 24-hour ambulatory blood pressure monitoring (ABP) was not required due to the equal effectiveness of the ABP and HBP measurement techniques for the diagnosis of WCH and HT (17, 18). Eventually, HT is defined as a BP of 135/85 mmHg or greater on mean HBP values (16). WCH is defined as an OBP of 140/90 mmHg or greater, but a mean HBP value of lower than 135/85 mmHg, sustained NT as an OBP of lower than 140/90 mmHg together with an average HBP of lower than 135/85 mmHg, and masked HT as an OBP of lower than 140/90 mmHg but a mean HBP of 135/85 mmHg or greater (16). Prevalence of smoking, sustained NT, WCH, and HT were detected in each group, and results were compared in between. Mann-Whitney U test, Independent-Samples T test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 417 cases (217 females), totally. The first and second phases took periods of eight and four months, respectively. During the first phase, we were able to detect 50 cases (31 females) with underweight. On the other hand, we were able to detect just nine cases (six females) in the obesity group during the second phase therefore the obesity group was not taken for comparison. Despite the nonsignificant differences according to age in between, female ratios were detected as 62.0% (31 cases), 53.9% (149 cases), and 40.6% (37 cases) in the underweight, normal weight, and overweight groups, respectively (Table 1). So there was a statistically significant ($p<0.05$) male predominance in the overweight group. Beside that there were nonsignificant differences according to the prevalence of smoking between the three groups. There were gradual and statistically significant increases in the prevalence of WCH beside the gradual and significant decreases in the sustained NT from the underweight towards the normal weight and overweight groups. Eventually, the prevalence of WCH reached 68.1% (62 cases) in the overweight group. In other words, only 31.8% (29 cases) of the overweight group had sustained NT despite the very young mean age of the patients. Probably due to the very young mean age, there was only one case of HT among the study cases.

Table 1: Blood pressure variability of the study cases

Variables	Underweight (n= 50)	*p*-value	Normal weight (n= 276)	*p*-value	Overweight (n= 91)
Mean age (year)	24.7 ± 9.1 (15-63)	Ns*	24.3 ± 4.3 (15-39)	Ns	24.7 ± 5.2 (15-33)
Female ratio	62.0% (31)	Ns	*53.9% (149)*	*<0.05*	*40.6% (37)*
Smoking	14.0% (7)	Ns	15.2% (42)	Ns	17.5% (16)
Sustained NT†	*80.0% (40)*	*<0.05*	*64.1% (177)*	*<0.001*	*31.8% (29)*
WCH‡	*20.0% (10)*	*<0.05*	*35.5% (98)*	*<0.001*	*68.1% (62)*
HT§	0% (0)	Ns	0.3% (1)	Ns	0% (0)

*Nonsignificant ($p>0.05$) †Normotension ‡White coat hypertension §Hypertension

Table 2: Comparison of the previous study cases

Variables	Sustained NT* (n= 54)	*p*-value	WCH† (n= 66)	*p*-value	HT‡ (n= 49)	*p*-value§
Female ratio	*38.8%*	*<0.001*	*65.1%*	Ns‖	55.1%	*<0.05*
Mean age (year)	57.3 ± 11.0 (36-80)	Ns	55.3 ± 8.6 (36-75)	Ns	53.0 ± 9.3 (38-76)	Ns
Smoking	*44.4%*	*<0.001*	*13.6%*	*<0.05*	*24.4%*	*<0.01*
Overweight	31.4%	Ns	31.8%	Ns	24.4%	Ns
Obesity	*20.3%*	*<0.05*	*31.8%*	*<0.001*	*55.1%*	*<0.001*
*IGT***	*1.8%*	*<0.05*	*6.0%*	Ns	*8.1%*	*<0.01*
*DM****	*14.8%*	Ns	*18.1%*	*<0.01*	*34.6%*	*<0.001*
Hyperbetalipoproteinemia	*5.5%*	*<0.001*	*19.6%*	Ns	*12.2%*	*<0.05*
Hypertriglyceridemia	*7.4%*	*<0.001*	*21.2%*	Ns	*18.3%*	*<0.01*
Dyslipidemia	*12.9*	*<0.001*	*33.3%*	Ns	*28.5%*	*<0.01*

*Normotension †White coat hypertension ‡Hypertension §Value as a result of the comparison between the sustained NT and HT cases ‖Nonsignificant ($p>0.05$) **Impaired glucose tolerance ***Diabetes mellitus

Discussion

WCH is a condition characterized by elevated BP in medical settings combined with normal ABP or self-measured HBP. As already detected in some other studies (17, 18), both methods were equally effective for the diagnosis of WCH and HT. Similarly, recent HT guidelines propose self-measurement of HBP as an important technique to evaluate response to antihypertensive therapy, to improve compliance with therapy, and as an alternative to ABP to confirm or refute the WCH (19). In the above study (17), we observed very high prevalence of WCH in society, 33.3% in the second, 46.6% in the third, 50.0% in the fourth, 48.9% in the fifth, 36.9% in the sixth, 19.2% in the seventh, and 8.3% in the eighth decades of life, and prevalence of HT initially started to be higher than 40% in the sixth decade, and it reached up to 75% in the eighth decade of life. On the other hand, the prevalence of HT was detected as just 3% in the third, 8% in the fourth, and 21% in the fifth decades of life (17). The high prevalence of WCH in society was also shown in some other reports (20, 21). So as a hypothesis, we come to the result that all HT cases, 75% in the eighth decade of life (17), may arise from the previously WCH cases but WCH may actually be an acute phase reactant for several consequences other than HT alone. Although it was postulated in a recent review (22) that patients with WCH are characterized by absence of target organ damage induced by HT, absence of risk of future cardiovascular disease related to HT, and absence of lowering of BP from antihypertensive treatment, we evaluated WCH not as a cause of HT or atherosclerosis alone but as an acute phase reactant mainly alarming overweight and obesity and many associated disorders in the future, in the present study. When we compared the underweight, normal weight, and overweight groups according to BP variability, beside the significantly decreased prevalence of sustained NT from the underweight towards the normal weight and overweight groups, the prevalence of WCH increased in the same direction, significantly. Eventually, the prevalence of WCH reached up to 68.1% in the overweight group, and only 31.8% of the overweight group have sustained NT although their very young mean. Similarly, in the above study (17), we detected the prevalence of WCH as 33.3% even in the second, and 46.6% in the third decades of life (17), despite the lower prevalence of overweight and obesity in these age groups. On the other hand, when we compared the sustained NT, WCH, and HT groups in another study (18), WCH cases were found in between according to the frequencies of almost all of the following disorders including obesity, IGT, DM, hypertriglyceridemia, hyperbetalipoproteinemia, and dyslipidemia, and nearly all of the disorders showed a gradual and significant progression in frequencies from the sustained NT towards the WCH and HT cases (Table 2). As a surprising result of the above study (18), the prevalence of smoking significantly decreased from the sustained NT towards HT and WCH groups, but actually 38.8% of the sustained NT, 65.1% of the WCH, and 55.1% of the HT cases were female and we totally studied 45 smokers, 39 of those were males. So the highest female ratio of the WCH group showed the lowest smoking ratio and the lowest female ratio of the sustained NT group showed the highest smoking ratio. On the other hand, 20% and 35.5% of WCH cases in the underweight and the normal weight groups, respectively, may indicate that WCH may be an acute phase reactant influenced by several factors instead of BMI alone (23-25).

Authors in the Adult Treatment Panel III reported that some people may be classified as overweight just due to the larger muscular mass that may also explain the significant male predominance of the overweight group in the present study (59.3%, $p<0.05$). But actually most of them have excess body fat tissue, too, and both overweight and obesity predispose to CAD, stroke, dyslipidemia, DM, HT, and numerous other pathologies (15). Similarly, the differences between the normal weight and overweight groups according to the decreasing prevalence of sustained NT and increasing prevalence of WCH were significant in the present study ($p<0.001$ for both). So the larger muscular mass of the males probably does not protect them from the definition of excess weight according to the BMI.

Relationship between excess weight and HT is well-described under the heading of metabolic syndrome, and clinical manifestations of the syndrome include overweight and obesity, dyslipidemia, HT, insulin resistance, and proinflammatory as well as prothrombotic states. Overweight and obesity lead to both structural and functional abnormalities of the cardiovascular system. In general, overweight and obese individuals will have an increased circulating blood volume as well as an increased volume of cardiac output, thought to be the result of increased oxygen demand of the extra body tissue. The prolonged increase in circulating blood volume can lead to myocardial hypertrophy and decreased compliance, in addition to the common comorbidity of HT. In addition to HT, the prevalence of high fasting plasma glucose, high serum total cholesterol, and low high density lipoprotein cholesterol, and their clustering all raised parallel to the increased BMI value (26). Combination of these cardiovascular risk factors will eventually lead to an increase in left ventricular stroke work with a higher risk of arrhythmias, cardiac failure, and sudden cardiac death. The prevalence of CAD and stroke, especially ischemic stroke, increased parallel to the increased BMI values (27). The above prospective cohort study showed that the BMI was one of the independent risk factors of stroke and CAD (26). Eventually, the risk of death from all causes including cardiovascular diseases, cancers, or other diseases increases throughout the range of moderate and severe weight excess for both genders in all age groups (2).

As a conclusion, due to the gradually increased prevalence of WCH from the underweight towards the normal weight and overweight groups and the very low prevalence of sustained NT in the overweight group although the very young mean age of them and the already known increased prevalence of HT, IFG, IGT, DM, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, CAD, COPD, cirrhosis, CRD, and stroke and an increased all-cause

mortality rate in the same direction, WCH may actually be an acute phase reactant mainly alarming overweight and obesity and many associated health problems in future.

References

1. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999 – 2004. JAMA 2006; 295(13): 1549-1555.
2. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999; 341(15): 1097-1105.
3. Jee SH, Sull JW, Park J, Lee SY, Ohrr H, Guallar E, et al. Body-mass index and mortality in Korean men and women. N Engl J Med 2006; 355(8): 779-787.
4. Helvaci MR, Aydin LY, Aydin Y. Chronic obstructive pulmonary disease may be one of the terminal end points of metabolic syndrome. Pak J Med Sci 2012; 28(3): 376-379.
5. Helvaci MR, Kaya H, Duru M, Yalcin A. What is the relationship between white coat hypertension and dyslipidemia? Int Heart J 2008; 49(1): 87-93.
6. Satia-Abouta J, Patterson RE, Schiller RN, Kristal AR. Energy from fat is associated with obesity in U.S. men: results from the Prostate Cancer Prevention Trial. Prev Med 2002; 34(5): 493-501.
7. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med 2003; 348(17): 1625-1638.
8. Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ: Comperative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. Lancet 2002; 360(9343): 1347-1360.
9. Karter Y, Curgunlu A, Altinisik S, Erturk N, Vehid S, Mihmanli I, et al. Target organ damage and changes in arterial compliance in white coat hypertension. Is white coat innocent? Blood Press 2003; 12(5-6): 307-313.
10. Polonia JJ, Gama GM, Silva JA, Amaral C, Martins LR, Bertoquini SE. Sequential follow-up clinic and ambulatory blood pressure evaluation in a low risk population of white-coat hypertensive patients and in normotensives. Blood Press Monit 2005; 10(2): 57-64.
11. Ohkubo T, Asayama K, Kikuya M, Metoki H, Hoshi H, Hashimoto J, et al. How many times should blood pressure be measured at home for better prediction of stroke risk? Ten-year follow-up results from the Ohasama study. J Hypertens 2004; 22(6): 1099-1104.
12. Ugajin T, Hozawa A, Ohkubo T, Asayama K, Kikuya M, Obara T, et al. White-coat hypertension as a risk factor for the development of home hypertension: the Ohasama study. Arch Intern Med 2005; 165(13): 1541-1546.
13. Nakashima T, Yamano S, Sasaki R, Minami S, Doi K, Yamamoto J, et al. White-coat hypertension contributes to the presence of carotid arteriosclerosis. Hypertens Res 2004; 27(10): 739-745.
14. Fagard RH, Van Den Broeke C, De Cort P. Prognostic significance of blood pressure measured in the office, at home and during ambulatory monitoring in older patients in general practice. J Hum Hypertens 2005; 19(10): 801-807.
15. 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) final report. Circulation 2002; 106(25): 3143-3421.
16. O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, et al. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. J Hypertens 2003; 21(5): 821-848.
17. Helvaci MR, Seyhanli M. What a high prevalence of white coat hypertension in society! Intern Med 2006; 45(10): 671-674.
18. Helvaci MR, Kaya H, Seyhanli M, Cosar E. White Coat Hypertension Is Associated with a Greater All-cause Mortality. J Health Sci 2007; 53(2): 156-160.
19. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289(19): 2560-2572.
20. Hozawa A, Ohkubo T, Kikuya M, Yamaguchi J, Ohmori K, Fujiwara T, et al. Blood pressure control assessed by home, ambulatory and conventional blood pressure measurements in the Japanese general population: the Ohasama study. Hypertens Res 2002; 25(1): 57-63.
21. Celis H, Fagard RH. White-coat hypertension: a clinical review. Eur J Intern Med 2004; 15(6): 348-357.
22. Verdecchia P, Staessen JA, White WB, Imai Y, O'Brien E. Properly defining white coat hypertension. Eur Heart J 2002; 23(2): 106-109.
23. Helvaci MR, Kaya H, Yalcin A, Kuvandik G. Prevalence of white coat hypertension in underweight and overweight subjects. Int Heart J 2007; 48(5): 605-613.
24. Helvaci MR, Kaya H, Seyhanli M, Yalcin A. White coat hypertension in definition of metabolic syndrome. Int Heart J 2008; 49(4): 449-457.
25. Helvaci MR, Kaya H, Sevinc A, Camci C. Body weight and white coat hypertension. Pak J Med Sci 2009; 25(6): 916-921.
26. Zhou B, Wu Y, Yang J, Li Y, Zhang H, Zhao L. Overweight is an independent risk factor for cardiovascular disease in Chinese populations. Obes Rev 2002; 3(3): 147-156.
27. Zhou BF. Effect of body mass index on all-cause mortality and incidence of cardiovascular diseases--report for meta-analysis of prospective studies open optimal cut-off points of body mass index in Chinese adults. Biomed Environ Sci 2002; 15(3): 245-252.

An Unusual Persistent Mullerian Duct Syndrome in a child in Abha city: A Case Report

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Abstract

Background: Persistent Mullerian duct syndrome (PMDS) is a rare condition that is characterized by the presence of the Mullerian duct structures and is phenotypically and genotypically male. It could result from insufficiency of Mullerian inhibiting factor (MIF) or its receptors.

Case presentation: A 9 month-old Syrian boy was admitted to Abha Maternity and Children Hospital with a previous history of a huge left inguinal swelling since 8 hours, vomiting 4 times, and with yellowish discharge. Routine examinations and investigations were done and the boy was diagnosed with left unilateral inguinal hernia with obstruction and during surgery left ovotestis with fallopian tubes and rudimentary uterus were detected. The histopathology showed no signs of malignancy. After two weeks from left inguinal hernia repair, the boy presented with right incarcerated hernia. The boy underwent right inguinal herniotomy and right gonadopexy. During the operation, right ovotestis, with vas and fallopian tube were detected. The tube was resected and the sac was dissected; vas and vessels were secured. The boy had no sexual dysfunction and chromosomal investigation showed normal male karyotype. The testosterone level was less than the normal range (0.087 nmol/l).

Conclusion: The PMDS is a rare condition and during early stages cannot be detected; the only diagnostic procedure is when the children are tested for other diseases such as hernia or cryptorchidism. The correct and early diagnosis depends on genetic investigation and endocrinology. Surgery is the treatment of choice.

Key words: Persistent Mullerian duct syndrome (PMDS), Obstructed inguinal hernia, male, Mullerian inhibiting factor, Mullerian duct derivatives.

Background

Persistent Mullerian duct syndrome (PMDS) is a rare condition that has presented in only 150 cases in the literature (1). It is characterized by the presence of the Mullerian duct structures and is phenotypically and genotypically male but the exact etiology is still a debate. It could result from insufficiency of Mullerian inhibiting factor (MIF) or its receptors(2).

The PMD patients are supposed to have normal genitalia and sexual characteristics. Among males, inguinal hernia is characterized by descending of the testis and presence of inguinal hernia. The second type of PMD is ectopia and hernia of both testis (3, 4).

Most of the inguinal hernias present in the groin (75%). Hernias have many complications including obstruction of the bowel and strangling among older subjects(5). Also, ectopic testis diagnosed among PMD patient could result in cryptorchidism among males. The tumors of the testicular germ cell tumors have been reported but are very rare among the Mullerian duct derivatives. If the patients was diagnosed to be phenotypically male, tumor and PMD are not suspected until the time of surgery for hernia repair or treatment of cryptorchidism(6, 7).

Case presentation

A 9 months-old Syrian boy was admitted to Abha Maternity and Children Hospital with a previous history of huge left inguinal swelling since 8 hours, vomiting 4 times, yellowish discharge and these symptoms arre the most common symptoms of persistent inguinal hernia according to the literature review(6, 7). Routine examinations and investigations were normal. No history of medical chronic condition, surgical operation, allergy to medications was present and he was diagnosed with left unilateral inguinal hernia with obstruction and the patient was prepared for surgery. The child had urgent left inguinal herniotomy, gonadopexy and diagnostic laparoscopy after 3 days of admission. During operation there was left and right ovotestis with fallopian tubes and rudimentary uterus; thus the boy was referred for consultation in the OPD after 2 weeks (Figure 1).

The histopathology of the tissue from the left fibroid and vas side of the testis showed normal testis composed of capsule, lobule and convoluted seminiferous tubules. The tubules were enclosed by thick basal lamina surrounded by muscles cells. The tubules contained spermatogenic cells and Sertoli cells. No malignancy was seen. At discharge, the HB was 9.7 mg/dl, WBCs were 6.87x103 and normal UE.

After two weeks from left inguinal hernia repair, the boy presented with right incarcerated hernia. The boy underwent right inguinal herniotomy and right gonadopexy. During the operation, right ovotestis, with vas and fallopian tube were found. The tube was resected and the sac was dissected; vas and vessels were secured. 2 biopsies were taken from the vas site and the fimbrial site.

The boy had no sexual dysfunction and chromosomal investigation showed normal male karyotype 46 XY. The testosterone level was less than the normal range (0.087 nmol/l). The ALT level was within normal range, Fe, BUN and creatinine were lower than the normal range and complete blood picture was done. The pathological report showed immature testicular tissue with no signs of malignancy.

Discussion

Pseudo-hermaphroditism is a condition that occurs in males where the testis presents but the internal genital organs are not fully virilized(8, 9).

PMDS is a rare condition that can presented Mullerian duct derivatives and is seen in males. There is still debate about the exact etiology but the deficiency of MIF hormone or its receptors could result in PMDs(10-12).

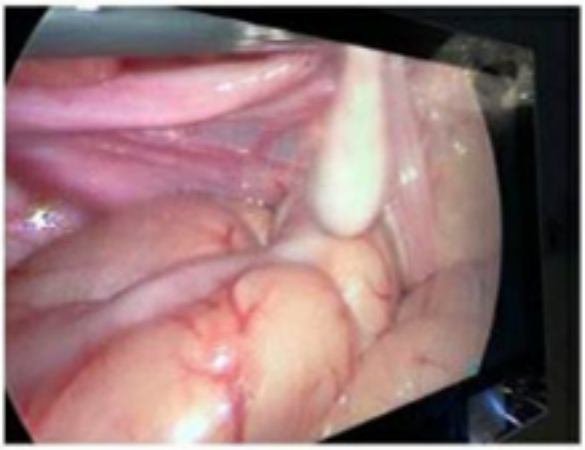
The MIF is responsible for relapse of the Mullerian duct among male embryos thus any defect on its release from the Sertoli cells in fetal growth since the seventh week of gestation may lead to the persistence of a uterus and fallopian tube in males(13, 14).

This could result in cryptorchidism or inguinal hernia(15, 16)as in the case of our patients who developed left and right inguinal hernia.

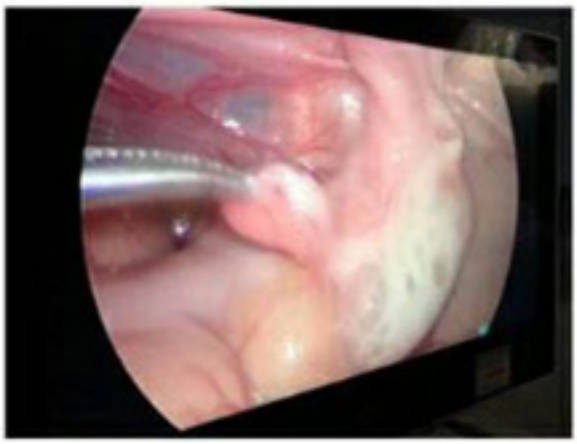
The testicles were kept due to absence of malignancy after pathological examination. Also, the tube was resected and the sac was dissected,; vas and vessels were secured. However, other studies showed increased risk of embryonal carcinoma, yolk sac tumor and seminoma among PMDS patients but this difference could be attributed to the fact that our patient was still 9 months old as the risk of tumor is increased by age (1, 2, 4, 7).

Our patient had a low level of testosterone and the chromosomal investigation showed normal male karyotype with 46XY chromosome pattern. In the same respect, normal male development of the epididymis, seminal vesicles and sperm duct needs testosterone from the Leydig cells (17). Also, the AMH deficiency or deficiency of its receptors in the male fetus could result in PMDs development. The testosterone level is not influenced by PMDs thus the chromosomal pattern is presented as 46XY and normal external genital organs as well as development of Wolffian ducts derivatives. However, the patient is phenotypically male, and cryptorchidism could occur (6, 18).

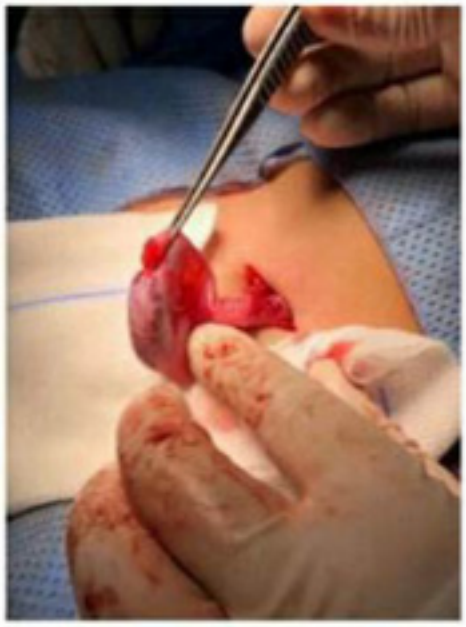
Figure 1:



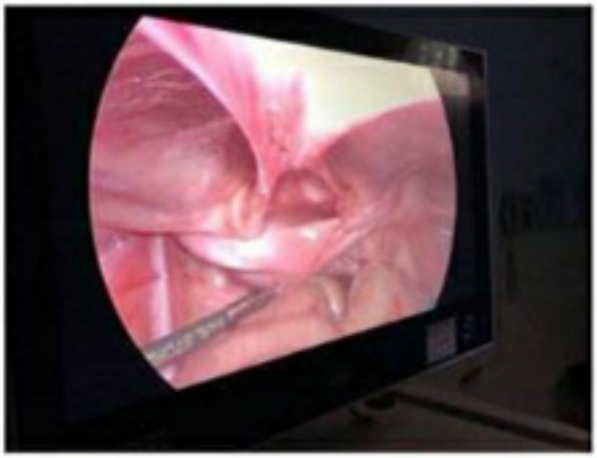
Fallopian tube



Ovotestis



Left ovotestis



Uterus

Conclusion

The PMDS is a rare condition and during early stages cannot be detected but the only diagnostic procedure is when the children are tested for other diseases such as hernia or cryptorchidism. The correct and early diagnosis depends on genetic investigation and endocrinology. Surgery and removal of the PMDs derivatives is the treatment of choice and further investigations are needed.

Conflict of Interest:
The authors declare that there is no conflict of interest regarding the publication of this paper.

References

1. Prakash N, Khurana A and Narula B (2009): Persistent Mullerian duct syndrome. Indian Journal of Pathology & Microbiology, 52:546-548.
2. Renu D, Rao BG, Ranganath K, et al. (2010): Persistent mullerian duct syndrome. The Indian Journal of Radiology & Imaging, 20:72-74.
3. Lawal TA, Egbuchulem KI and Ajao AE (2014): obstructed inguinal hernia in children: case-controlled approach to evaluate the influence of socio-demographic variables. Journal of the West African College of Surgeons, 4:76-85.
4. Gawad N, Davies DA and Langer JC (2014): Determinants of wait time for infant inguinal hernia repair in a Canadian children's hospital. Journal of Pediatric Surgery, 49:766-769.
5. Gutte AA, Pendharkar PS and Sorte SZ (2008): Transverse testicular ectopia associated with persistent Mullerian duct syndrome - the role of imaging. Br J Radiol, 81:e176-178.

6. Ren X, Wu D and Gong C (2017): Persistent Müllerian duct syndrome: A case report and review. Experimental and Therapeutic Medicine, 14:5779-5784.
7. Kaul A, Srivastava KN, Rehman SM, et al. (2011): Persistent Mullerian duct syndrome with transverse testicular ectopia presenting as an incarcerated inguinal hernia. Hernia : the journal of hernias and abdominal wall surgery, 15:701-704.
8. Saleem M, Ather U, Mirza B, et al. (2016): Persistent mullerian duct syndrome: A 24-year experience. Journal of Pediatric Surgery, 51:1721-1724.
9. Wei CH, Wang NL, Ting WH, et al. (2014): Excision of Mullerian duct remnant for persistent Mullerian duct syndrome provides favorable short- and mid-term outcomes. Journal of Pediatric Urology, 10:929-933.
10. Rehman A, Hasan Z, Amanat S, et al. (2008): Combined persistent Mullerian Duct Syndrome, Transverse Testicular Ectopia and Mosaic Klinefelter's Syndrome. Journal of the College of Physicians and Surgeons-Pakistan : JCPSP, 18:375-377.
11. Elias-Assad G, Elias M, Kanety H, et al. (2016): Persistent Mullerian Duct Syndrome Caused by a Novel Mutation of an Anti-Mullerian Hormone Receptor Gene: Case Presentation and Literature Review. Pediatric Endocrinology Reviews : PER, 13:731-740.
12. Salehi P, Koh CJ, Pitukcheewanont P, et al. (2012): Persistent Mullerian duct syndrome: 8 new cases in Southern California and a review of the literature. Pediatric Endocrinology Reviews: PER, 10:227-233.
13. Yuksel B, Saygun O and Hengirmen S (2006): Persistent mullerian duct syndrome associated with irreducible inguinal hernia, bilateral cryptorchidism and testicular neoplasia: a case report. Acta chirurgica Belgica, 106:119-120.
14. Agrawal AS and Kataria R (2015): Persistent Mullerian Duct Syndrome (PMDS): a Rare Anomaly the General Surgeon Must Know About. The Indian Journal of Surgery, 77:217-221.
15. Shamim M (2007): Persistent Mullerian duct syndrome with transverse testicular ectopia presenting in an irreducible recurrent inguinal hernia. JPMA The Journal of the Pakistan Medical Association, 57:421-423.
16. Odi TO, Abdur-Rahman LO and Nasir AA (2010): Persistent Mullerian duct syndrome: a case report and review of the literature. African journal of paediatric surgery : AJPS, 7:191-193.
17. Renu D, Rao BG, Ranganath K, et al. (2010): Persistent mullerian duct syndrome. The Indian journal of radiology & imaging, 20:72-74.
18. Gujar NN, Choudhari RK, Choudhari GR, et al. (2011): Male form of persistent Mullerian duct syndrome type I (hernia uteri inguinalis) presenting as an obstructed inguinal hernia: a case report. Journal of medical case reports, 5:586.

Prevalence of abdominal obesity and its associated comorbid condition in adult Yemeni people of Sana'a City

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Abstract

Objective: Abdominal obesity is a metabolic problem that has become increasingly common worldwide over the past several decades. Its prevalence is increased in both advanced and developing countries including Yemen. The aim of this cross sectional study was to investigate the prevalence of Abdominal obesity in a sample of Yemeni adult individuals and its association with other comorbid conditions namely, hypertension, diabetes, dyslipidemia (high triglyceride, low high density lipoprotein) and metabolic syndrome (MS)..

Methodology: A sample of 1118 adult Yemeni people equal to or over 18 years was randomly chosen to represent the population living in Sana'a City during a period of two years from April 2016 to April 2018. All the study group underwent full clinical history and examination which included measurement of BP and waist circumference and the following laboratory investigations (FBS, serum TG, HDL, and LDL).

Results: The prevalence of abdominal obesity in this study was 24.5% (7.9% male and 44.2% female). Central obesity in this study was significantly correlated with age and sex. The highest prevalent comorbidity in patients with abdominal obesity was high BP (41.3%), followed by high serum TG (40 %), higher prevalence of MS (40%), low serum HDL (37.8%) high LDL (20.1%) raised fasting blood glucose (22.1%) than those without abdominal obesity (5.5%, 31.3%, 16.6%, 8.5%, 12.5% and increased FBS 10% respectively).

Conclusion: Hypertension, diabetes, dyslipidemia and MS are strongly correlated with abdominal obesity.

Key words : central obesity, hypertension, dyslipidemia, MS

Introduction

Obesity is a worldwide epidemic. Beyond the fat mass per se, the pattern of fat distribution has a profound influence on cardiometabolic risk. Visceral abdominal fat (VAF) is metabolically active and pro-inflammatory and presents a higher cardiometabolic risk association and calcification of the coronary arteries than the body mass index (BMI) and has more impact on health than subcutaneous fat, presenting a risk factor for increased incidence of metabolic syndrome (1, 2). Abdominal obesity (AO) is directly associated with increased VAF, and it is also associated with endothelial dysfunction, inflammation, insulin resistance, diabetes mellitus, hypercholesterolemia, metabolic syndrome [MetS], and cancer (1, 3). There are several methods available to measure AO. Waist circumference (WC) provides an indicator of central adiposity that is the most practical and easiest method used in large-scale epidemiological studies (4). It is a good predictor of cardiometabolic morbidity and mortality, and it has also a positive association with visceral abdominal fat. However, WC does not allow us to differentiate between visceral fat and subcutaneous fat; methods such as absorptiometry by dual energy X-ray (DEXA), impedance, or densitometry can be used to handle this differentiation (5–7). WC measurement requires correct and standardized procedures, which depend mainly on training and adequate equipment. A standardized technique requires that the person being measured removes bulky or tight garments, as well as shoes with heels, empties their bladder then stands in the upright position, with arms loosely positioned to the side. The tape is passed around the body and positioned mid-way between the iliac crest and costal margin of the lower rib, ensuring that it is Population Organization (References) Recommended waist circumference threshold for abdominal obesity Men Women Europid IDF ≥94 cm ≥80 cm Caucasian WHO ≥94 cm [increased risk]≥102 cm [still higher risk] ≥80 cm [increased risk]≥88 cm [still higher risk] United States AHA/NHLBI [ATP III] ≥102 cm ≥88 cm Canada Health Canada ≥102 cm ≥88 cm European European cardiovascular societies ≥102 cm ≥88 cm Asian [including Japanese] IDF ≥90 cm ≥80 cm Asian WHO ≥90 cm ≥80 cm Japanese Japanese obesity society ≥85 cm ≥90 cm China Cooperative task force ≥85 cm ≥80 cm Middle East, Mediterranean IDF ≥94 cm ≥80 cm Sub-Saharan African IDF ≥94 cm ≥80 cm Ethnic Central and South American IDF ≥90 cm ≥80 cm. Waist circumference cutoffs are recommended for the diagnosis of abdominal obesity according to ethnicity and gender (8,9). In 2009, a method to standardize the diagnosis of metabolic syndrome was established, upon discussions held by the International Diabetes Federation (IDF) and the American Heart Association/National Heart, Lung, and Blood Institute. In this context, it was suggested that ethnicity and gender should be considered for the diagnosis of AO (9)

In decades past, many clinicians were taught in medical school that the adipose cell is a vehicle for energy storage and nothing more. Today, there is a different perception of the adipose cell; specifically, it is an active endocrine organ that communicates with gut hormones and a master regulator in the brain to control appetite and satiety. It also exerts pathologic effects on other organs and critical metabolic and immunologic processes .Four major hormones—ghrelin, insulin, peptide YY (PYY) from the gut, and leptin from fat tissue—participate in appetite and satiety regulation in communication with each other and the central control of energy balance, the arcuate nucleus in the hypothalamus. Ghrelin is a short-term appetite hormone, the “hunger hormone”, that brings on feelings of hunger at mealtimes. Secreted in the gastric fundus, ghrelin rises immediately before meals and falls as insulin levels rise in response to the meal(10,11). It also increases during weight loss, which may be a factor in making successful weight loss so difficult. However, ghrelin levels decrease in persons who have had gastric bypass surgery, which may aid in maintaining weight loss (10). Insulin, in addition to its multiple other metabolic functions, acts as a satiety signal to the brain, causing feelings of fullness. PYY, secreted in the distal small intestine in response to food, signals satiety to the hypothalamus to counteract the influence of ghrelin. Levels of PYY are significantly lower in obese versus normal-weight persons,(8) but are elevated after gastric bypass(11). Leptin was the original “satiety factor,” discovered to much excitement by Friedman and coworkers in 1994(12). This hormone is produced in adipose tissue in proportion to body fat; the more fat present, the more leptin secreted. Initially, it was hoped that exogenous leptin administration would be a “magic bullet” for curing obesity and establishing the condition as a metabolic disorder instead of a personal failing(9). Despite its effectiveness in mice with a genetic defect in the leptin molecule, exogenous leptin does not produce meaningful weight loss in obese humans, apparently because the brain becomes resistant to it. However, leptin is one of many neuro hormonal pathways that have evolved genetically to prevent starvation and ensure survival. In addition, the hypothalamus contains neurons that can either stimulate or inhibit food intake, and many of the gut hormones exert actions on both sides of the equation(13). The possibilities for routes to intervention among this wealth of pathways remain promising and rational in the search for weight control treatments. Current thinking now holds that fat tissue is an active participant in weight regulation. In one current theory, it is the basis of adiposopathy, defined by Bays and colleagues as pathogenic adipose tissue whose toxicity may be worsened by fat accumulation and a sedentary lifestyle in genetically susceptible individuals(14). This dysfunctional tissue releases increased amounts of free fatty acids (FFAs) and abnormal amounts of inflammatory factors such as cytokines from macrophages. Such changes can promote insulin resistance in skeletal muscle and the liver, increased insulin secretion, dyslipidemia, hypertension, and type 2 diabetes, all components of the metabolic syndrome, which increases the risk of atherosclerosis (14-16). Muscle biopsies in obese patients show that deposits of fat are stored in liver when fat can no longer be stored subcutaneously, with some cases resulting in steatohepatitis and eventually fibrosis. Excess fat may be associated with androgen elevations in women (or decreases in men);

increases in plasminogen-activator inhibitor 1, which encourages thrombosis; and asthma, as a consequence of pro inflammatory changes. Even osteoarthritis may be an outcome of increased inflammation, although it is also mediated by the mechanical load of excess weight on the joints(17,18). Not everyone who is obese has metabolic syndrome or type 2 diabetes—although these are perhaps the most prevalent complications of obesity. Genetic susceptibility is yet another confounding component of obesity. The ability to differentiate genetically susceptible humans is not yet within reach. Better predictors of who will and will not respond to adiposity with endocrine and other consequences are still needed. In the meantime, ongoing research on appetite and satiety regulation has made it clear that obesity is a disease largely beyond an individual's control(19) rather than a function of inadequate willpower. The development and availability of medications and procedures that address the underlying pathobiology of obesity herald a new approach to stemming the tide of the obesity epidemic.

Material and Method

This was a cross sectional population based study conducted in Sana'a city for a period of 2 years between April 2017 and April 2018. A sample of 1,118 adult Yemeni people (508 male and 610 aged ≥18 years) was randomly selected. The data collection was from those attending Al-Kuwait University Hospital and Consultation Clinic. All the participants in this study underwent complete clinical history (regarding their age, occupation, habits, any history of hypertension, diabetes mellitus, dyslipidemia and medication). Anthropometric measurements included measurement of waist circumference and systolic and diastolic blood pressure. Waist circumference was manually measured on standing subjects with soft tape midway between the lowest rib and the iliac crest. WC was divided into abdominal overweight (85–95 cm in males and 80–90 cm in females) and abdominal obesity groups (WC ≥ 95 cm in males and ≥ 90 cm in females) (20,21). WC ≥ 85 cm in males and ≥ 80 cm in females were defined as elevated WC. Two blood pressure recordings were obtained from the right arm of patients with standard mercury sphygmomanometer in a sitting position after 10 minutes of rest; measurements were taken in 3-5 minute intervals and the mean values were calculated . Blood pressure was classified as normotensive (SBP < 120 mmHg and DBP < 80 mmHg), pre-hypertensive (SBP: 120–139 mmHg and/or DBP: 80–89 mmHg) and hypertensive (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg) by the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (22,23); fasting blood glucose, total cholesterol, triglyceride, LDL and HDL cholesterol were measured.

The American Diabetes Association criteria was used to classify FBG as normal glucose (FBG < 5.6 mmol/L), impaired fasting glucose (IFG) (FBG ≥ 5.6 mmol/L ≤ FBG < 7.0 mmol/L), and diabetic (FBG ≥ 7.0 mmol/L).

Type 2 diabetes mellitus was defined according to the American Diabetes Association (24) A1C ≥ 6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay or FPG ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 hours. In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing or 2-hour plasma glucose ≥200 mg/dl (11.1mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing or in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose 200 mg/dl (11.1mmol | l).

Dyslipidemia was classified according to ATP III, TG: Normal < 1.69 mmol/L, Borderline high 1.69–2.26 mmol/L, High 2.26–5.65 mmol/L, Very high ≥ 5.65 mmol/L; TC: Desirable < 5.17 mmol/L, Borderline high 5.17–6.24 mmol/L, High ≥ 6.24 mmol/L; HDL-C: High 1.56 mmol/L, Optimal 1.03–1.56 mmol/L, Low <l.03 mmol/L; LDL-C: Optimal <2.59 mmol/L, Near optimal 2.59–3.38 mmol/L, Borderline high 3.38–4.16 mmol/L, High 4.16–4.94 mmol/L, Very high ≥4.94 mmol/L.(25).

Metabolic syndrome was diagnosed by the presence of three or more of the following criteria (26).

- Fasting glucose ≥100 mg/dL (or receiving drug therapy for hyperglycemia)
- Blood pressure ≥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 ≥102 cm (40 in) in men or ≥88 cm (35 in) in women; if Asian American, ≥90 cm (35 in) in men or ≥80 cm (32 in) in women (The international diabetes federation [IDF] criteria allow the use of a body mass index [BMI] >30 kg/m2 in lieu of the waist circumference criterion.)

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 ≤ 0.05.

Results

A study sample included 1,118 persons aged between 18-83; of them 508 (45.4%) were male and 610 (54.6%) were female . The Mean age ± SD was 47.4 ±10.2 years, with an age range of 30–77 years with no significant age difference between men and women.

The prevalence of abdominal obesity according to WC was 24.5%. The physical and metabolic characteristic of the study population by gender are shown in Table 1. Women have significantly higher prevalence of abdominal obesity, systolic and diastolic BP, high serum TG, high LDL, low serum HDL as well as high prevalence of MS.

Table 1: The clinical and laboratory characteristics of the study group

Variable		Men=508 (45.4%)	Women =610 (54.7%)	Total =1118	p-value
WC					
-	Normal	468(92.1%)	240(55.8%)	708(75.5%)	0.000
-	Obese	40(7.9%)	190(44.2%)	230(24.5%)	
BP					
-	Normal	458(91.2%)	516(84.6%)	974(87.1%)	0.003
-	High	50(9.8%)	94(15.5%)	144(12.9%)	
FBS					
-	Normal	434(85.4%)	524(85.9%)	958(85.7%)	0.65
-	IFG	28(5.5%)	16(2..6%)	45(3.9%)	
-	Diabetes	26(9.1%)	70(11.5%)	95(10.4%)	
TG					
-	Normal	310(61%)	440(72.1%)	750(67.1%)	
	High	198(39%)	170(27.9%)	368(32.9%)	0.000
HDL					
-	Normal	412(81.1%)	544(89.2%)	956(85.5%)	0.000
-	High	96(18.9%)	66(10.5%)	162(14.5%)	
LDL					
-	Normal	304(59.8%)	296(48.5%)	600(53.7%)	0.000
-	High	204(40.2%)	310(51.5%)	518(46.3%)	
-	MS	85 (16.7%)	155 (25.4%)	240 (21.4%)	0.000

Table 2: The prevalence of both clinical and laboratory characteristics between obese and non-obese

Factors	Total =1118	With central obesity= 230	Without central obesity=888	P- value
Age	47.5±10.2	41.2±11.4	38.4±11.4	0.0321
Male gender	508 (45.4%)	40(17.3%)	468(52.7%)	0.0001
FBS mg/dl	140 (12.5%)	51(22.1%)	89(10%)	0.0001
BP mmHg	144(12.8%)	95(41.3%)	49 (5.5%)	0.0001
TG mg/dl	368(32.9%)	92(40%)	276(31.3%)	0.011
LDL	245 (21.9%)	134(20.1%)	111(12.5%)	0.0001
HDL	162 (14.4%)	87(37.8%)	75(8.5%)	0.0001
MS	240(21.4%)	92 (40%)	148(16.6%)	0.0001

The highest prevalent comorbidity in patients with abdominal obesity was high BP (41.3%), followed by high serum TG (40 %), high prevalence of MS (40%), low serum HDL (37.8%) high LDL (20.1%) raised fasting blood glucose (22.1%) than those without abdominal obesity (5.5%, 31.3%, 16.6%, 8.5%, 12.5% and increased FBS 10% respectively).

Discussion

The prevalence of abdominal obesity is increasing dramatically worldwide(27,28). In the United States, the overall age-adjusted prevalence of abdominal obesity increased significantly from 46.4% (95% confidence interval [CI], 42.1%–50.8%) in 1999–2000 to 54.2% (95% CI, 51.3%–57.0%) in 2011–2012(27).

Obesity is a major risk factor for hypertension, type 2 diabetes, coronary heart disease, and certain types of cancer(29,30,31,32,33). Obesity is classified as general obesity (defined as body mass index ≥30 kg/m2) and abdominal obesity (defined as waist circumference [WC] ≥90 cm for men and WC ≥80 cm for women), based on World Health Organization (WHO) recommendations for Asians(34,35). In particular, abdominal obesity has a close relationship with central fat localization and cardiovascular disease, independently of general obesity(36,37,38). The overall prevalence of abdominal obesity among the study population in the present study was found to be 24.5% which is comparable to that found in Nigeria (21.8%) [39] , Tanzania (24.8%)(40) and Brazil (30%) (41), lower than that was found in South Asia (68.9%) (42), USA (56%)(43) and Mexico (74%) (44). The prevalence of abdominal obesity in population-based studies from the Arab world was found to be variable and was in the range of 23 % to 46.5% (45,46).

In our study, there was significant gender difference which is consistent with the findings from Saudi Arabia (46) and Taiwan (23) .

The highest prevalent abdominal obesity co morbidity in our study population was hypertension (41.3%)(47) followed by atherogenic dyslipidemia as high TG (40%) low serum HDL (37.8%) and high serum LDL (20.1%) (48), followed by higher prevalence of MS (41.3%) (49.50) and raised fasting blood glucose (22.1%) (51) than those without central obesity (5.5%, 31.3%, 16.6%, 8.5%, 12.5% and increased FBS 10%) respectively .

This finding was in keeping with the existing knowledge that obesity is clearly linked to essential hypertension. Hypertension was also the most common comorbid condition in abdominal obese subjects (47, 48). The mechanism linking abdominal obesity with hypertension might be explained by the activation of the renin–angiotensin–aldosterone system which primarily leads to the activation of the sympathetic activity, promotion of the leptin resistance by increased pro-coagulatory activity. The cumulative effect of this cascade is endothelial dysfunction and inflammatory changes. Additional mechanisms include the enhanced renal sodium reabsorption with a resultant increase in volume expansion usually observed in abdominally obese patients (52). In our study 40% of the obese patients had dyslipidemia (51). This fact can be explained by the accumulation of adipose tissue and the release of free fatty acids which are easily directed to the liver for higher production of TG and very low density lipoprotein (51,52). Raised fasting blood glucose was the lowest comorbidity among abdominal obese subjects (53.54).

Conclusion

Our study demonstrates an alarming high prevalence of abdominal obesity among Yemeni patients that increases the burden on an overstrained Yemeni health system with uprising CVDs and other AO related health problems e.g. hypertension, dyslipidemia, DM. As obesity is the main modifiable risk factor for these comorbid conditions, raising community awareness and promotion of healthy lifestyle together with organizing training courses for health educators are highly recommended. There is also an urgent need to develop strategies for prevention, detection, and treatment of AO that could contribute to decreasing the incidence of grave consequences such as cardiovascular disease and diabetes.

Abbreviations: World Health Organization (WHO), waist circumference (WC), abdominal obesity (AO) , Metabolic Syndrome (MS), Adult Treatment Panel (ATP) serum triglyceride (TG),High Density Lipoprotein (HDL), Fasting Blood Sugar (FBS), National Cholesterol Education Program Adult Treatment Panel (NCEP ATP),

References

1- Shah RV, Murthy VL, Abbasi AS, Blankstein R, Kwong RY, Goldfine AB, et al. Visceral adiposity and the risk of metabolic syndrome across body mass index: the MESA study. JACC Cardiovasc Imaging. 2014;7(12):1221–1235. doi:10.1016/j.jcmg.2014.07.017

2- Carmienke S, Freitag MH, Pischon T, Schlattmann P, Fankhaenel T, Goebel H, et al. General and abdominal obesity parameters and their combination in relation to Epidemiology of Abdominal Obesity http://dx.doi.org/10.5772/65342 85 mortality: a systematic review and meta-regression analysis. Eur J Clin Nutr. 2013; 67 (6):573–585. doi:10.1038/ejcn.2013.61

3- Martins IS, Marino SP. The potential of central obesity antropometric indicators as diagnostic tools. Rev Saúde Pública. 2003;37(6):760–767.

4- Olinto MTA, Nácul LC, Dias-da-Costa JS, Gigante DP, Menezes AMB, Macedo S. Intervention levels for abdominal obesity: prevalence and associated factors. Cad Saúde Pública. 2006;22(6):1207–1215. doi:10.1590/S0102-311X2006000600010

5- Lee K, Lee S, Kim YJ, Kim YJ. Waist circumference, dual-energy X-ray absortiometrically measured abdominal adiposity, and computed tomographically derived intra-abdominal fat area on detecting metabolic risk factors in obese women. Nutrition. 2008;24:625–631. doi:10.1016/j.nut.2008.03.004

6- Lean ME, Han TS, Deurenberg P. Predicting body composition by densitometry from simple anthropometric measurements. Am J Clin Nutr. 1996;63:4–14.

7- Menezes TN, Rocha FL, Belém PLO, Pedraza DF. Abdominal obesity: a critical review of the measurement techniques and cutoff points of anthropometric indicators adopted in Brazil. Ciência & Saúde

8- World Health Organization (WHO). Waist Circumference and Waist-Hip Ratio: Report of a WHO Expert Consultation, Geneva, 8–11 December 2008. Geneva: WHO; 2011.
9- Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation task force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009;120:1640–1645. doi:10.1161/CIRCULATIONAHA.109.192644
10- Batterham RL, Cohen MA, Ellis SM, et al. Inhibition of food intake in obese subjects by peptide YY3-36. N Engl J Med. 2003;349:941-948.
11- Investigating Minds. March 30, 2009. http://im-promise-of-leptin_30.html. 0tb.blogspot.com/2009/03/obesityreviving-
12 - Kashyap SR, Gatmaitan P, Brethauer S, Schauer P. Bariatric surgery for type 2 diabetes: weighing the impact for obese patients. Cleve Clin J Med. 2010;77:468-476.
13- Suzuki K, Simpson KA, Minnion JS, ShillitoJC, Bloom SR. The role of gut hormones and the hypothalamus in appetite regulation. Endocr J. 2010;57:359-372.
14- Bays H. Adiposopathy—defining, diagnosing, and establishing indications to treat 'sick fat': what are the regulatory considerations? US Endocrine Dis. 2006;12-14.
15- Bays H, Ballantyne C. Adiposopathy: why do adiposity and obesity cause metabolic disease? Future Lipidol. 2006;1:389-420.
16- Guilherme A, Virbasius JV, Puri V, Czech MP. Adipocyte dysfunctions linking obesity to insulin resistance and type 2 diabetes. Nat Rev Mol Cell Biol. 2008;9:367-377.
17- Klein S. Obesity as a chronic disease: epidemiology, morbidity, and mortality. http://cme. medscape.com/viewarticle/567413. Accessed November 1, 2012.
18- Aronne LJ, Nelinson DS, Lillo JL. Obesity as a disease state: a new paradigm for diagnosis and treatment. Clin Cornerstone. 2009;9:9-25.
19- Allison DB, Downey M, Atkinson RL, et al. Obesity as a disease: a white paper on evidence and arguments commissioned by the Council of the Obesity Society. Obesity (Silver Spring). 2008;16:1161-1177.
20- Hu L, Huang X, You C, Li J, Hong K, Li P, et al. Prevalence and Risk Factors of Prehypertension and Hypertension in Southern China. PLoS One. 2017; 12(1): e170238 doi: 10.1371/journal.pone.0170238 .
21- Hou X, Lu J, Weng J, Ji L, Shan Z, Liu J, et al. Impact of waist circumference and body mass index on risk of cardiometabolic disorder and cardiovascular disease in Chinese adults: a national diabetes and metabolic disorders survey. PLoS One. 2013; 8(3):e57319
22- Canadian Organ Replacement (CORR) 2001 Annual Report. Ottawa, ON, Canada: Canadian Institute for Health Information; 2001.
23- European Society of Hypertension-European Society of Cardiology Guidelines Committee: Guidelines for the management of arterial hypertension. J Hypertens 2003, 21:1011-1053.
24- American Diabetes Association. Standards of Medical Care in Diabetes 2011.
DIABETES CARE, VOLUME 34, SUPPLEMENT 1, JANUARY 2011
25- 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). JAMA2001;285(19):2486-97. A.y
26- Ford E.S., Maynard L.M., Li C. Trends in mean waist circumference and abdominal obesity among US adults, 1999–2012. JAMA. 2014;312:1151–1153.
27- Yoo S., Cho H.J., Khang Y.H. General and abdominal obesity in South Korea, 1998-2007: gender and socioeconomic differences. Prev Med. 2010;51:460–465.
28- Lilja M., Eliasson M., Stegmayr B., Olsson T., Soderberg S. Trends in obesity and its distribution: data from the Northern Sweden MONICA Survey, 1986–2004. Obesity (Silver Spring) 2008;16:1120–1128.
29- Welty T.K. Health implications of obesity in American Indians and Alaska Natives. Am J Clin Nutr. 1991;53:1616S–1620S.
30- Must A., Spadano J., Coakley E.H., Field A.E., Colditz G., Dietz W.H. The disease burden associated with overweight and obesity. JAMA. 1999;282:1523–1529.
31- Lee Z.S., Critchley J.A., Chan J.C. Obesity is the key determinant of cardiovascular risk factors in the Hong Kong Chinese population: cross-sectional clinic-based study. Hong Kong Med J. 2000;6:13–23.
32- Hu F.B., Wang B., Chen C. Body mass index and cardiovascular risk factors in a rural Chinese population. Am J Epidemiol. 2000;151:88–97.
33- Ahn S., Zhao H., Smith M.L., Ory M.G., Phillips C.D. BMI and lifestyle changes as correlates to changes in self-reported diagnosis of hypertension among older Chinese adults. J Am Soc Hypertens. 2011;5:21–30.
34- WHO . WHO Expert Committee; 1995. Physical Status: The Use of and Interpretation of Anthropometry.
35- WHO, IASO, IOTF . International Diabetes Institute; Melbourne: 2000. The Asia-Pacific Perspective: Redefining Obesity and its Treatment.
36- Pouliot M.C., Despres J.P., Lemieux S. Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. Am J Cardiol. 1994;73:460–468.
37- Yusuf S., Hawken S., Ounpuu S. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. Lancet. 2005;366:1640–1649.
38- Reis J.P., Macera C.A., Araneta M.R., Lindsay S.P., Marshall S.J., Wingard D.L. Comparison of overall obesity and body fat distribution in predicting risk of mortality. Obesity (Silver Spring) 2009;17:1232–1239.
39- Chukwuonye II, Chuku A, Onyeonoro UU, Okpechi IG, Madukwe OO, Umeizudike TI, et al. Prevalence of abdominal obesity in Abia State, Nigeria: results of a population based house-to-house survey. Diabetes Metab Syndr Obes Targets Ther. 2013;6:285–291. doi:10.2147/DMSO.S43545

40- Munyogwa MJ and Mtumwa AH
The Prevalence of Abdominal Obesity and Its Correlates among the Adults in Dodoma Region, Tanzania: A Community-Based Cross-Sectional Study
Adv Med. 2018; 2018: 6123156.
41- Linhares RS, Horta BL, Gigante DP, Dias-da-Costa JS, Olinto MTA. Distribution of general and abdominal obesity in adults in a city in southern Brazil. Cad Saúde Pública. 2012;28(3):438–447. doi:10.1590/S0102-311X2012000300004
42- Misra A, Shivastava U. Obesity and dyslipidemia in South Asians. Nutrients. 2013;5:2708– 2733. doi:10.3390/nu5072708
43- Beltrán-Sánchez H, Harhay MO, Harhay MM, McElligott S. Prevalence and trends of metabolic syndrome in the adult US population, 1999–2010. J Am Coll Cardiol. 2013;62 (8):697–703. doi:10.1016/j.jacc.2013.05.064
44- Barquera S, Campos-Nonato I, Hernández-Barrera L, Pedroza A, Rivera-Dommarco JA. Prevalence of obesity in Mexican adults, 2000–2012. Salud Pública Méx. 2013;55(2):S151–S160
45- Badran M and Laher I Obesity in Arab speaking countries.
Journal of Obesity Volume 2011, Article ID 686430, 9 pages doi:10.1155/2011/686430
46- Hazzaa M. Al-Hazzaa, Nada A. Abahussain, Hana I. Al-Sobayel, Dina M. Qahwaji, Nouf A. Alsulaiman, and Abdulrahman O. Musaiger.
Prevalence of Overweight, Obesity, and Abdominal Obesity among Urban Saudi Adolescents: Gender and Regional Variations.
47- Amole OI, Adesina AS. The prevalence of abdominal obesity and hypertension among adults in Ogbomoso, Nigeria. African journal of primary health care and family medicine 2011, 188
48- Khairun Nisa Berawi, Sutopo Hadi, Nur Indrawati Lipoeto, Irza Wahid and Jamsari; Dyslipedemia Incidents Between General Obesity and Central Obesity of Employees with Obesity at Universities. Lampung biomedical and pharmacological J
Vol. 11(1), 201-207 (2018)
49- Barroso, AT, Marins BL, Alves R. Association of central obesity with the incidence of cardiovascular diseases and risk factors. International journal of cardiovascular science s 2017,30 (5) 416-424
50- Iloh GUP, Ikwudinma AO. Abdominal obesity in adult Nigerian Africans: Prevalence and co-occurrence with cardio-metabolic risk factors in a resource poor setting of a rural hospital in EasternNigeria. AmJHealth Res. 2013;1(3):73–80.
51- LEE Wei-Jei ; CHEN Hsin-Hung ; WEU WANG ; WEI Po-Li ; LIN Ching-Mei ; HUANG Ming-Te. Metabolic syndrome in obese person referred from weight reduction surgery in Taiwan. J Formos Med Assoc 2003; 102; 459-464
52- Xavier HT, Izar MC, Faria Neto JR, Assad MH, Rocha VZ, Sposito AC, et al; Sociedade Brasileira de Cardiologia. [V Brazilian Guidelines on Dyslipidemias and Prevention of Atherosclerosis]. Arq Bras Cardiol. 2013;101(4 Suppl 1):1-20. doi: 105935/abc20135010. [
53- Pimenta AM, Kac Gilberto, Gazzinelli A, Corrêa-Oliveira R, Velásquez- Meléndez G. Association between central obesity, triglycerides and hypertension in a rural area in Brazil. Arq Bras Cardiol. 2008;90(6):386-92. doi: 10.1590/S0066-782X2008000600006
54- Termizy H M, Mafauzy M. Metabolic syndrome and its characteristics among obese patients attending an obesity clinic. 2009. Singapore Med J 2009; 50: 390- 394

Smoking may even cause irritable bowel syndrome

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Abstract

Background: Smoking induced chronic vascular endothelial inflammation may even cause irritable bowel syndrome (IBS).

Method: IBS is diagnosed according to Rome II criteria in the absence of red flag symptoms.

Results: The study included 647 patients with IBS and 340 control cases. Mean age of the IBS patients was 41.4 years. Interestingly, 64.2% of the IBS patients were female. Prevalence of smoking was higher in the IBS cases (36.4% versus 20.5%, p<0.001). Similarly, prevalence of antidepressants use was higher in the IBS patients (48.0% versus 15.5%, p<0.001). Additionally, prevalence of urolithiasis was also higher in the IBS group (23.3% versus 9.4%, p<0.001). Mean body mass index values were similar in the IBS and control groups (27.5 versus 27.7 kg/m2, p>0.05, respectively). Prevalence of white coat hypertension was also similar in them (29.3% versus 31.4%, p>0.05, respectively). Although prevalence of hypertension and diabetes mellitus and mean values of total cholesterol, triglycerides, low density lipoproteins, and high density lipoproteins were all similar in them, mean value of fasting plasma glucose (FPG) was significantly higher in the IBS group (110.1 versus 105.6 mg/dL, p= 0.013).

Conclusion: IBS may be a low-grade inflammatory process being initiated with infection, inflammation, psychological disturbances-like stresses, and eventually terminates with dysfunctions of gastrointestinal and genitourinary tracts and other systems of the body. Although there may be several possible causes of IBS, smoking induced chronic vascular endothelial inflammation may even cause IBS. The higher FPG in the IBS patients should be researched with further studies.

Key words: Smoking, irritable bowel syndrome, metabolic syndrome, fasting plasma glucose

Introduction

One of most frequent applications to Internal Medicine Polyclinics are due to recurrent upper abdominal discomfort (1). Although gastroesophageal reflux disease, esophagitis, duodenal or gastric ulcers, erosive gastritis or duodenitis, celiac disease, chronic pancreatitis, and malignancies are found among possible causes, irritable bowel syndrome (IBS) may be one of the most frequently diagnosed diseases, clinically. Flatulence, periods of diarrhea or constipation, repeated toilet visits due to urgent evacuation or early filling sensation, excessive straining, feeling of incomplete evacuation, frequency, urgency, reduced feeling of well-being, and eventually disturbed social life are often reported by the IBS patients. Although many patients relate onset of symptoms to intake of food, and often incriminate specific food items, a meaningful dietary role is doubtful in the IBS. According to literature, 10-20% of the general population have IBS, and it is more common among females with unknown causes (2). Psychological factors seem to precede onset or exacerbation of gut symptoms, and many potentially psychiatric disorders including anxiety, depression, or sleep disorders frequently coexist with the IBS (3). For example, thresholds for sensations of initial filling, evacuation, urgent evacuation, and utmost tolerance recorded via a rectal balloon significantly decreased by focusing the examiners' attention on gastrointestinal stimuli by reading pictures of gastrointestinal malignancies in the IBS cases (4). So although IBS is described as a physical instead of a psychological disorder according to Rome II guidelines, psychological factors may be crucial for triggering of the physical changes in the body. IBS is actually defined as a brain-gut dysfunction according to the Rome II criteria, and it may have more complex mechanisms affecting various systems of the body with a low-grade inflammatory state (5). For example, IBS may even terminate with chronic gastritis, urolithiasis, and hemorrhoid in a significant proportion of patients (6-8). Similarly, some authors studied the role of inflammation via colonic biopsies in 77 patients with IBS (9). Although 38 patients had normal histology, 31 patients demonstrated microscopic inflammation and eight patients fulfilled criteria for lymphocytic colitis. However, immunohistology revealed increased intraepithelial lymphocytes as well as increased CD3 and CD25 positive cells in lamina propria of the group with "normal" histology. These features were more evident in the microscopic inflammation group who additionally revealed increased neutrophils, mast cells, and natural killer cells. All of these immunopathological abnormalities were the most evident in the lymphocytic colitis group who also demonstrated HLA-DR staining in the crypts and increased CD8 positive cells in the lamina propria (9). A direct link between the immunologic activation and IBS symptoms was provided by work of some other authors (10). They demonstrated not only an increased incidence of mast cell degranulation in the colon but also a direct correlation between proximity of mast cells to neuronal elements and pain severity in the IBS (10). In addition to these findings, there is some evidence for extension of the inflammatory process behind the mucosa. Some authors addressed this issue in 10 patients with severe IBS by examining full-thickness jejunal biopsies obtained via laparoscopy (11). They detected a low-grade infiltration of lymphocytes in myenteric plexus of nine patients, four of whom had an associated increase in intraepithelial lymphocytes and six demonstrated evidence of neuronal degeneration. Nine patients had hypertrophy of longitudinal muscles and seven had abnormalities in number and size of interstitial cells of Cajal. The finding of intraepithelial lymphocytosis was consistent with some other reports in the colon (9) and duodenum (12). On the other hand, smoking is a well-known cause of chronic vascular endothelial inflammation all over the body. We tried to understand whether or not smoking induced chronic vascular endothelial inflammation all over the body is found among one of the possible causes of the IBS.

Material and methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. Consecutive patients with upper abdominal discomfort were taken into the study. Their medical histories including smoking habit, hypertension (HT), diabetes mellitus (DM), and already used medications including antidepressants at least for a period of six months were learned. A routine check up procedure including fasting plasma glucose (FPG), triglycerides, low density lipoproteins (LDL), high density lipoproteins (HDL), erythrocyte sedimentation rate, C-reactive protein, albumin, thyroid function tests, creatinine, urinalysis, hepatic function tests, markers of hepatitis A virus, hepatitis B virus, hepatitis C virus, and human immunodeficiency virus, a posterior-anterior chest x-ray film, an electrocardiogram, a Doppler echocardiogram in case of requirement, an abdominal ultrasonography, an abdominal X-ray graphy in supine position, and a questionnaire for IBS was performed. IBS is diagnosed according to Rome II criteria in the absence of red flag symptoms including pain and diarrhea that awakens/interferes with sleep, weight loss, fever, and abnormal physical examination findings. An additional intravenous pyelography was performed just in suspected cases from presenting urolithiasis as a result of the urinalysis and abdominal X-ray graphy. So urolithiasis was diagnosed either by medical history or as a result of clinical findings. Patients with a history of eating disorders including anorexia nervosa, bulimia nervosa, compulsive overeating, or binge eating disorder, insulin using diabetics, and patients with devastating illnesses including malignancies, acute or chronic renal failure, cirrhosis, hyper- or hypothyroidism, and heart failure were excluded to avoid their possible effects on weight. Current daily smokers at least for six months and cases with a history of five pack-year were accepted as smokers. Body mass index (BMI) of each case was calculated by the measurements of the same physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared (13). Cases with an overnight FPG level of 126 mg/dL or higher on two occasions or already using antidiabetic medications were defined as diabetics. An oral glucose tolerance test with 75 grams glucose was performed in cases with FPG levels between 100 and

126 mg/dL, and diagnosis of cases with 2-hour plasma glucose levels of 200 mg/dL or higher is DM (13). Office blood pressure (OBP) was checked after a 5-minute rest in seated position with mercury sphygmomanometer on three visits, and no smoking was permitted during the previous 2 hours. Ten-day twice daily measurements of blood pressure at home (HBP) were obtained in all cases, even in normotensives in the office due to the risk of masked HT after a 10-minute education session about proper blood pressure (BP) measurement techniques (14). The education included recommendation of upper arm while discouraging wrist and finger devices, using a standard adult cuff with bladder sizes of 12 x 26 cm for arm circumferences up to 33 cm in length and a large adult cuff with bladder sizes of 12 x 40 cm for arm circumferences up to 50 cm in length, and taking a rest at least for a period of 5 minutes in the seated position before measurements. An additional 24-hour ambulatory blood pressure monitoring (ABP) was not required due to an equal efficacy of the method with HBP measurement to diagnose HT (15). Eventually, HT is defined as a mean BP of 140/90 mmHg or higher on HBP measurements and white coat hypertension (WCH) is defined as an OBP of 140/90 mmHg or higher, but a mean HBP value of lower than 140/90 mmHg (14). Eventually, all patients with the IBS were collected into the first and age and sex-matched controls were collected into the second, groups. Mean BMI, FPG, total cholesterol (TC), triglycerides, LDL, and HDL values and prevalences of smoking, antidepressants use, urolithiasis, WCH, HT, and DM were detected in each group and compared in between. Mann-Whitney U test, Independent-Samples T test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 647 patients with the IBS and 340 control cases, totally. The mean age of the IBS patients was 41.4 ± 14.4 (15-86) years. Interestingly, 64.2% (416) of the IBS patients were female. Prevalence of smoking was significantly higher in cases with the IBS (36.4% versus 20.5%, p<0.001). Similarly, prevalence of antidepressants use was higher in cases with the IBS (48.0% versus 15.5%, p<0.001). Beside that prevalence of urolithiasis was also higher in the IBS group (23.3% versus 9.4%, p<0.001). Mean BMI values were similar both in the IBS and control groups (27.5 versus 27.7 kg/m2, p>0.05, respectively). Additionally, prevalence of WCH was similar in both groups, too (29.3% versus 31.4%, p>0.05, respectively). Although prevalence of HT and DM and mean values of TC, triglycerides, LDL, and HDL were all similar in both groups (p>0.05 for all), mean value of FPG was significantly higher in the IBS group with unknown reasons, yet (110.1 versus 105.6 mg/dL, p= 0.013) (Table 1).

Table 1: Comparison of patients with irritable bowel syndrome and control cases

Variables	Patients with IBS*	*p*-value	Control cases
Number	647		340
Mean age (year)	41.4 ± 14.4 (15-86)	Ns†	41.6 ± 14.4 (15-82)
Female ratio	***64.2% (416)***	Ns	64.1% (218)
Prevalence of smoking	***36.4% (236)***	***<0.001***	***20.5% (70)***
Prevalence of antidepressants use	***48.0% (311)***	***<0.001***	***15.5% (53)***
Prevalence of urolithiasis	***23.3% (151)***	***<0.001***	***9.4% (32)***
Mean BMI‡ (kg/m2)	27.5 ± 5.7 (15.0-51.1)	Ns	27.7 ± 5.9 (16.5-49.0)
Prevalence of WCH§	29.3% (190)	Ns	31.4% (107)
Prevalence of HT‖	13.9% (90)	Ns	14.7% (50)
Mean FPG** (mg/dL)	***110.1 ± 38.2 (66-338)***	***0.013***	***105.6 ± 33.0 (70-323)***
Prevalence of DM***	8.6% (56)	Ns	10.0% (34)
Mean TC**** (mg/dL)	198.7 ± 41.7 (105-352)	Ns	198.3 ± 42.5 (110-296)
Mean triglycerides (mg/dL)	159.9 ± 96.4 (20-622)	Ns	147.6 ± 103.7 (27-857)
Mean LDL***** (mg/dL)	125.3 ± 34.7 (10-282)	Ns	125.0 ± 32.4 (54-231)
Mean HDL****** (mg/dL)	46.8 ± 13.5 (24-124)	Ns	46.1 ± 10.2 (26-72)

*Irritable bowel syndrome †Nonsignificant (p>0.05) ‡Body mass index §White coat hypertension ‖Hypertension **Fasting plasma glucose ***Diabetes mellitus ****Total cholesterol *****Low density lipoproteins ******High density lipoproteins

Discussion

Smoking may be found among one of the most common causes of vasculitis all over the world. It is a major risk factor for the development of atherosclerotic endpoints including coronary heart disease (CHD), peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), cirrhosis, chronic renal disease (CRD), and stroke (16, 17). Its atherosclerotic effects are the most obvious in Buerger's disease. Buerger's disease is an obliterative disease characterized by inflammatory changes in small and medium-sized arteries and veins, and it has never been reported in the absence of smoking in the literature. Although the well-known strong atherosclerotic effects of smoking, some studies reported that smoking in humans and nicotine administration in animals are associated with a decreased BMI (18). Evidence revealed an increased energy expenditure during smoking both on rest and light physical activity (19), and nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (20). According to an animal study, nicotine may lengthen intermeal time and simultaneously decreases amount of meal eaten (21). Additionally, BMI seems to be the highest in the former, the lowest in the current and medium in never smokers (22). Smoking may be associated with postcessation weight gain but evidence suggests that risk of weight gain is the highest during the first year after quitting and declines over the years (23). Similarly, although CHD was detected with similar prevalence in both genders in a previous study (24), prevalence of smoking and COPD were higher in male patients with CHD against the higher prevalences of BMI, WCH, LDL, triglycerides, HT, and DM in female patients with CHD as the other atherosclerotic risk factor. This result may indicate both the strong atherosclerotic and weight decreasing roles of smoking (25). Similarly, the incidence of a myocardial infarction is increased sixfold in women and threefold in men who smoke at least 20 cigarettes per day compared to the never smoked cases (26). In other words, smoking is more dangerous for women regarding the atherosclerotic endpoints probably due to the higher BMI and its consequences in them. Parallel to the above results, the proportion of smokers is consistently higher in men in the literature (17). So smoking is probably a powerful atherosclerotic risk factor with some suppressor effects on appetite. Smoking induced loss of weight gain may be related with the smoking induced chronic vascular endothelial inflammation all over the body, since loss of appetite is one of the major symptoms of inflammation in the body. Physicians can even understand healing of their patients from their normalizing appetite. Several toxic substances found in cigarette smoke get into the circulation via the respiratory tract, and cause a vascular endothelial inflammation until its clearance from the circulation. But due to the repeated smoking habit of the individuals, the clearance process never terminates. So the patients become ill with loss of appetite, permanently. In another explanation, smoking induced weight loss is an indicator of being ill instead of being healthy (20-22). After smoking cessation, appetite normalizes with a prominent weight gain in the patients but the returned weights are their physiological weights, actually.

There may be several underlying mechanisms terminating with the symptoms of IBS in smokers. First of all, smoking induced chronic vascular endothelial inflammation all over the body may even disturb epithelial functions both for absorption and excretion in the gastrointestinal and genitourinary tracts. These functional problems may terminate with the symptoms and signs of IBS including loose stool, diarrhea, constipation, and urolithiasis. Secondly, diarrheal losses induced urinary changes may even terminate with the urolithiasis (6, 7). Thirdly, smoking induced sympathetic nervous system activation may cause motility disorders in the gastrointestinal and genitourinary tracts. Lastly, immunosuppression secondary to the smoking induced chronic vascular endothelial inflammation all over the body may even cause gastrointestinal and genitourinary tract infections causing loose stool, diarrhea, and urolithiasis since some types of bacteria can provoke urinary supersaturation and modify the environment to form crystal deposits in the urine. In fact, 10% of urinary stones are struvite stones which are built by magnesium ammonium phosphate produced during infection with bacteria that possess the enzyme, urease. Similarly, prevalence of urolithiasis was significantly higher in the IBS group in the present study (23.3% versus 9.4%, $p<0.001$).

Chronic endothelial damage may be the leading cause of aging by causing tissue hypoxia all over the body. Probably whole afferent vasculature including capillaries are mainly involved in the process since much higher BP of the afferent vasculature may be the major underlying cause via recurrent endothelial injuries. Thus the term of venosclerosis is not as famous as atherosclerosis in the literature. Secondary to the chronic endothelial damage, inflammation, edema, and fibrosis, vascular walls become thickened, their lumens are narrowed, and they lose their elastic nature which reduces blood flow and increases BP further. Some of the well-known accelerators of the disseminated atherosclerotic process are physical inactivity, excess weight, smoking, alcohol, and chronic inflammatory or infectious processes including sickle cell diseases, rheumatologic disorders, tuberculosis, and cancers for the development of terminal endpoints including obesity, HT, DM, PAD, COPD, pulmonary hypertension (PHT), CRD, CHD, cirrhosis, mesenteric ischemia, osteoporosis, and stroke, all of which terminate with early aging and premature death. They were researched under the title of metabolic syndrome, extensively (27, 28). Although early withdrawal of the causative factors may delay development of the endpoints, the endothelial changes cannot be reversed completely after the development of obesity, HT, DM, PAD, COPD, PHT, CRD, CHD, or stroke due to their fibrotic nature (29, 30).

Obesity may be found among one of the endpoints of the metabolic syndrome, since after development of obesity, nonpharmaceutical approaches provide limited benefit either to heal obesity or to prevent its complications.

Overweight and obesity may lead to a chronic low-grade inflammatory process on vascular endothelium, and risk of death from all causes including cardiovascular diseases and cancers that increase parallel to the range of excess weight in all age groups (31). The low-grade chronic inflammatory process may cause genetic changes on the epithelial cells, and the systemic atherosclerotic process may decrease clearance of malignant cells by the immune system, effectively (16). The effects of excess weight on BP were shown by several studies (32) in that the prevalence of sustained normotension (NT) was significantly higher in the underweight (80.3%) than the normal weight (64.0%, $p<0.05$) and overweight cases (31.5%, $p<0.05$), and 52.8% of cases with HT had obesity against 14.5% of cases with t NT ($p<0.001$) (33). So the dominant underlying cause of the metabolic syndrome appears as gaining weight, which is probably the major cause of insulin resistance, hyperlipoproteinemias, impaired fasting glucose, impaired glucose tolerance, and WCH via a chronic low-grade inflammatory process on vascular endothelium all over the body (34). Even prevention of the accelerated trend of gaining weight with exercise, even in the absence of a prominent weight loss, will probably result with resolution of many parameters of the metabolic syndrome (35-38). But according to our experience, excess weight may actually be a consequence of physical inactivity instead of an excessive eating habit thus prevention of gaining weight cannot be achieved by diet alone (39). Additionally, limitation of excess weight as an excessive fat tissue around the abdomen under the heading of abdominal obesity is meaningless, instead it should be defined as overweight or obesity by means of BMI since adipocytes function as an endocrine organ, and they produce a variety of cytokines and hormones anywhere in the body (34). The eventual hyperactivities of sympathetic nervous system and renin-angiotensin-aldosterone system are probably associated with chronic endothelial inflammation, insulin resistance, and elevated BP. Similarly, the Adult Treatment Panel III reported that although some people classified as overweight have a large muscular mass, most of them have excessive fat tissue predisposing to hyperlipoproteinemias, HT, DM, CHD, and stroke (13).

As a conclusion, IBS may be a low-grade inflammatory process being initiated with infection, inflammation, psychological disturbances-like stresses, and eventually terminated with dysfunctions of the gastrointestinal and genitourinary tracts, and other systems of the body. Although there may be several possible causes of IBS, smoking induced chronic vascular endothelial inflammation all over the body may even cause IBS. The higher FPG in the IBS patients should be researched with further studies.

References

1. Valenkevich LN, Iakhontov OI. Modern myths of clinical gastroenterology. Eksp Klin Gastroenterol 2004; 105(3): 72-74.
2. Rhee PL. Definition and epidemiology of irritable bowel syndrome. Korean J Gastroenterol 2006; 47(2): 94-100.
3. Lee OY. Psychosocial factors and visceral hypersensitivity in irritable bowel syndrome. Korean J Gastroenterol 2006; 47(2): 111-119.
4. Wang W, Pan G, Qian J. Effect of psychological factors on visceral sensation of patients with irritable bowel syndrome. Zhonghua Yi Xue Za Zhi 2002(5); 82: 308-311.
5. Park H. The pathophysiology of irritable bowel syndrome: inflammation and motor disorder. Korean J Gastroenterol 2006; 47(2): 101-110.
6. Helvaci MR, Kabay S, Gulcan E. A physiologic events' cascade, irritable bowel syndrome, may even terminate with urolithiasis. J Health Sci 2006; 52(4): 478-481.
7. Helvaci MR, Algin MC, Kaya H. Irritable bowel syndrome and chronic gastritis, hemorrhoid, urolithiasis. Eurasian J Med 2009; 41(3): 158-161.
8. Helvaci MR, Kaya H, Algin MC, Yalcin A. A physiologic events' cascade: irritable bowel syndrome may even terminate with chronic gastritis. Med J Malaysia 2008; 63(2): 140-142.
9. Chadwick VS, Chen W, Shu D, Paulus B, Bethwaite P, Tie A, et al. Activation of the mucosal immune system in irritable bowel syndrome. Gastroenterology 2002; 122(7): 1778-1783.
10. Barbara G, Stanghellini V, De Giorgio R, Cremon C, Cottrell GS, Santini D, et al. Activated mast cells in proximity to colonic nerves correlate with abdominal pain in irritable bowel syndrome. Gastroenterology 2004; 126(3): 693-702.
11. Tornblom H, Lindberg G, Nyberg B, Veress B. Full-thickness biopsy of the jejunum reveals inflammation and enteric neuropathy in irritable bowel syndrome. Gastroenterology 2002; 123(6): 1972-1979.
12. Wahnschaffe U, Ullrich R, Riecken EO, Schulzke JD. Celiac disease-like abnormalities in a subgroup of patients with irritable bowel syndrome. Gastroenterology 2001; 121(6): 1329-1338.
13. 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) final report. Circulation 2002; 106(25): 3143-3421.
14. O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, et al. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. J Hypertens 2003; 21(5): 821-848.
15. Helvaci MR, Seyhanli M. What a high prevalence of white coat hypertension in society! Intern Med 2006; 45(10): 671-674.
16. Helvaci MR, Aydin Y, Gundogdu M. Smoking induced atherosclerosis in cancers. HealthMED 2012; 6(11): 3744-3749.

17. Fodor JG, Tzerovska R, Dorner T, Rieder A. Do we diagnose and treat coronary heart disease differently in men and women? Wien Med Wochenschr 2004; 154(17-18): 423-425.
18. Grunberg NE, Greenwood MR, Collins F, Epstein LH, Hatsukami D, Niaura R, et al. National working conference on smoking and body weight. Task Force 1: Mechanisms relevant to the relations between cigarette smoking and body weight. Health Psychol 1992; 11: 4-9.
19. Walker JF, Collins LC, Rowell PP, Goldsmith LJ, Moffatt RJ, Stamford BA. The effect of smoking on energy expenditure and plasma catecholamine and nicotine levels during light physical activity. Nicotine Tob Res 1999; 1(4): 365-370.
20. Hughes JR, Hatsukami DK. Effects of three doses of transdermal nicotine on post-cessation eating, hunger and weight. J Subst Abuse 1997; 9: 151-159.
21. Miyata G, Meguid MM, Varma M, Fetissov SO, Kim HJ. Nicotine alters the usual reciprocity between meal size and meal number in female rat. Physiol Behav 2001; 74(1-2): 169-176.
22. Laaksonen M, Rahkonen O, Prattala R. Smoking status and relative weight by educational level in Finland, 1978-1995. Prev Med 1998; 27(3): 431-437.
23. Froom P, Melamed S, Benbassat J. Smoking cessation and weight gain. J Fam Pract 1998; 46(6): 460-464.
24. Helvaci MR, Kaya H, Gundogdu M. Gender differences in coronary heart disease in Turkey. Pak J Med Sci 2012; 28(1): 40-44.
25. Helvaci MR, Aydin Y, Gundogdu M. Atherosclerotic effects of smoking and excess weight. J Obes Wt Loss Ther 2012; 2:145.
26. Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998; 316(7137): 1043-1047.
27. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005; 365(9468): 1415-1428.
28. Helvaci MR, Kaya H, Sevinc A, Camci C. Body weight and white coat hypertension. Pak J Med Sci 2009; 25(6): 916-921.
29. Helvaci MR, Aydin LY, Aydin Y. Digital clubbing may be an indicator of systemic atherosclerosis even at microvascular level. HealthMED 2012; 6(12): 3977-3981.
30. Anderson RN, Smith BL. Deaths: leading causes for 2001. Natl Vital Stat Rep 2003; 52(9): 1-85.
31. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999; 341(15): 1097-1105.
32. Helvaci MR, Kaya H, Yalcin A, Kuvandik G. Prevalence of white coat hypertension in underweight and overweight subjects. Int Heart J 2007; 48(5): 605-613.
33. Helvaci MR, Kaya H, Duru M, Yalcin A. What is the relationship between white coat hypertension and dyslipidemia? Int Heart J 2008; 49(1): 87-93.
34. Franklin SS, Barboza MG, Pio JR, Wong ND. Blood pressure categories, hypertensive subtypes, and the metabolic syndrome. J Hypertens 2006; 24(10): 2009-2016.
35. Azadbakht L, Mirmiran P, Esmaillzadeh A, Azizi T, Azizi F. Beneficial effects of Dietary Approaches to Stop Hypertension eating plan on features of the metabolic syndrome. Diabetes Care 2005; 28(12): 2823-2831.
36. Helvaci MR, Ayyildiz O, Gundogdu M, Aydin Y, Abyad A, Pocock L. Excess weight or smoking. World Family Med 2018; 16(10): 14-19.
37. Helvaci MR, Ayyildiz O, Gundogdu M, Aydin Y, Abyad A, Pocock L. Body mass and blood pressure. World Family Med 2019; 17(1): 36-40.
38. Helvaci MR, Kaya H, Borazan A, Ozer C, Seyhanli M, Yalcin A. Metformin and parameters of physical health. Intern Med 2008; 47(8): 697-703.
39. Helvaci MR, Algin MC, Abyad A, Pocock L. Physical inactivity or an excessive eating habit. Middle East J Nursing 2018; 12(1): 14-18.

Early Onset Dementia: A Systematic Review of the Literature to Inform Qualitative Experiences

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Abstract

There is increasing recognition that EOD (Early Onset Dementia) represents an important social problem affecting economic and social impacts (Campbell et al., 2008; Johannessen et al., 2018). Recent research calls for greater efforts to be made in consulting with the PwD (people with dementia) directly (Allen 2001; Bamford & Bruce 2000). The condition is understood to occur between the ages of 45-65 (Mercy, 2008). This makes EOD a sub-group of dementia with numerous differences when compared to later onset dementia. These include the likelihood of still being in work and having a family to raise. Being responsible for an income and for dependent others is particularly difficult for those affected. Additionally, the social and psychological context for younger people is different (Beattie, 2004). PwEOD (people with Early Onset Dementia) are more likely to be physically fitter than those with later onset dementia which may impact on their physical care needs. The existing expectation within health and social care agencies for PwEOD is in keeping within an older person's framework of care which may well be inappropriate. This may have occurred in the past due to biomedical assumptions regarding the condition (Kitwood, 1997; van Vliet et al., 2017). This also suggests that little attention has been paid to subjective experiences (van Vliet, 2017). The need to elicit the views and subjective experiences of PwEOD is therefore gaining increasing recognition within health and social care research (van Vliet, 2010). Literature has been modestly growing in the subject area to demonstrate how PwEOD have expressed their views and experience of dementia successfully (Page and Keady, 2010; Ohman et al., 2001). However, most of the extant literature is based on family carers (Cabote, 2015; Kobiske and Bekhet, 2018). Whilst carers' views are important they should not be used as a substitute for the views of younger people with dementia (Goldsmith 1996, Whitlatch 2001). Given the limited research available, both the views of PwEOD and their family carers are incorporated into the systematic literature review.

Key words: Early onset dementia (EOD), qualitative, people with early onset dementia (PwEOD), family kin, meta-ethnography, stigma, liminality and chronicity, biographical disruption, losses, coping

Introduction

Personal accounts describing EOD have potential to inform clinical and care provision as well as informing other dementia subsets. Examining first person accounts makes this a valuable exercise. This may be assumed as PwEOD (People with Early Onset Dementia) possess more faculties with which to tell about lived experience from first person accounts.

Method

Study aim: This systematic review paper sought to address the following question:

'How do PwEOD as a diagnosed sub group of other dementias and their immediate family experience living with EOD?'

Study inclusion: Studies were included and excluded according to the following criteria: a diagnosis of EOD between the ages of 45-65 [1]; research dated between 1998-2018;[2] in English language; qualitative and peer reviewed papers. The key aim of study inclusion was to capture the experience of living with EOD through the available literature in the field. Personal experiences were sought in the literature on PwEOD and their immediate family living with the experience post-diagnosis. The scoping review uncovered the relative lack of studies to date on the experiences of PwEOD, therefore studies were inclusive of spouses, partners, children and adult dependents as people living with the PwEOD. Searches were kept broad and unconstrained by further filters in order to capture a fuller picture of the issues and experiences connected to EOD.

Study exclusion: Studies focusing solely on people presenting with dementia younger than 45; studies with a predominant interest in; dementia caused by HIV, traumatic brain injury, Down's syndrome, congenital birth conditions likely to include dementia, Huntington's chorea and alcohol-related dementia were excluded. Systematic literature reviews were excluded.

Scoping: A scoping exercise of the literature took place prior to the systematic literature review which identified EOD as a sub-group of dementia under-represented in the literature. Google Scholar and Abertay's Library Search including serendipitous searches using prior knowledge of the research field extended the search in preparation for the systematic review.

Search strategy: The author then searched databases which were selected for their social and clinical perspectives through EBSCOhost; Web of Science and Cinahl plus with text, Psychology and Behavioural Sciences Collection, Scopus and Sage. The search terms were: dement*, early onset dementia, young onset dementia, presenile-Alzheimer* and working age dementia. These were searched as single terms using Boolean phrasing; 'OR' then once the searches were captured, refined with; 'AND' then stored for scrutiny at the next stage.

Selection of papers: The search located five-hundred-and-fifty-two (522) papers. Duplicates were removed (n=22). The remaining studies' (n=500) abstracts and titles were screened. Twenty-two studies (n=22) were retained and full texts read. This left sixteen studies (n=16) to be included. The reference lists of the twenty-two studies were also examined. Although two were added from references, they were finally excluded for failing to meet the criteria. With reference to the final six studies excluded, these are listed in the appendices (Appendix 1).

Approach to systematic and meta-analysis synthesis of studies

The review was guided by the systematic approach preferred by PRISMA (Reporting Systematic Reviews and Meta-Analysis Studies (Liberati, 2009). Figure 1 illustrates the process of papers being excluded or included for the systematic review based upon the study question. This process sets a standard for the assessment and critique of health focussed studies and interventions assisting the processes for summarising evidence accurately and reliably. However, it is the case that the methods of meta-analysis are not transferable to qualitative health research for a number of pragmatic and epistemological reasons; for example, computer literature searches, statistical data and priorities in quantitative research may fail to capture forms of qualitative research which lack the appeal of more clinical protocols and interventions (Britten et al., 2002). As such, criteria for judging the quality of published research whilst contested in the past have since found established qualitative protocols for comparing studies (Britten et al., 2002). The potential audiences for viewing research through this lens include practitioners across a broad health practice background as well as policy-makers and qualitative researchers (Britten et al., 2002). Therefore, there exists several well recognised methods by which to conduct a systematic review of qualitative literature (Greenwood & Smith, 2016).

[1] This definition is in keeping with Mercy (2008), excluding two other studies limiting EOD to 45-60. All others searched for the systematic review including the scoping review referred to 45-65 as the most commonly used criteria for EOD.

[2] Searches between 1998-2018 captured the advent and widespread prescription of anti-cholinesterase inhibitor treatment and linked with a key driver as laid out in the Scottish Government's 2009 report making dementia a healthcare priority for development.

The role of meta-ethnography in qualitative research

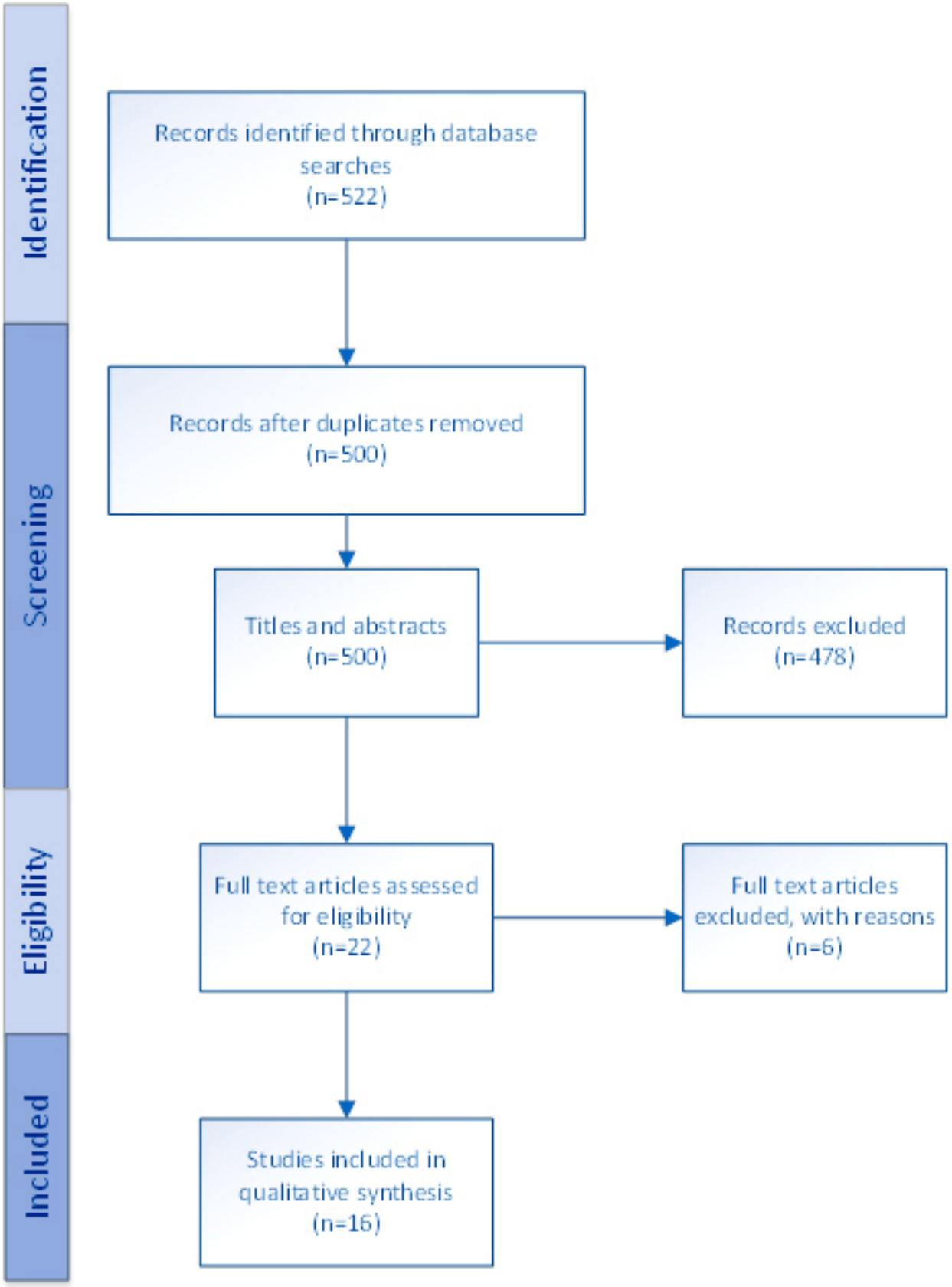
The impetus for developing methods of qualitative synthesis has arisen from a need to complement quantitative research. This looked to gain a more complete understanding of phenomena, especially in terms of organisational processes and provision of services (Greenhalgh, 1998). Therefore a need existed to bring together isolated studies for comparison (Sandelowski et al., 1997). Meta-ethnography provides a way to compare qualitative studies accommodating induction and interpretation (Greenwood & Smith, 2016). It also can synthesise conceptual innovations such as metaphorical and emotionally relevant phenomena (Strike and Posner, 1983). It has origins in the interpretive paradigm and as such, it possesses an alternative to traditional aggregative methods of synthesis which retain qualities or concepts of the qualitative method of study it aims to synthesise.

The benefit of applying meta-ethnography to the synthesis of qualitative research and suitability for this study was informed by Noblit and Hare's (1988) seven-step process (Table 1). Narrative literature reviews capture concepts and information in a more eclectic fashion but have in the past been criticised for being singular descriptive accounts based upon the implicit bias of the researcher (Fink, 1998). They have also been condemned for lacking critical assessment. Adopting a more systematic approach to the literature was therefore useful in order to approach a more comprehensive contemporary review of the field. This approach was particularly helpful in investigating EOD as a lesser known sub-group of dementia. Meta-ethnography has proven a sound technique for synthesising qualitative research in health studies (Paterson et al., 1998). It has been successfully employed in publications to date including: lay meanings of medicines (Britten et al., (2002); lay experiences of diabetes and diabetes care (Campbell et al; 2003); what values people seek when they provide unpaid care for an older person (Al-Janabi et al., 2008) and locating how coping experiences appear in chronic fatigue syndrome sufferers (Larun and Malterud, 2007).

Table 1:

Noblit & Hare's 7 step qualitative synthesis	
1.	Getting started: determine the research questions
2.	Deciding what is relevant to the initial interest: defining the focus of the synthesis, locate relevant studies, inclusion decisions and quality assessment of included studies
3.	Reading the studies: reading the articles multiple times to identify the main concepts
4.	Determining how the studies are related: listing the emergent concepts and identifying the related concepts
5.	Translating the studies into one another: listing the concepts into a table and then looking for these concepts in each of the included articles
6.	Synthesising translations: building a line of argument by exploring the relationships between concepts
7.	Expressing the synthesis: how the synthesis is reported

Figure 1: PRISMA flowchart



Results

Participant and study design

The inclusion criteria sought studies spanning 1998-2018. However, the studies ranged from 2009 to 2018. The mean date was 2015. All studies were performed in Western countries (Norway-6; America-1; England-; 6; The Netherlands-1; Ireland-1 & Australia-1). Where English was not the dominant language it was widely taught and well spoken (Norway and The Netherlands). The participants were predominantly drawn from health environments or services structured to assist PwD or PwEOD such as statutory or voluntary bodies. There were a total of 229 participants after making amendments for those participants drawn from the same sample groups where multiple study authors were included. Johannessen et al., (2014) and Johannessen and Moller (2011) used the same participants. Johannessen et al., (2016) and Johannessen et al., (2017) also shared participants databases throughout the studies. Data were collected through face to face interview mostly using a semi-structured format. These were situated within the statistics of the studies quoted above; (PwEOD (4); their family members (2); both spouses (2) and dependents (8) whether still regarded as children living at home or adult children living independently elsewhere). These studies drew together the theoretical approaches to the data founded in: grounded theory (5); autobiographical life story narrative (3); phenomenological hermeneutic analysis (2); Thematic Analysis (TA) (2); qualitative semi structured interview (1); conceptual model (1); action research study (1) Interpretative phenomenological analysis (IPA) (1).

Ethnicity was referred to infrequently (n=1) and where ethnic origins were detailed, the sample groups were white/Western. Allen et al., (2009) was the only study to include 25% Asian participants within an English sample. Other studies made no attempt to refer to ethnicity and so a presumption is made that natives of the country of origin satisfied the sample cohorts. This is excepting Sikes and Hall (2017) which reported that the sample participant group was ‘mainly white, British, middle-class, participants’.

Type of dementia was not a focus except for Johannessen et al., (2017) which focused on people with fronto-temporal lobe dementia. Other data reported were related to whether participants (both PwEOD and family) were working, living at home, in studies, in a care home, retired or medically signed off work and living on retirement funds or state benefits. The source for participants overwhelmingly arose from clinical or health focused environments. This particular feature was examined in the discussion of the studies. Having noted the brief characteristics of the studies above, the following tables and sub-sections developed overall themes along with the development of the line of argument.

Table 2: Participant and study design

	Author, year & country	Title	Aims	Sample size	Ages & participant cohort	EOD classification	Ambient relationship setting & recruitment
1	**Johannessen, A. Moller, A. Haugen, P. Biong, B. (2014) Norway**	A shifting sense of being: a secondary analysis & comparison of 2 qualitative studies on young onset dementia	To investigate and interpret metaphorical expressions of lived experience of PwEOD	20	54-67 PwEOD	YOD	Recruited from 4 hospital memory clinics (drawn from an original study: Johannessen and Moller, 2013)
2	**Johannessen, A. Moller, A. (2011) Norway**	Experiences of persons with EOD in everyday life: a qualitative study.	Locate experience of EOD, implications for practice and development.	20 AD 6 FTD & 3 others	54-67 PwEOD	YOD	Recruited from 4 hospitals memory clinics (chosen for cost and saving time on recruitment) telephone and follow up in hospital.
3	**Pipon-Young, E. Lee, K. Jones, F. Guss, R. (2011) England**	"I'm not all gone, I can still speak": The experiences of younger people with dementia. An action research study.	Investigating the experiences and challenges of EOD with diagnosis, support, problems and areas requiring change.	8	60-67 PwEOD	7 AD 1 mixed dementia	Via clinicians in the NHS. Interviewed at home and hospital.
4	**Rostad, D. Hellzen, O. Enmarker, I. (2013) Norway**	The meaning of being young with dementia and living at home.	Understanding the challenges and experiences of PwEOD living at home.	4	55-62 PwEOD	3 AD 1 mixed dementia	Recruitment via a health coordinator with experience of the client group. Interviewed at home, welfare centre & day care.
5	**Johannessen, A. Helvik, A. Engedal, K. Thorsen, K. (2017)Norway**	Experience & needs of spouses of persons with YO fronto-temporal lobe dementia during the progression of the disease.	Aim to find out what life is like for PwEOD's (FT) partners & their needs.	16	51-69 spouses	9 wives, 6 husbands 1 male cohabitant	7 memory clinics, 1 municipality dementia team and a nursing home. Interviewed at home, in town and at work

	Author, year & country	Title	Aims	Sample size	Ages & participant cohort	EOD classification	Ambient relationship setting & recruitment
6	**Hoppe, S. (2018) The Netherlands**	A sorrow shared is a sorrow halved: the search for empathetic understanding of family members of a person with EOD.	How Dutch family members find empathy for PwEOD in their family and assess barriers to providing care	7 EOD +41 family members, = 48 partners, PwEOD, 11 group constellations.	55-65Family kin	EOD	Recruited from the Alzheimer's Society and 3 care institutions. Interviews at home at researcher's office in cafes for about 1 to 2 hours.
7	**Flynn, R, Mulcahy, H. (2013) Ireland**	EOD: the impact on family caregivers	Explore caring from family perspective in looking after PwEOD.	7 (over 16)	Under 65 when diagnosed. Family kin	EOD	Regional manager recruited via letter to volunteer participants meeting criteria. At offices of Alzheimer's Society Ireland.
8	**Johannessen, A. Engdal, K. Thorsen, K. (2016) Norway**	Coping efforts & resilience among adult children who grow up with a parent with YOD: a qualitative follow up study.	How adolescent/adult dependents experience their parents' EOD and how they coped with life situations.	14	18-30 Adult dependents	EOD	7 memory clinics, 1 municipality dementia team and a nursing home and from Norwegian National Support Group for Adult Children. Interviews held at convenience of respondent.
9	**Johannessen, A. Engdal, K. Thorsen, K. (2015) Norway**	Adult children of parents with young onset dementia narrate the experience of their youth through metaphors.	To investigate & interpret metaphorical expression of adult dependents of PwEOD. What sense can be made?	14	18-30 Adult dependents	EOD	Heterogeneity attained through diverse geography in Norway/2 memory clinics/1 municipality/nursing home & support group for PwEOD. Interviewed at convenience at home or place of choice

	Author, year & country	Title	Aims	Sample size	Ages & participant cohort	EOD classification	Ancient relationship setting & recruitment
10	**Hutchinson, K. Roberts, C. Kurrle, S. Daly, M. (2016) Australia**	The emotional well-being of young people having a parent with early onset dementia.	To explore the lived experiences of young people with parents with EOD from the perspective of a social model of disability.	12	19-33 + 1 x 10 year old Child/adult dependents	YOD	Advertising via Alzheimer's Australia for volunteers. Interviewed at work, at home or in local library.
11	**Gelman, C. Rhames, K. (2018) America**	In their own words: the experience and needs of children in younger onset Alzheimer's disease & other dementia families.	What are the experiences & needs of children with YOD families & the impact of a diagnosis on children of those families.	(14) 4 families 4 mothers 10 children	10-25 Child/adult dependents	YOD	Flyers were displayed at support organisations $25 payment for information. Interviews lasted an hour at participant's preferred location.
12	**Allen, J. Oyebade, J. Allen, J. (2009) England**	Having a father with young onset dementia. The impact on well being of young people	To investigate and explore the impact on young people's well being in light of them having a PwEOD	12	8-31 (mean 19) Child/adult dependents	British 75% Asian 25% Families of EOD	Recruited from Alzheimer's Society throughout the Midlands. Interviewed from 45-90 minutes
13	**Sikes, P. Hall, M. (2018) England**	"It was then that I though what? This is not my dad". The implications of the 'still the same person' narrative for children & young people who have a parent with dementia	To investigate the 'still the same' narrative through children of PwEOD to assist future plans to support others in the same situation.	19	8-31 age selecting accordance with the UN and WHO guidelines of what qualifies for ages in youth Child/adult dependents	EOD	2 interviews based upon self selecting participants from web advertisement.

	Author, year & country	Title	Aims	Sample size	Ages & participant cohort	EOD classification	Ambient relationship setting & recruitment
14	**Sikes, P. Hall, M. (2017) England**	"Every time I see him, he's the worst he's ever been and the best he'll ever be": Grief and sadness in children and young people who have a parent with dementia.	Aims to represent grief related to perceptions and experience of children and young people who have a parent with EOD. Gathering the information will assist future planning.	22	6-31 age selecting accordance with the UN and WHO guidelines of what qualifies for ages in youth Child/adult dependents.	EOD	Snowballing, advertised on website, self selecting, temporal effect desired so interviewed over two years.
15	**Hall, M, Sikes, P. (2016) England**	From "What the Hell is going on? To the "Mushy middle ground" to "Getting used to it as a new normal": Young people's biographical narratives around navigating parental dementia.	To navigate through EOD family experience seeking temporal journeys of a biographical nature looking to location disruption to lives.	22	7-31 Child/adult dependent	EOD	Advertised through social media (Facebook, Twitter, Alzheimer's Society, Young Dementia UK). 2 0r 3 interviews over 16 months.
16	**Lakeridge S. Simpson J. (2012) England**	The experience of caring for a partner with YOD: How younger carers cope	To explore the coping strategies adopted by 6 carers to assist with adaptation in their relationship with their partner with YOD.	6	3 male 3 female Spouses		Recruited from regional branches of Alzheimer's office. 50-90 minute interviews in participant's home or local Alzheimer's office.

Drawing a line of argument from the seven step process

Noblet and Hare (1988) refer to a meta-ethnographic line of argument which emerges to articulate a larger phenomenon drawn from the data. This was achieved by following the steps. After selecting an aim and study question (steps one and two), the studies were read to fulfil step three. This was followed by populating the tables with typical broad characteristics (Table 2). Investigation of experiences were then described (Table 3). Following this, steps four, five and six produced more concepts (Table 4) and themes (Table 5) were populated taking care to ensure the data remained true to the original studies. Step seven provided for a discussion through the line of argument of what fresh data was discovered.

Table 3: Investigation of experiences

	Author, year	Title	Experience investigated	Sample method	Inclusion criteria	Data collection	Approach to data analysis
1	**Johannessen, A. Moller, A. Haugen, P. Biong, B. (2014) Norway**	A shifting sense of being: a secondary analysis & comparison of 2 qualitative studies on young onset dementia.	Interpret metaphorical expressions	Anthropological	YOD catchment from hospital appointments	Thematic question interview based	Grounded theory
2	**Johannessen, A. Moller, A. (2011) Norway**	Experiences of persons with EOD in everyday life: a qualitative study.	Living with EOD	Theoretical	Post diagnosis	Semi-structured interviews	Grounded theory
3	**Pipon-Young, E. Lee, K. Jones, F. Guss, R. (2011) England**	"I'm not all gone, I can still speak": The experiences of younger people with dementia. An action research study.	Living with EOD - changes to health and practical needs. Transitional experience and health expectations.	Purposive	More than 6 months from diagnosis	Semi-structured interviews	1st phase: thematic 2nd phase: framework
4	**Rostad, D. Hellzen, O. Enmarker, I. (2013) Norway**	The meaning of being young with dementia and living at home.	Living with a diagnosis of EOD	n/s*	Diagnosed with EOD, living at home and diagnosed with EOD	Narrative constructed interviews	Pheno-menological & hermeneutic
5	**Johannessen, A. Helvik, A. Engedal, K. Thorsen, K. (2017)Norway**	Experience & needs of spouses of persons with YO fronto-temporal lobe dementia during the progression of the disease	Spouses living with FTLD during disease progression	Sampling	YoFTLD + family members	Qualitative interviews	Grounded theory
6	**Hoppe, S. (2018) The Netherlands**	A sorrow shared is a sorrow halved: the search for empathetic understanding of family members of a person with EOD	PwEOD & family members	Purposive sampling	EOD + family	Semi-structured qualitative interviews	NViVO transcription of interviews to extract 3 cases

	Author, year	Title	Experience investigated	Sample method	Inclusion criteria	Data collection	Approach to data analysis
7	Flynn, R, Mulcahy, H. (2013) Ireland	EOD: the impact on family caregivers	Physical, social, emotional and financial experience sought	Purposive	Open invitation to those within criteria	Face to face semi-structured in-depth	Chou (2000) conceptual analysis tool
8	Johannessen, A. Engdal, K. Thorsen, K. (2016) Norway	Coping efforts & resilience among adult children who grow up with a parent with YOD: a qualitative follow up study	Transition and resilience	Purposive sampling	EOD diagnosis made 6 months include adult children	Interview face to face	Grounded theory
9	Johannessen, A. Engdal, K. Thorsen, K. (2015) Norway	Adult children of parents with young onset dementia narrate the experience of their youth through metaphors	Emotional trauma and distress	Purposive sampling	Family of EOD	Individual qualitative interviews Seeking metaphors from interview	Phenomenological, hermeneutic. T.A.
10	Hutchison, K. Roberts, C. Kurrle, S. Daly, M. (2016) Australia	The emotional well-being of young people having a parent with early onset dementia	Purposive sampling	Children of PwEOD	Semi-structured interviews		Social model of disability
11	Gelman, C. Rhames, K. (2018) America	In their own words: the experience and needs of children in younger onset Alzheimer's disease & other dementia families	Experience of social impact	Purposive sampling	Children of PwEOD	Face to face interviews	Thematic narrative analysis
12	Allen, J. Oyebade, J. Allen, J. (2009) England	Having a father with young onset dementia. The impact on well-being of young people	Emotional impact and psychological experience	Purposive sampling	Children of PwEOD	Face to face interviews	Grounded theory
13	Sikes, P. Hall, M. (2018) England	"It was then that I thought what? This is not my dad". The implications of the 'still the same person' narrative for children & young people who have a parent with dementia	Autobiographical meanings	Purposive and self-referring	Children and young people of PwEOD	Collection of in depth personal stories and biographies	Autobiographical/life histories interviews &T.A

	Author, year	Title	Experience investigated	Sample method	Inclusion criteria	Data collection	Approach to data analysis
14	**Sikes, P. Hall, M. (2017) England**	"Every time I see him, he's the worst he's ever been and the best he'll ever be": Grief and sadness in children and young people who have a parent with dementia.	Seeking individual grief related responses to having a parent with EOD	Self-referring from internet advertisement & snowballing	Children and young people of PwEOD	Invitation to tell a story to the researcher	Auto/ biographical, specifically life historical and narrative approach
15	**Hall, M, Sikes, P. (2016) England**	From "What the Hell is going on? To the "Mushy middle ground" to "Getting used to it as a new normal": Young people's biographical narratives around navigating parental dementia	How different biographies meet common ground with the study cohort	Self-selecting from advertisement	Children of PwEOD	Narrative biographical seeking interview	Thematic approach as in K Reissman
16	**Lakeridge, S. Simpson, J. (2012) England**	The experience of caring for a partner with YOD: How younger carers cope	General experience of caring for someone with EOD	Purposive sampling	Primary carer of PwEOD	Semi-structured interview using IPA	IPA

Overall themes

By the time Table five was completed at stages five and six in accordance with Noblit and Hare's seven step process, new data emerged to realise conceptual themes crystallised into themes which formed the expression of the new information. The expression of the synthesis followed the tables discussed theme by theme.

Table 4: Conceptual themes

	Author/Title/ Year	Concepts							
		Losses	Chronicity and lost time	Biographical disruption	Stigma & judgment	Diagnosis	Isolation & social identity	Emotions	Coping
1	Johannessen, A. Moller, A. Haugen, P. Biong, B. (2014) Norway	Loneliness	Life changes will appear		Masking & hiding	Difficult and lengthy to achieve	Sliding away & falling from life once taken for granted	Anger Fear Reticence Living in limbo	Coping Claiming dignity
2	Johannessen, A. Moller, A. (2011) Norway	Lack of normality. Confusion in every day contexts. Dignity lost	Dislocation & lack of certainty. Constraint s on time and planning		Dismissed by others. Status lost	Diagnostic struggles & shock	Feeling outside others and time Relationship changes	Diminished & rejected. Irritation	Stronger together, going on
3	Pipon-Young, E. Lee, K. Jones, F. Guss, R. (2011) England	Losing ideas of how to relate		Calm for now but afraid of the future	Saving face with others, shielding truth	Diagnosis feels in the wrong time & stage	'Out of step'	Resilience	Keeping 'in the swim' & retaining new social identities
4	Rostad, D. Hellzen, O. Enmarker, I. (2013) Norway	Loss of power, Loss of humanity, Loss of identity,	Wrong time for diagnosis		Reduced sense of belonging in the eyes of others,		Trapped by circumstances		Preservation of hope and resilience. Desiring to live well and managing.
5	Johannessen, A. Helvik, A. Engedal, K. Thorsen, K. (2017) Norway			Moving apart	Stigma	Distanced emotional reactions		Coping	Calm & resilience
6	Hoppe, S. (2018) The Netherlands	From certainty of health to the uncertainty of disease		Lifestyle burnout when too young	Barriers to acceptance of EOD condition	In between ideas of health and illness	Living in a state of confusion	Trepidation Guilt	Communing with friends increasing strength
7	Flynn, R, Mulcahy, H. (2013) Ireland	No means to support and care	Waiting times for news and change			Different diagnoses given. Big delays. Diagnosis denial	Doubts over how to go forward differently	Fear Loneliness	

	Author/Title/ Year	Concepts							
		Losses	Chronicity and lost time	Biographical disruption	Stigma & judgment	Diagnosis	Isolation & social identity	Emotions	Coping
8	Johannessen, A. Engdal, K. Thorsen, K. (2016) Norway	Lost childhood of child dependent						Feeling freedom. Feeling like themselves. Guilt on top of freedom	Relief. Making a stand
9	Johannessen, A. Engdal, K. Thorsen, K. (2015) Norway	The loss of a parent sliding away. The shock of losing the parent inside & no one left behind.		Stilted development	Covering up the diagnosis		Waiting to begin life	Confused	Emotional chaos. Escaping from doubt to cope
10	Hutchison, K. Roberts, C. Kurrle, S. Daly, M. (2016) Australia	Loss compounded with grief			Being judged			Fear of being trapped, hopelessness, frustration, 24/7 nature of caring is overwhelming. Normality of family weighted against normality of self	24/7 nature of caring is overwhelming. Normality of family weighted against normality of self.
11	Gelman, C. Rhames, K. (2018) America	Abruption – interruption of child/adolescent development. Losing the natural order of parents & children.	Waiting for others to 'get it'-disbelief of diagnosis	Living with lies, terror, dread & 'freak-outs				Fear, Embarrassment exasperation	Adaption, acceptance, growth & change
12	Allen, J. Oyebade, J. Allen, J. (2009) England	Loss of status; working parent, credible parent, comforted child.	Waiting to become a child but needing to be a parent instead. Parentification.	Loss of parent loss of childhood & youth	Disjunction of childhood experience.	Delays in diagnosis.		Fear, fright, unease Despair.	Engaged, Knowledgeable. Better understanding of way forward.

	Author/Title/ Year	Concepts							
		Losses	Chronicity and lost time	Biographical disruption	Stigma & judgment	Diagnosis	Isolation & social identity	Emotions	Coping
13	**Sikes, P. Hall, M. (2018) England**	The loss and receding of the self (parent) Leaving the idea of the parent, loss of role, 'mum is an utter bitch'	The slipping away of parent & child	Disconnect of parenting	The 'Hollywooding' of the demented-the romanticising of dementia		No warning of losses & happenings	Crumbling spirit,	
14	**Sikes, P. Hall, M. (2017) England**	Missing important stages and rites of passage in life.	Life on hold, Worrying about death & funerals 'out of time'				Liminal grief. Uncertainty of future.	Envy of other families in health deemed normal. Post-carer symptoms of depression.	Relief after death or after caring
15	**Hall, M, Sikes, P. (2016) England**	Shock realisation of death after illness for children of PwEOD	Irrational behaviour only takes on meaning after time. Time lag of diagnosis.	Disruption to the natural expectation of life with dementia- children don't understand dementia is terminal.		Epiphanic moment of realisation. Time lag in diagnosis	Stuck in the middle ground of not knowing what may happen next	Shock sadness of unexpected death. Sadness of loss of parent in life & death.	
16	**Lakeridge, S. Simpson, J. (2012) England**	Loss of social status. Uncertainty over position in future life beyond caring. Threat to self over EOD being diagnosed.			Rejected by social life and society Left out of the loop as carers of EOD which is not understood by other health care roles/services	Lack of awareness of EOD as a condition. Futility of giving a negative diagnosis.	Denial of what is happening in everyday life.	Anxiety, Self denial, In denial, Shock, Disappointment Distress, Anger, Bitterness at treatment as carers, Feeling bullied by service providers into accepting unwanted services.	Finding help from others in same position.

Conceptual themes and Schultz's first and second order constructs

The table below concluded the development of the line of argument. Noblit and Hare adopted Schutz's notion of first and second order constructs assisting the progression of themes. Schutz utilised the term first-order construct in referring to the everyday constructs and understandings of ordinary lay people. The second-order construct referred to those constructs familiar to social science researchers. The table below (Table 5) reveals how the themes took their place within the constructs drawn in accordance with Schutz's terms. The final themes that arose were: i) biographical disruption ii) diagnosis, iii) losing life, friends and competences, iv) liminality and chronicity, v) stigma, and vi) coping with cautious optimism. The table below finalised the creation of new concepts which are followed by discussion of the themes.

Table 5: Second and third order interpretations

Key concepts	1st order interpretation			2nd order interpretation		
Losses encountered through experience with condition	Loneliness experience throughout changes to life can disrupt and cause other feelings & experiences	Dignity lost to those personally affected	Confusion & uncertainty over lost health can be felt with diagnosis			
	Loss of power, social status, financial, role.	Loss of self experienced.	Missing 'normal' shape of rite of passage in life			
	Loss of financial/ emotional security is another side effect of a diagnosed chronic illness which can threaten the ability to work.	Loss of childhood experienced before natural time can occur.			The nature of the perceived limiting nature of a dementia diagnosis appears to compound the idea of losses especially in EOD as there are increased fears of job loss, threat to home and future hopes less thought of in older age dementia.	
Liminality	Feeling outside life and out of step with events.	Trapped in the middle of nowhere.			The process on the way to diagnosis including & post period can alter the perception of the self in life, others & life activities	

Key concepts	1st order interpretation			2nd order interpretation		
	Doubts and fears about going forward with uncertainty	No sense of belonging to or possessing order to life living with EOD				
	Out of step with others and expectations of health personnel & family can occur with EOD. It can make the person feel displaced in their own lives.					
Biographical disruption	Stilted development for especially younger children of PwEOD.	Dependents not able to experience transition to develop.				
	Loss of normal sequence to life e.g. child-teenager-adult	Disruption & abruption			Biographical disruption heightens negative experience of diagnosis; this can alienate hopes & expectations of moving forward positively through life stages	
	Parentification of younger family members of PwEOD					

Key concepts	1st order interpretation			2nd order interpretation		
Stigma & dealing with the presentation of self	Rejection by others.			Passing type attempts to negate others' negative attention drawn to illness effects. Goffman's micro sociological understanding.	Masking occurs in PwEOD & their families as they try to cope with social responses – Goffman.	'Hollywoodin g' by society of the condition prohibits those directly affected from speaking their truth which is less glamorous.
	Lack of cohesion & sense of belonging with others.	Covering up deficiencies.	Indecision through shame.			Stigma can seem worse due to the younger onset nature of an illness unexpected.
Diagnosis & the nature of changes emerging from disclosure	Diagnosis difficult to gain & to realize, not being taken seriously by others.	Other conditions are preferred in diagnosis due to professional reluctance to consider dementia.	Emotional exhaustion at eventual diagnosis- mild relief/ depression.			
	Epiphanic welcome & feared news at eventual diagnosis.					
Chronicity & the articulation of & effects of time	Dislocation & lack of certainty about present, past & future.	Waiting for confirmation, services, results, sense of self to emerge.				The indecision, shock & lack of knowing with an EOD diagnosis leads to lapses, lags & sensory feelings of not fulfilled as expected.
	Difficulties to plan time after being given a diagnosis.					

Key concepts	1st order interpretation			2nd order interpretation		
Coping & emerging from suffering positively	There can be 'room to live with it' helps to see life more positively after.	Collaboration from others helps to be positive.				
	With understanding plans can be made to bond with post diagnosis life.	Lessons to teach others emerge; can occur with acceptance			Once a stage of acceptance has been met, beyond this is a reintegration with a normal life once more but as changed, informed with an optimistic outlook of self & others.	
	Desiring to manage & flourish with new knowledge					

Line of argument

PwEOD – Biographical disruption

A prevailing theme within eleven of the synthesised sixteen papers reflected disruption of future life plans for PwEOD and their families (Pipon-Young et al., 2011; Hall and Sikes, 2018; Gelman and Rhames, 2016; Johannessen et al, 2016; Johannessen et al, 2017;Johannessen et al, 2015; Johannessen and Moller, 2011; Rostad and Hellzen, 2013;Allen et al, 2009; Sikes and Hall, 2017; Sikes and Hall, 2018).

A synthesis of these studies showed how participants' awareness of feeling too young to face a dementia diagnosis prevailed (Pippon-Young et al., 2011). For dependents, living with a parent with EOD could alter the experience of ideas of childhood. Hall and Sikes (2017) suggested how life could be on hold. From this position, Hall and Sikes (2018) noted how there was no parental template to draw upon for support. Sikes and Hall (2018) expanded upon their own authorship of other papers and described the 'Hollywooding' of the experience of dementia. This referred to the way film and media positioned dementia to a lay public. However, participants reported that this perspective did not equate to their lived reality. Gelman and Rhames (2018) reflected upon the chaos and uncertainty of living with EOD and how life lacked any sense of continuity. Johannessen et al., (2016) and Johannessen et al, (2017) noted that the overall burden of EOD on the family was a major biographical consideration. Shock was recorded prior to and beyond diagnosis with the reshaping of life plans (Johannessen and Moller, 2011; Rostad and Hellzen, 2013). Sikes and Hall (2017) suggested that life could be experienced as hectic prior to diagnosis. Following this, post diagnosis held no changes to a life continuing in crisis or fear of crisis. These feelings extended to include both children and teenagers who were immersed in the difficulties in trying to achieve, enjoy and establish lifetime goals that others took for granted (Hutchinson et al., 2016; Hoppe, 2018; Hall and Sikes, 2016). Extending from this, Allen et al., (2009) and Johannessen et al., (2015) described levels of parentification which became normal ways to react to living within a family. Gelman and Rhames, (2016), spoke of developmental hitches occurring to both emotional and psychological development. The ways that this could be reported lay with noticing that a sibling had stopped smiling and laughing. Hall and Sikes (2016) reported a lack of awareness in children that dementia was terminal.

Some studies discussed how being in the workplace represented feelings of exposure with others noticing changes (Johannessen and Moller, 2011). This could lead to queries by colleagues over observable drops and changes in performance (Johannessen and Moller, 2011). Although early retirement caused by EOD could be a life changing departure it could come as a relief when struggles became overwhelming (Johannessen and Moller, 2011). Johannessen et al., (2016) reported how the younger members of families with a PwEOD struggled to define themselves. This had consequences for their own identity. Johannessen et al., (2015) suggested that the integrity and identity of the family as a whole was diminished in certain participant groups. The parental role was eroded through illness as was the child/teenager's role interrupted. Therefore, this could feel like, as discussed, how life changing situations at home felt like a continuous life threat (Hall and Sikes, 2018).

In conclusion it appeared that although biological disruption is a common theme, it can be experienced differently. Participants could experience it with a sense of not knowing what the future held thus making plans and expectations

hard to follow or to enjoy. This could arise from not understanding the trajectory of the illness and at the same time understanding that changes would be unpredictable making life plans difficult to gauge and direct.

Diagnosis

A dominant theme appeared throughout fourteen of the studies indicating that the periods before and after diagnosis could be pivotal (Flynn and Mulcahy, 2013; Johannessen and Moller, 2011; Allen et al, 2009; Hall and Sikes 2018; Johannessen et al., 2017; Lockeridge and Simpson, 2012; Sikes and Hall, 2017; Sikes and Hall, 2018; Johannessen et al., 2016; Johannessen et al., 2015; Pipon-Young, 2011; Rostad and Hellzen 2013; Gelman and Rhames, 2018;and Hutchinson et al, 2016).

A summary and synthesis of similarities reflected that the period running up to diagnosis could be triggered by major crisis events attracting the intervention of authorities as well as minor events which were not exposed to public scrutiny (Lockeridge and Simpson, 2012). It could prove an exhausting journey (Sikes and Hall, 2018). Diagnosis could provide the catalyst for lifestyle changes (Gelman and Rhames, (2018). However, Lockeridge and Simpson (2012) reported that the road towards the clarity and certainty provided by diagnosis was not always welcomed. When dementia was feared or suspected it could take some time to convince a family member to address the matter through a clinical diagnosis (Lockeridge and Simpson, 2012). It was also acknowledged (Allen et al., 2009) that family carers felt despondent over the quality of diagnosis; the competence of the doctor being able to diagnose dementia and ability to offer any supportive strategy thereafter. Johannessen et al., (2017) reflected how each member of the triad reacted to diagnosis; the clinician, the PwEOD and family. Some evidence uncovered how participants' credibility was affected (Johannessen et al., 2017; Johannessen and Moller, 2011) as participants felt they were not believed by a clinical audience. However, Johannessen et al., (2017) and Sikes and Hall (2017) reported relief at diagnosis as it gave a rational account of the recent past. But contrasted to this was experiences of loneliness could set in with no one to talk to about the diagnosis (Johannessen et al., 2015). In Johannessen and Moller (2013), diagnosis meant that an explanation was provided for odd behaviour or withdrawal from previous interests. However, this was tempered by the fact that EOD still represented a terminal illness (Johannessen and Moller, 2011).

Experiences and feelings of blame did permeate the diagnostic period. Such conflicts meant that there was a variety in responses from those affected personally by EOD (Hall and Sikes, 2018). Because doctors were unlikely to suspect EOD often subjective criticism and blame directed towards the family members occurred (Johannessen et al., (2017). Some spouses were not often welcomed in the consulting room and their input was not valued (Johannessen et al., 2017). Often diagnosis was finally achieved after investigation of a string of plausible conditions had proven fruitless (Allen, 2009).

The certainty of diagnosis could allow for exploration of potential future pathways. Attempts could be made to incorporate new approaches to health like new treatment therapies and healthier lifestyles (Hall and Sikes, 2018). While some participants felt relief in reaching a diagnosis, suicidal feelings could manifest immediately after diagnosis (Hutchinson et al, 2016). However, diagnosis could also provide the catalyst for making life changes such as giving up career plans for both the PwEOD and their family (Gelman and Rhames., 2018). Acceptance helped make the best of the situation (Rostad et al., (2013). Contrasting with acceptance was the way that the diagnosis period was experienced outside the clinician's consulting room with one participant being outpaced by his wife's determination to locate a diagnosis. This meant that the participant lagged in their knowledge and acceptance of the diagnosis (Rostad et al., 2013) Lockeridge and Simpson (2012) illustrated how spouses felt conflicted whilst pursuing a diagnosis. They reported that they felt a level of deceit in reporting symptoms at home.

To conclude, when facing a diagnosis of EOD, there were obstacles. These were present prior to diagnosis with lack of realisation of EOD and a desire to not acknowledge a life changing condition. Medical authorities often failed to identify the condition and as a coping mechanism blamed the family who were consulting. Families coped in different ways where optimism could be a feature but predominantly negative feelings were voiced. Whether positive or negative experiences prevailed, families found their lives following very different paths after the delivery of a diagnosis.

Losing life, friends and competencies

Eight studies reflected themes connected to losses; (Rostad et al., 2013; Gelman and Rhames,2018; Flynn and Mucahy, 2013; Allen et al.,2009; Sikes and Hall, 2018; Hutchinson et al., 2016; Sikes and Hall, 2017 and Johannessen et al., 2014).

The synthesis located the diverse effects which could be considered as losses. Rostad et al., (2013) represented ideas expressed over losses to humanity. This was described as loss of self-identity, esteem, determination and respect which extended to becoming dependent upon others. This led to increased inactivity and passivity. Gelman and Rhames (2018) stated that a lack of finite resources to provide for and recognise needs in the family led to permanent feelings of loss. Sikes and Hall (2018) reported loss of the PwEOD and bereavement and grieving occurring before the death occurred and discussed how life was lived alongside these feelings. In Allen et al., (2009) there was a reported loss of a father role in the family and the loss of expectation of being parented. In Hutchinson et al., (2016) a loss was recorded in opportunities due to mandatory care responsibilities being required to be covered in the household. Sikes and Hall (2017) reported a downward spiral effect of losing a normal perspective. In the Johannessen et al., (2014) study, losses were discussed as losing social role, health, quality of life, ability to work and cognitive capacity.

Flynn and Mulcahy, (2013) positioned their study to understand losses as being service driven and they often fell short of sufficiency for the PwEOD and their family carers. Restrictions were financial, social, emotional and physically felt by the participant group; the family carers (Sikes and Hall, 2017).

To conclude, losses could be understood personally as well as socially.

Experiences around how 'normal' life was now dislocated, particularly after the certainty of a diagnosis, were notable and diverse. These experiences could venture into aspects of life which were connected to feelings and perceptions of identity, autonomy and selfhood. This could reflect how it was difficult to isolate claims into disparate concepts. Instead they tended to rely upon linking and merging into each other. Conceptual losses could thus be understood within a number of interlinking experiences.

Liminality and chronicity

Themes drawn from eleven of the sixteen studies revealed experiences around liminality. This effect can arise when people feel 'out of this world', 'betwixt and between' and in situations divorced from their perception of normal life. Notions of chronicity prevailed with feeling that time did not follow a normal pattern: (Rostad et al., 2013;Johannessen and Moller,2011;Johannessen et al., 2014; Lockeridge and Simpson, 2012; Gelman and Rhames,2018; Hutchison et al., 2016; Johannessen et al., 2015; Sikes and Hall, 2017; Sikes and Hall. 2018;Flynn and Mulcahy,2013 and Johannessen et al., 2017).

The synthesised results led to the following understanding: Johannessen and Moller (2011) noted feelings of confusion and not knowing what was happening to them in the interim period prior to diagnosis. Gelman and Rhames (2018) reported experiences of chaotic feelings of 'otherness' and 'outsiderhood' in relation to change as well as leading to feelings of failure to cope (Rostad et al., 2013; Johannessen et al., 2014; Johannessen and Moller, 2011). These experiences read to reflect a sensory experience which was experienced as a fracturing away from others and perceived normality (Allen et al., 2009). Spouses could feel rejected and confused over how to cope (Johannessen et al., 2017). Lockeridge and Simpson (2012) outlined being lost with feelings of rejection and how carers could feel bullied into accepting services they did not wish or feel necessary. Allen et al (2009) reported in accordance with the Gelman paper feelings of disconnection whereby other family members could appear co-dependent with the PwEOD. This could lead to epiphanic, revelationary and euphoric traits present whereby certain family members could advocate for the day when the PwEOD recovered or different causes could be found for symptoms. Johannessen et al., 2017; Sikes and Hall (2017) reported how family carers observed feelings of rejection and confusion about everyday life. Johannessen et al., (2016) articulated lifetime rites of passage and aggregated experiences that were under threat such as marriage, graduations and childbirth. Therefore, there was an articulated experience of achievements going unnoticed. Within this failed recognition, a detachment could form with dependents based upon feelings of exclusion and indifference (Hutchinson et al., (2016). This led to background fears of impending decline and death. Sikes and Hall (2017) reported further reflections around the experiences of time and waiting. By the time a diagnosis did arrive, emotional exhaustion prevented diagnosis from providing a 'Eureka moment'. There nonetheless remained a feeling that life was on hold and there was no destination end to the journey. Themes related to chronicity were noted. Time could feel more burdensome in the way that every declaration and event had to be waited upon. Such experiences were provoked by waiting for news, diagnosis, service provision and uncertainty about the future (Johannessen et al., (2016); Sikes and Hall (2018). Johannessen et al., (2015) articulated the conceptual meme of feeling 'zombified' by the experience and taint of EOD. The family reported coping in ways that were more; more dislocated, spatially lost and remote (Flynn and Mulcahy, 2013; Johannessen et al., 2017. Johannessen et al., (2015) recorded metaphorical experiences of 'slipping away' of being 'in another world' and 'spinning in a centrifugal machine'.

These concluded experiences of life in limbo including thematic descriptions of dealing with the often chaotic experiences of EOD. The experiences were overarching the confusion that EOD symptoms often provoked in PwEOD and reflected how family felt wrong-footed over daily routines and how to react in a 'new normal' life. These led to situations of feeling 'betwixt and between' with regard to not finding or locating a comfortable place to occupy in the family as the roles of child/adult, young adult/parent lost definition.

Stigma

Eleven of the sixteen studies reflected stigma was prevalent being reported by both PwEOD and with spouses and dependents; Hutchinson et al., (2016);Pipon-Young et al., 2011, Allen et al.,(2009); Johannessen and Moller, (2011);Sikes and Hall, (2017); Johannessen et al., (2016); Lockeridge and Simpson,(2012); Hoppe (2018); Gelman and Rhames, (2018); Johannessen et al., (2014) and Hoppe,(2018).

Johannessen and Moller (2011) reported how suicidal thoughts could be the outcome of not being confident about being in company with others due to their cognitive abilities. This could be shown in self-harm (Allen et al., 2009). However, most stigma emerged with interaction with others. This is where stigma could manifest obviously. Pipon-Young et al., (2011) discussed 'saving face' as a way by which people covered up their dementia through embarrassment and coped socially with potentially discriminating features of their lives. Johannessen and Moller (2011) described how PwEOD could feel marginalised through having no control over what others knew about them. Stigma by association [3] affected participants across some studies (Allen et al.),

(3) Stigma by association is the placing of strain on family members arising from the connection

2009; Hutchinson et al., 2016). Dependents felt stigmatised by having a parent with EOD. At any time the participants reflected how difficult it was to manage their accounts to others often changing information dependent upon to whom they were directing their conversation (Hutchinson et al., 2016) Participant family carers vacillated between guilt and a form of coping. This form of coping allowed family carers to operate daily life whilst trying to shield the PwEOD from difficulties in the aftermath of a dementia diagnosis. Some studies reported how strategies were found to cope and deflect stigma both in the self and other family members (Sikes and Hall, 2017; Johannessen et al., 2016); Lockeridge and Simpson (2012) and Hoppe (2018). Crucially these experiences of being judged negatively emerged when interfacing with medical services (Sikes and Hall, 2017; Johannessen et al., 2016). Gelman and Rhames (2018) reported stigma like experiences reported through loss of status, self-efficacy and credibility. As a result of stigma, dependents could be left with feelings of irrecoverable lack of confidence.

The experiences concluding EOD stigma demonstrated how PwEOD, their spouses and children were affected in different ways; some of which were rooted in the micro-relationships within the family and physician relationships, others emerged within social life in society.

Coping with cautious optimism.

Under the theme of coping, eleven of the sixteen studies reported evidence of participants thriving with EOD (Johannessen et al., (2017); Johannessen et al., (2016); Rostad et al., (2013); Pipon-Young et al., (2011); Lockeridge and Simpson (2012); Millenaar et al., (2016); Johannessen et al., (2015);Gelman and Rhames (2018) Allen et al., (2009); Hutchinson et al., (2016) and Hall and Sikes, (2018).

Pipon-Young et al., (2011) related how PwEOD negotiated positive ways to live well with dementia; ; keeping active and involved and sharing a social life. Rostad et al., (2013) Lockeridge and Simpson (2012) and Johannessen. Rostad et al., (2013) Lockeridge and Simpson (2012) and Johannessen et al., (2017) reported participants as being able to reach acceptance and live with their diagnosed condition. Mental health issues affected coping resulting from unmet needs and lack in provision of support (Millenaar et al., 2016) with reference to young carer literature [4]. Johannessen et al., (2016) and Johannessen et al., (2015) showed that part of coping was enabled by detaching from everyday suffering in life to gain a safe perspective. Getting used to a 'new normal' was possible alongside negotiating the difficulties of life drawing parallels with Parsonian obligations to work and contribute to self and society (Hall and Sikes, 2018). This impacted upon coping themes related to competing in a job market. Gelman and Rhames (2018) and Allen et al., (2009) drew upon claims that coping meant adjusting to living with fear and taking one day at a time. Hutchinson et al., (2016) reported how the identity could be developed which enhanced strategies of coping. Overarching the views on coping was securing a blend of normality which could be achieved provided economic pressures could be minimised or set aside. Resilience helped dependents distance themselves from traumatic family events and overwhelming tension. This meant that part of being a 'new normal' could result in not being economically competitive.

Conclusion

The review focused on the experiences of living with EOD. The results indicated that there was variation in the sample sizes, patient type, models and study design. Meta-ethnography was the selected approach to systematically review the literature. The main themes extracted were; i) biographical disruption ii) diagnosis, iii) losing life, friends and competences, iv) liminality and chronicity, v) stigma, and vi) coping with cautious optimism. The findings do reflect broad consensus that EOD prompts some different needs within the dementias' classifications. To this end, further research and development in the field is suggested in order to provide more knowledge for those providing and receiving care and services with particular sensitivity to each personal perspective in the triad of PwEOD, spouse and children.

Gaps in the literature and rationale for study

The literature review conducted in this chapter reflected a gap in the literature capturing the lived experience of PwEOD as reported in their own voice. As a result, only four studies were located reflecting the views of PwEOD were expanded with the experiences of family kin reporting on life at home with the PwEOD. This study aim therefore intended to investigate the direct experiences of PwEOD as they chose to reveal what living with the condition was like in everyday life. This review contributes to the modest extant knowledge of PwEOD. Of the available literature meeting criteria, there is still a tendency for the literature to seek family kinship views as opposed to drawing upon the PwEOD's views where these opinions and views could be provided. Given the gaps in current research, it was important to investigate further the challenges and opportunities for researchers and practitioners in researching, planning, implementing, and evaluating appropriate educational, supportive, and therapeutic services for individuals affected by EOD. Without a firm policy steer, PwEOD in the UK may be at risk of not receiving age-sensitive appropriate care.

Strengths and limitations of the study

Methodological strengths of this review include its reproducible and systematic nature including the application of a meta-ethnographic tool (Noblit and Hare, 1988). This review contributes to the modest extant knowledge of PwEOD. The process allowed similar concepts to be compared through a system of values enabling a full review of all available literature meeting the criteria.

(4)Domestic estimates in Scotland suggest mental health difficulties amongst young carers indicate are reported twice as much as is reported by non-carers (Scottish Government, 2017).

There were a number of limitations with the review. Weaknesses were located around the paucity of studies located highlighting experience of having EOD. This was dealt with by expansion to encompass family kin. This allowed inclusion of a wide variation in age ranges and eclectic family role dyads. The literature illustrated that there are many legitimate perspectives affected by EOD. However, as thevariation in the studies was so wide, the synthesis could not fully account for the influence of these factors in the findings. Finally, included studies were conducted within Western cultures and within traditional 'nuclear families'. This had the effect of restricting generalisability of findings to other family structural systems. Studies were included from clinical settings which may distort some of the findings and assumptions.

Clinical implications

Participant views are deemed to be important for the planning of service provision and delivery. The results suggest strongly that planners of health and social care will be required to be answerable to an audience which is differently populated. Within any population of EOD there may likely be people who form part of the working population with children who still require support from parents both financially and emotionally. Care providers and planners must be cognisant that EOD is a chronic condition which whilst terminal, occurs in individuals and families with acute and vital ongoing needs. It is critical that qualitative research takes on board the nature of biographical disruption in an EOD diagnosis and considers the needs of a younger population. This is critical to the needs of other workers in the family including the vulnerability of children.

One noteworthy consideration in qualitative studies gathering person-centred-views is awareness of location and channel through which studies are performed. The studies relied upon hospital based or clinically led studies. Most made provision to ensure participant convenience and comfort. However, it is the case that ethical concern must be drawn to what extent participant groups may suspect that there are right answers or wrong answers. Medicine still is situated as the dominant hegemony governing care in times of medical frailty where people fear demise and death. It may be imagined that by complying with a particular view it may help participants to gain access to medication, clinical trials or enhanced service provision. For these reasons such concern should be taken over recruitment paths. This will ensure that participants are not unclear about what their data may realise for them personally in the short to medium term. In order to ethically and respectfully manage the expectations of participants, the aims and likely outcomes of studies should very clearly be illustrated to potential participants.

Future research implications

Further contributions to the research body including qualitative studies on experience could sensitise policy-makers, health and social care providers to the factors likely to enhance service provision and care. EOD is a classification which brings its own separate concerns from those presenting in later onset dementias. Therefore, it may be fruitful for future research to explore further the experience of PwEOD. This would relate to both the personal impacts as a distinct condition with different symptoms to that of older onset conditions as well as experiences of coping within work and family settings.

References

Al-Janabi H, Coast J, Flynn TN. (2008) What do people value when they provide unpaid care for an older person? A meta-ethnography with interview follow-up. Soc Science Medicine67(1):111–21.

Allen, J., Oyebode, J., Allen, J., (2009) Having a father with young onset dementia. The impact on well-being of young people.Dementia http://em.sagepub.com vo.l 8 (4) 455-480

Allen K. (2001) Communication and Consultation: Exploring Ways for Staff to Involve People with Dementia in Developing Services.Bristol: The Policy Press.

Bamford C. & Bruce E. (2000) Defining the outcomes of community care: the perspectives of older people with dementia and their carers. Ageing and Society 20, 543–570.

Beattie, A., Daker-White, G., Gilliard, J., Means, R., (2004) 'How can they tell?' A qualitative study of the views of younger people about their dementia and dementia care services. Health and Social Care in the Community 12(4), 359–368. Blackwell Publishing, Ltd.

Britten N, Campbell R, Pope C, Donovan J, Morgan M, Pill R. (2002) Using meta ethnography to synthesise qualitative research: a worked example. Journal of Health Service Research & Policy;7(4):209–15.

Cabote, C., Bramble, M., McCann, D., (2015) Family Caregivers' Experiences of Caring for a Relative With Younger Onset Dementia: A Qualitative Systematic Review.Journal of Family Nursing Vol. 21(3):443-68.

Campbell R, Pound P, Pope C, Britten N, Pill R, Morgan M, et al. (2003) Evaluating metaethnography: a synthesis of qualitative research on lay experiences of diabetes and diabetes care. Soc Sci Med;56:671–84.

Flynn, R. Mulcahy, H., (2013) Early onset dementia: the impact on family care-givers. British Journal of Community Nursing.18(12), 598-606.

Fink, A. (1998). Conducting Research Literature Reviews: From Paper to the Internet, Sage Publications, London.

Gelman, C., Rhames, K., (2018). In their own words: The experience and needs of children of younger-onset Alzheimer's Disease and other dementias families. Dementia. Vol. 17 (3) 337-358

Greenhalgh T. (1998) Meta-analysis and beyond: applying secondary research methods to primary care. British Journal of General Practice;48:1540–1.

Greenwood, N., Smith, R., 2016. The experiences of people with young-onset dementia: A meta-ethnographic review of the qualitative literature. Maturitas 92 (2016) 102–109

Goldsmith, M., (1996) Hearing the Voice of People with Dementia. Opportunities and Obstacles. Jessica Kingsley Publishers. London

Hall, M., Sikes, P., (2018) From "What the Hell is going on?" to the "Mushy middle ground" to "Getting used to a new normal": Young people's biographical narratives around navigating parental dementia. Illness, Crisis and Loss Vol. 26 (2) 124-144

Hart, C. (1998). Doing a Literature Review: Releasing the Social Science Research Imagination, Sage Publications, London

Hoppe, S., (2018) A sorrow shared is a sorrow halved: The search for empathetic understanding of family members of a person with early onset dementia. Culture, Medicine and Psychiatry. 41 (1): 180-201.

Hutchinson, K. Roberts, J. Kurrle, S Daly, M. (2014)The emotional well-being of younger people having a parent with younger dementia.Dementia 1–20

Johannessen, A., Moller, A., (2011) Experiences of persons with early-onset dementia in everyday life: a qualitative study, Dementia 12 (4) 410–424,

Johannessen, A., Moller, Haugen, Per K., (2014) A shifting sense of being: A secondary analysis and comparison of two qualitative studies on young-onset dementia. International Journal of Qualitative Studies on Health and Wellbeing. Volume 9, Issue 1.

Johannessen, A., Engedal, K., Thorsen, (2015) Adult children of parents with young-onset dementia narrate the experiences of their youth through metaphors. Volume 8 pp. 245-254. Dove Medical Press Ltd.

Johannessen, A., Engedal, K., Thorsen, K.,(2016) Coping efforts and resilience among adult children who grew up with a parent with young-onset dementia: a qualitative follow-up study. International Journal of Qualitative Studies on Health and Wellbeing. Volume 11, issue 1

Johannessen, A., Helvik., A., Engedal, K., Thorsen, K., (2018) Experiences and needs of spouses of persons with young-onset frontotemporal lobe dementia during the progression of the disease. Scandinavian Journal of Caring Sciences Volume 31, issue 4

Kitwood T. (1997) The experience of dementia. Aging and Mental Health 1 (1),13–22

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. British Medical Journal. 339:b2700.

Lockeridge, S. Simpson, J., (2013) The experience of caring for a partner with young onset dementia: how younger carers cope. Dementia 12 (5) 635–651

Larun L, Malterud K. (2007) Identity and coping experiences in chronic fatigue syndrome: a synthesis of qualitative studies. Patient Educ Couns;69(1):20–8

Mays N, Pope C, Popay J. (2005) Systematically reviewing qualitative and quantitative evidence to inform management and policymaking in the health field. Journal of Health Services Research & Policy;10(Supp 1):6-20.

Mercy, L., Hodges, J., Dawson, K., Barker, R., Brayne, C., (2008) Incidence of early-onset dementias in Cambridgeshire. American Academy of Neurology. https://doi.org/10.1212/01.wnl.0000334277.16896.fa (accessed 10th May, 2018.

Noblit GW, Hare RD. (1998) Meta-ethnography: synthesising qualitative studies. London: Sage.

Ohman, A., Nygard, L., Borell, L., (2001) The vocational situation in cases of memory deficits or younger onset dementia Scandinavian Journal of Caring Sciences.15-1 pp. 34-43.

Page S and Keady J. (2010) Sharing Stories: A meta-ethnographic analysis of twelve Autobiographies written by people with dementia between 1989-2007. Ageing & Society 30 (3) 511-526

Paterson, B.,Thorne, S.,Dewis, M.,(1998) AdaptingtoandmanagingdiabetesJournalofNursing Scholarship Vol. 30:57– 62

Pipon-Young, F. Lee, K. Jones, F. Guss, R., (2012) I'm not all gone, I can still speak: the experiences of younger people with dementia. An action research study, Dementia 11 (5) 597–616

Pound P, Britten N, Morgan M, Yardley L, Pope C, DakerWhite G, et al. (2005) Resisting medicines: A synthesis of qualitative studies of medicine taking. Social Science and Medicine;6: 133-155.

Rose, H., Cohen, K., (2010). The experiences of young carers: a meta-synthesis of qualitative findings. Journal of Youth Studies. Volume 13. Issue 4.

Rostad, D., Hellzén, O., Enmarker, I., (2013) The meaning of being young with dementia and living at home, Nurs. Rep. 3 (1) 3, http://dx.doi.org/10.4081/ nursrep.

Sandelowski M, Docherty S, Emden C. (1997) Qualitative metasynthesis: issues and techniques. Res Nurs Health;20:365–71

Schütz A. Collected papers 1. (1962) The Hague, Netherlands: Martinus Nijhoff.

Scottish Government. (2017). Proposal for Scotland's National Dementia Strategy 2016-19: March 2016. http://www.gov.scot/Topics/Health/Policy/Dementia. (Accessed 26/05/2018).

Sikes, P. Hall, M., (2017) "Every time I see him he's the worst he's ever been and best he'll ever be": grief and sadness in children and young people who have a parent with dementia. Mortality Volume 22, issue 4

Sikes, P., Hall, M., (2018) "It was then that I thought 'what? This is not my Dad': The implication of the 'still the same person' narrative for children and young people who have a parent with dementia. DementiaVolume 17 (2) 180-198

Strike K, Posner G. Types of synthesis and their criteria. (1983) In: Ward S, Reed L, editors. Knowledge structure and use. Philadelphia, PA: Temple University Press. pp. 344–61.

Whitlatch, C., (2002) Including people with dementia in family care-giving research. Aging and Mental Health 5 (1), S20- S22

Van Vliet, D., de Vugt., M., Bakker, C., Koopmans, R., Verhey, F., (2010). Impact of early onset dementia on caregivers: a review International Journal of Psychiatry

Yardley, L., (2000) Dilemmas in Qualitative Research. Psychology & Health Journal, Vol. 15 Issue 2, p215-229.

Appendices

Appendix 1

Excluded papers	Rationale for failing to meet final inclusion
Millenaar et al., (2016). Exploring perspectives of young onset dementia caregivers with high versus low unmet needs. Ch 3. In Young Onset Dementia. Towards a better understanding of care needs & experience. Neuro Psych Publishers. The Netherlands 2016	Seeking outcomes for future service needs- no investment in reported experiences
Millenaar et al., (2016). The experiences and needs of children living with a parent with young onset dementia. In Young Onset Dementia. Towards a better understanding of care needs & experience. Neuro Psych Publishers. The Netherlands 2016	Quantitative approach to study findings
Beattie et al., (2004) "How can they tell?" A qualitative study of the views of younger people about their dementia and dementia care services.	Too focused on service outcomes
Williams et al., (2001) From pillar to post- a study of younger people with dementia	Seeking epidemiological data for service development
Kaiser et al., (2007) The psychosocial impact of young onset dementia on spouses	Stress on quantitative information and concern with clinical conditions not experience
Harris & Keady (2009) Selfhood in younger onset dementia: Transitions and testimonies	Focus groups
Johannessen et al., (2017) Experiences and needs of spouses of persons with young-onset fronto-temporal lobe dementia during the progression of the disease	Focus on gaining information to inform GPs and IT services

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