ORIGINAL REPORT

Cardiovascular and Metabolic Profile of Subjects with Acne in a Cohort of Middle-aged Patients: A General Population Study of 1,932 Subjects

Suvi-Päivikki SINIKUMPU[1], Jari JOKELAINEN[2], Kaisa TASANEN[1] and Laura HUILAJA[1]
[1]Department of Dermatology, University Hospital of Oulu, and Medical Research Center, Research Unit of Clinical Medicine, University of Oulu and [2]Northern Finland Birth Cohorts, Arctic Biobank, Infrastructure for Population Studies, Faculty of Medicine, University of Oulu, Oulu, Finland

Acne vulgaris is one of the most common inflammatory skin diseases, but there are few studies of adult acne and its association with general health. The aim of this study was to examine the prevalence and clinical characteristics of adult acne at the population level among 1,932 subjects belonging to the Northern Finland Birth Cohort 1966 Study. In addition, cardiovascular and metabolic profiles of acne cases and their controls were analysed. The prevalence of adult acne was 7.9% ($n = 150$) with no statistical difference between the sexes. The majority of subjects presented with papulopustular acne (77.1%). Comedo acne (10.8% of all subjects) was more common in females than in males ($p < 0.005$). Males with acne had more abnormality in their metabolic factors than did acne-free controls; plasma glucose and insulin levels at 60 min after the 75 g glucose load were higher in males with acne than in controls ($p < 0.01$ for both). Corresponding associations were not seen in females. In conclusion, adult acne is common in middle-age, presenting a slightly different clinical picture in females than in males. In addition, male subjects with acne may have a higher risk of metabolic disturbances than do controls, and thus, comprehensive evaluation of patients with adult acne is needed.

Key words: acne; adult acne; cardiovascular risk factors; metabolic risk factors; epidemiology.

Accepted Apr 25, 2023; Published Jul 10, 2023

Acta Derm Venereol 2023; 103: 5921.

DOI: 10.2340/actadv.v103.5921

Corr: Suvi-Päivikki Sinikumpu, Department of Dermatology, Oulu University Hospital, PB 20, FIN-90029 Oulu, Finland. E-mail: suvi-paivikki.sinikumpu@oulu.fi

SIGNIFICANCE

Many patients experience acne after adolescence. However, there are few studies of adult acne. The aim of this study was to examine the prevalence of acne in the general population belonging to the Northern Finland Birth Cohort 1966 Study at the age of 46 years ($n = 1,932$). Acne was found to be common in middle-age; it was present in 7.9% of cases ($n = 150$). The most common type of adult acne was papulopustular acne, but comedo acne was also seen. Moreover, the study found that males with acne had more metabolic abnormalities, such as differences in insulin and glucose secretion, compared with acne-free controls.

Acne vulgaris is an inflammatory skin disease that affects almost all adolescents during puberty (1). Later, a significant number of subjects experience persistent acne or develop late-onset adult acne. In adulthood, acne has been reported to be more common in females than males (2, 3). According to a survey performed in the UK, acne was self-reported by 26.3% of women and 12.0% of men aged 40–49 years (4). In turn, at a tertiary dermatology referral centre in Singapore, one-third of all patients with acne were post-adolescent (5). Adult acne may be common, as recent studies have reported its increasing prevalence (2, 6, 7).

Clinically, adult acne differs from adolescent acne: small nodules and cysts on the chin are characteristic of adult acne, and patients have inflammatory pustules and papules, but usually have fewer comedones (8, 9). The aetiology of adult acne is multifactorial, and both endogenous and exogenous factors are involved in its pathogenesis (3). In addition, subjects with adult acne have been reported to have endocrinological abnormalities (7, 10–14), such as a risk of metabolic syndrome (12). An Indian study with 100 young male subjects with acne (mean age 22.7 years) found an increased risk of insulin resistance in acne cases compared with those without acne (14). Correspondingly, a study performed in Brazil ($n = 219$ subjects, mean age 32.2 years) reported a more unfavourable lipid profile in females with acne than in controls (13). In addition to endogenous factors, stress, medication and diet are known to affect the risk of adult acne (3, 6, 8).

The majority of studies addressing adult acne have been conducted among specific patient groups, such as subjects from dermatology clinics, which may have caused bias (5, 7, 10, 12–14). In addition, many of the previous studies on adult acne have concerned rather young subjects (10, 13, 14). This study aimed to examine the prevalence and clinical characteristics of adult acne in the general population at the age of 46 years in subjects belonging to the Northern Finland Birth Cohort 1966 Study (NFBC1966) (15). A further aim was to describe the metabolic and cardiovascular demographics of subjects with adult acne.

METHODS

Study population

The study population belongs to the large NFBC1966, which is a longitudinal research programme. Originally, the NFBC1966 included all 12,058 children in the 2 northernmost provinces (covering 48% of Finnish territory and 13.2% of the population in 1966) of Finland, whose expected dates of birth fell in the year 1966 (15). The whole cohort has been evaluated regularly since birth by means of health questionnaires and clinical examinations. At the age of 46 years all cohort members living in the city of Oulu and its surroundings (100 km distance including rural areas) were invited to a comprehensive health study including several clinical examinations (e.g. dermatological evaluation and anthropometric measurements) and health questionnaires. The 46-year follow-up study was performed between April 2012 and May 2013 at the Faculty of Medicine of Oulu University. Cohort members were 45–47 years old at the time of the study.

Dermatological evaluation

For the purpose of this study, detailed dermatological status was comprehensively determined for all subjects by a specialist in dermatology or an experienced resident (16). This examination began with visual observation of the whole skin. The location and duration of all skin symptoms and their severity was recognized. Diagnosis and classification of acne was based on the evaluation by a dermatologist at the study visit and on internationally accepted criteria (17). Adult acne was classified using the following subtypes, according to its clinical presentation: 1: comedo acne; 2: papulopustular acne; 3: cystic acne; 4: the combination of 1 and 2; or 5: the combination of 2 and 3. In addition, acne was classified into 3 groups according to severity: mild, moderate or severe. Disease severity was based on a combination of both clinical findings and the extent of the disease. The duration of acne symptoms was classified as follows: 1: <1 year; 2: 1–5 years; 3: 6–10 years; and 4: >10 years. Those without acne at the dermatological examination were used as controls and matched by age and sex.

Anthropometric parameters

Cardiovascular and metabolic parameters were comprehensively studied in all subjects, and these risk factors are described in detail in Appendix S1.

Table I. Clinical characteristics of subjects with adult acne

	Men ($n=882$) *n* (%)	Women ($n=1,028$) *n* (%)	Total ($n=1,910$) *n* (%)	*p*-value
Adult acne				0.366
Yes	64 (7.3)	86 (8.4)	150 (7.9)	
No	818 (92.7)	941 (91.6)	1,759 (92.1)	
Severity of adult acne				0.119
Mild	40 (62.5)	63 (74.1)	103 (69.1)	
Moderate	22 (34.4)	22 (25.9)	44 (29.5)	
Severe	2 (3.1)	0 (0.0)	2 (1.3)	
Clinical characteristics of adult acne				0.005
Comedone	2 (3.1)	14 (16.7)	16 (10.8)	
Papulo-pustules	53 (82.8)	62 (73.8)	115 (77.7)	
Cysts	0 (0.0)	4 (4.8)	4 (2.7)	
Comedones and papulo-pustules	6 (9.4)	4 (4.8)	10 (6.8)	
Papulo-pustules and cysts	3 (4.7)	0 (0.0)	3 (2.0)	
Duration of symptoms, years				0.012
<1	1 (1.6)	6 (7.1)	7 (4.8)	
1–5	11 (18.0)	19 (22.4)	30 (20.5)	
6–10	3 (4.9)	16 (18.8)	19 (13.0)	
>10	46 (75.4)	44 (51.8)	90 (61.6)	

Some data are missing because some study cases have denied the subsequent use of data.

Ethics statement

The ethics committee of the Northern Ostrobothnia Hospital District approved the current study (§94/2011), which was performed according to the principles of the Declaration of Helsinki 1983. The subjects took part on a voluntary basis and gave their informed consent. The data was handled on the group level and was pseudonymized for analyses.

Statistical analyses

The characteristics of the study population are presented as proportions, means and medians. The Mann–Whitney *U* test and Person's χ^2 test were used to compare the distribution of cardiovascular and metabolic risk factors in acne cases and controls. Because of the known causality between physical activity, body mass index (BMI) and cardio/metabolic factors it was decided not to perform multivariable analyses. To correct for multiple testing, the false discovery rate (FDR) was controlled using the Benjamini-Hochberg method. Statistical analyses were performed using SAS software package (version 9.4, SAS Institute, Inc., Cary, NC, USA) and a *p*-value <0.05 was considered statistically significant.

RESULTS

A total of 3,181 persons of the NFBC1966 living in a given geographical area were invited to attend a clinical total-body skin examination of the 46-year follow-up study. Of those 1,932 participated (60.7%) and of these, 1,036 (53.7%) were females. The baseline characteristics of study cases are shown in **Tables I** and **II**.

The overall prevalence of adult acne was 7.9% ($n=150$). Acne was seen more commonly in females 8.4% ($n=86$) than in males 7.3% ($n=64$), but the difference was not statistically significant ($p=0.37$). The majority of cases presented with mild acne (69.1%), but males were more often affected with more severe acne than were females (not statistically significant) (Table I). The most common type of acne was papulopustular (85.5%), and females more commonly had comedo acne than did males ($p<0.005$). Over half of the subjects (61.6 %) reported their acne symptoms to have been present for more than 10 years (Table I).

When analysing the subjects' cardiovascular and metabolic profiles, it was found that male subjects with acne had more metabolic abnormalities than did controls. More precisely, males with acne had increased insulin secretion (assessed by Homeostasis Model Assessment – beta-cell function; HOMA-B) compared with male controls ($p<0.05$). Plasma glucose and insulin levels at 60 min after the 75 g glucose load were higher in males with acne than in controls ($p<0.01$ for both). Body mass index (BMI), waist circumference and visceral fat area tended to be higher in males with acne than in controls, but the difference was not statistically significant ($p>0.5$). Corresponding metabolic findings were not seen in females compared with acne-free controls (**Table III**).

After correcting for multiple comparisons using the Benjamini-Hochberg method, there were still

Table II. Baseline characteristics of study population

	Men				Women			
	Acne ($n=64$)	No acne ($n=818$)	Total ($n=882$)	p-value	Acne ($n=86$)	No acne ($n=941$)	Total ($n=1,027$)	p-value
Socioeconomic status, *n* (%)				0.645				0.404
Basic/secondary*	39 (60.9)	522 (63.8)	561 (63.6)		55 (64.0)	556 (59.3)	611 (59.7)	
Tertiary*	25 (39.1)	296 (36.2)	321 (36.4)		31 (36.0)	381 (40.7)	412 (40.3)	
Smoking, *n* (%)				0.951				0.602
Never smoked	28 (45.2)	372 (47.4)	400 (47.2)		50 (59.5)	516 (57.0)	566 (57.2)	
Former >6 months	19 (30.6)	218 (27.8)	237 (28.0)		15 (17.9)	208 (23.0)	223 (22.5)	
Former ≤6 months	1 (1.6)	18 (2.3)	19 (2.2)		2 (2.4)	11 (1.2)	13 (1.3)	
Current smokers	14 (22.6)	177 (22.5)	191 (22.6)		17 (20.2)	170 (18.8)	187 (18.9)	
Alcohol consumption, g/day, mean (SD)	19.0 (36.5)	16.9 (23.5)	17.1 (24.7)	0.284	5.6 (8.3)	6.5 (9.3)	6.4 (9.2)	0.527
Physical activity, *n* (%)				0.014				0.374
Inactive	22 (35.5)	145 (18.5)	167 (19.7)		14 (16.5)	208 (23.0)	222 (22.4)	
Slightly active	20 (32.3)	314 (40.1)	334 (39.5)		39 (45.9)	339 (37.4)	378 (38.1)	
Active	17 (27.4)	285 (36.4)	302 (35.7)		31 (36.5)	343 (37.9)	374 (37.7)	
Very active	3 (4.8)	40 (5.1)	43 (5.1)		1 (1.2)	16 (1.8)	17 (1.7)	

*Socioeconomic status was defined by education.
The information on smoking, physical activity, alcohol consumption was self-reported (26).
SD: standard deviation.
Some data are missing because some study cases have denied the subsequent use of data.

statistically significant differences between the males with acne and those without for the following parameters: plasma glucose and insulin levels at 60 min after the glucose load, and glucose area under the curve (AUC) during oral glucose tolerance test (OGTT).

DISCUSSION

This general population study demonstrated that adult acne is moderately common (7.9%) in both sexes in midlife. Increased insulin secretion and symptoms of metabolic syndrome were seen more commonly in males with acne than in acne-free controls. Similar findings have also been seen in earlier reports, but only in younger subjects with acne (10, 14). It is noteworthy that metabolic disturbances were not seen in the female subjects with acne.

The prevalence of adult acne was nearly 8% in the current study. This finding is in line with previous studies, which have confirmed that acne remains a common skin disease throughout life (4, 5). However, a higher prevalence than that in the current study has also been reported: in a US study ($n=1,013$), 12.0% of men and as many as 26.3% of women experienced acne in their 40s (4). Nevertheless, the US study was based on self-reporting and focused on selected patients visiting a dermatology clinic, which may have caused bias. On the contrary, in a multicentre study performed in China ($n=17,345$) the prevalence of adult acne among those aged 45–49 years was clearly lower than in the current study (1.2% for males and 0.9% for females) (18). In that study, subjects were asked to complete a questionnaire on acne after which they were examined by dermatologists. However, only a few centres were included in the study and the number of middle-aged subjects was very low ($n=12$ for those aged 45–49 years), which makes comparison with the current study challenging (18).

According to the literature, the clinical picture of adult acne differs from that in adolescents. Small nodules and cysts on the chin are characteristic of adult acne, and inflammatory pustules and papules are typical, whereas less comedones are usually seen (8, 9). The most prevalent type in the current study was papulopustular acne, but especially females also presented with comedo acne. The current study also found a few cases with cystic acne. Interestingly, while most of the current study cases presented with mild acne, there was also a high number of subjects (29.5%) with moderate or severe (1.3%) disease, which aligns with a previous study (18). In a Chinese study 26.0% of subjects had moderate and 5.6% had severe acne (18).

Unlike other studies, the current analysis found that acne affected both sexes equally. In the US study, acne was more common in females (4), and similar findings have also been demonstrated in other studies (2, 5, 18–20). This difference may derive from the fact that, in general, females are more likely to seek consultation than males (21), especially for acne (20). Interestingly, in the current study, males were more commonly affected with a severe form of acne than were females. It is of note that selection bias was minimized in the current cohort study representing general population (no selected subjects), and thus, it probably describes more precisely the true prevalence of adult acne in both sexes.

The current study found that male subjects with acne had more impaired glucose metabolism and insulin secretion than did controls. Moreover, they had higher BMI and waist circumference than controls, even though the difference did not reach statistical significance in these parameters. The current findings support previous studies that have found a similar association in younger males (14, 22). However, the current results indicate that this association is also seen in middle-aged males. In an Indian study performed in the dermatology clinic ($n=100$

Table III. Comparison of cardiovascular and metabolic risk factors between acne cases and control

	Men				Women			
	Acne ($n=64$)	No acne ($n=818$)	Total ($n=882$)	*p*-value	Acne ($n=86$)	No acne ($n=941$)	Total ($n=1,027$)	*p*-value
Body mass index, mean (SD)	27.5 (3.6)	27.2 (4.2)	27.2 (4.2)	0.289	26.7 (6.0)	26.6 (5.3)	26.6 (5.4)	0.931
Body mass index, *n* (%)				0.739				0.809
Underweight	18 (28.1)	253 (30.9)	271 (30.7)		42 (48.8)	431 (46.0)	473 (46.2)	
Normal	0 (0.0)	2 (0.2)	2 (0.2)		0 (0.0)	5 (0.5)	5 (0.5)	
Overweight	30 (46.9)	403 (49.3)	433 (49.1)		27 (31.4)	286 (30.5)	313 (30.6)	
Obese	16 (25.0)	160 (19.6)	176 (20.0)		17 (19.8)	215 (22.9)	232 (22.7)	
Body composition, mean (SD)								
Fat percentage	24.4 (6.7)	23.6 (7.0)	23.6 (7.0)	0.211	33.7 (8.6)	33.3 (8.4)	33.3 (8.4)	0.858
Fat mass, kg	22.0 (8.5)	21.0 (9.6)	21.1 (9.5)	0.149	25.5 (12.8)	24.9 (11.2)	24.9 (11.4)	0.916
Skeletal muscle mass, kg	37.3 (4.0)	36.9 (4.5)	37.0 (4.5)	0.278	25.6 (3.2)	25.8 (3.4)	25.8 (3.4)	0.581
Visceral fat area, cm^2	103.9 (35.1)	99.8 (38.3)	100.1 (38.1)	0.176	110.7 (44.5)	109.6 (43.4)	109.7 (43.4)	0.885
Waist circumference, cm	98.7 (11.0)	97.2 (11.4)	97.3 (11.4)	0.190	87.9 (13.6)	87.4 (13.1)	87.5 (13.1)	0.712
Hip circumference, cm	101.3 (6.3)	100.4 (7.5)	100.5 (7.4)	0.114	101.9 (12.2)	101.7 (10.8)	101.7 (10.9)	0.859
Waist : hip ratio	0.973 (0.064)	0.966 (0.061)	0.966 (0.061)	0.263	0.861 (0.062)	0.858 (0.058)	0.858 (0.058)	0.530
Insulin levels in OGTT, median (IQR)								
Fasting	8.8 (6.1, 13.4)	8.8 (5.6, 12.9)	8.8 (5.6, 12.9)	0.499	7.2 (5.3, 9.9)	6.8 (4.9, 10.5)	6.9 (4.9, 10.5)	0.815
30 min	59.8 (43.8, 116.4)	61.0 (41.9, 97.1)	60.9 (42.0, 97.2)	0.794	56.9 (44.5, 90.9)	55.3 (40.4, 85.9)	55.3 (40.6, 86.4)	0.795
60 min	101.7 (60.4, 166.6)	72.1 (47.2, 126.3)	73.5 (48.1, 127.5)	0.009	60.0 (40.8, 90.5)	56.6 (39.6, 97.6)	57.0 (39.6, 97.5)	1.000
120 min	49.2 (28.1, 117.1)	44.8 (27.1, 71.0)	44.8 (27.2, 74.9)	0.162	46.2 (28.4, 63.4)	42.8 (30.5, 65.5)	42.9 (30.3, 65.5)	0.983
OGTT AUC insulin	138.0 (94.5, 247.4)	115.6 (78.3, 174.6)	116.8 (79.0, 178.0)	0.035	99.2 (71.3, 149.1)	96.6 (71.0, 154.2)	97.1 (71.0, 153.0)	0.971
Glucose levels in OGTT, mmol/L, median (IQR)								
Fasting	5.6 (5.5, 6.0)	5.6 (5.3, 6.0)	5.6 (5.4, 6.0)	0.628	5.4 (5.1, 5.6)	5.3 (5.0, 5.6)	5.3 (5.0, 5.6)	0.465
30 min	8.7 (8.2, 9.5)	8.5 (7.5, 9.4)	8.5 (7.5, 9.4)	0.153	7.8 (6.7, 8.8)	7.6 (6.6, 8.6)	7.6 (6.6, 8.7)	0.735
60 min	8.8 (7.6, 10.7)	7.7 (6.3, 9.5)	7.9 (6.3, 9.5)	0.008	6.6 (5.4, 8.0)	6.7 (5.3, 8.2)	6.6 (5.3, 8.2)	0.726
120 min	6.0 (5.1, 7.2)	5.7 (4.9, 6.7)	5.7 (4.9, 6.8)	0.117	5.6 (5.2, 6.4)	5.7 (5.0, 6.7)	5.7 (5.0, 6.7)	0.642
OGTT AUC gluc	15.4 (13.7, 17.5)	14.2 (12.5, 16.4)	14.3 (12.6, 16.5)	0.014	12.8 (11.5, 14.4)	13.0 (11.2, 15.0)	13.0 (11.2, 14.9)	0.824
Glucose tolerance status, *n* (%)				0.870				0.541
Normal (< 6.1mmol/L)	37 (68.5%)	499 (71.3%)	536 (71.1%)		68 (89.5%)	650 (82.6%)	718 (83.2%)	
Impaired fasting glucose (6.1–6.9 mmol/L)	8 (14.8%)	83 (11.9%)	91 (12.1%)		2 (2.6%)	29 (3.7%)	31 (3.6%)	
Impaired glucose tolerance (≥ 7.0 mmol/L)	6 (11.1%)	67 (9.6%)	73 (9.7%)		3 (3.9%)	62 (7.9%)	65 (7.5%)	
Screen detected DM	1 (1.9%)	29 (4.1%)	30 (4.0%)		1 (1.3%)	28 (3.6%)	29 (3.4%)	
Previous DM	2 (3.7%)	22 (3.1%)	24 (3.2%)		2 (2.6%)	18 (2.3%)	20 (2.3%)	
Fasting indices								
HOMA2 β cell function, median (IQR)	91.4 (36.4)	80.8 (28.9)	81.5 (29.6)	0.046	85.1 (28.3)	83.4 (28.6)	83.5 (28.6)	0.484
HOMA 2 insulin resistance, median (IQR)	1.4 (1.0)	1.3 (0.9)	1.3 (0.9)	0.242	1.2 (0.9)	1.1 (0.8)	1.1 (0.8)	0.063
Fasting plasma glucose, mmol/L, mean (SD)	5.5 (0.7)	5.5 (0.6)	5.5 (0.6)	0.775	5.4 (0.6)	5.4 (0.5)	5.4 (0.5)	0.972
B-HbA1c, mmol/mol, mean (SD)	36.3 (7.4)	36.7 (6.3)	36.7 (6.4)	0.661	35.8 (6.5)	35.5 (5.0)	35.5 (5.1)	0.973
Fasting serum lipids, mmol/L (mean, SD)								
Total cholesterol	5.5 (1.0)	5.6 (1.0)	5.6 (1.0)	0.975	5.1 (0.9)	5.2 (0.8)	5.2 (0.8)	0.089
High-density lipoprotein	1.4 (0.3)	1.4 (0.3)	1.4 (0.3)	0.083	1.6 (0.4)	1.7 (0.4)	1.7 (0.4)	0.093
Low-density lipoprotein	3.8 (0.9)	3.7 (0.9)	3.7 (0.9)	0.339	3.2 (0.9)	3.3 (0.8)	3.3 (0.8)	0.636
Triglycerides	1.4 (0.6)	1.5 (1.0)	1.5 (1.0)	0.479	1.0 (0.5)	1.1 (0.6)	1.1 (0.6)	0.043
Dyslipidaemia treatment, *n* (%)				0.548				0.877
No	59 (95.2%)	738 (93.2%)	797 (93.3%)		83 (97.6%)	888 (97.4%)	971 (97.4%)	
Yes	3 (4.8%)	54 (6.8%)	57 (6.7%)		2 (2.4%)	24 (2.6%)	26 (2.6%)	
Blood pressure, mmHg, mean (SD)								
Systolic mean, min	129.8 (13.2)	130.0 (13.7)	130.0 (13.7)	0.907	119.9 (16.0)	119.9 (15.8)	119.9 (15.8)	0.954
Diastolic mean, min	87.7 (8.8)	87.0 (10.1)	87.0 (10.0)	0.559	82.2 (10.6)	82.7 (10.8)	82.7 (10.8)	0.811
High sensitivity CRP, mg/L (median, IQR)	0.727 (0.521, 1.543)	0.687 (0.383, 1.330)	0.696 (0.394, 1.363)	0.149	0.961 (0.354, 1.710)	0.774 (0.370, 1.640)	0.786 (0.369, 1.645)	0.532
High sensitivity CRP, *n* (%)				0.392				0.363
1	38 (60.3%)	526 (65.0%)	564 (64.7%)		44 (51.8%)	551 (59.5%)	595 (58.9%)	
2	21 (33.3%)	210 (26.0%)	231 (26.5%)		30 (35.3%)	266 (28.7%)	296 (29.3%)	
3	4 (6.3%)	73 (9.0%)	77 (8.8%)		11 (12.9%)	109 (11.8%)	120 (11.9%)	
Cardiovascular risk scores, median (IQR)								
Framingham Risk Score	8.7 (5.6, 11.5)	7.9 (5.9, 11.1)	8.0 (5.9, 11.1)	0.579	3.0 (2.3, 4.6)	3.1 (2.3, 4.6)	3.1 (2.3, 4.6)	0.861
FINRISK	2.5 (1.8, 3.5)	2.3 (1.8, 3.2)	2.4 (1.8, 3.3)	0.508	1.0 (0.7, 1.3)	0.9 (0.7, 1.3)	0.9 (0.7, 1.3)	0.153
CVD score	1.4 (1.0, 2.0)	1.4 (1.1, 2.0)	1.4 (1.1, 2.0)	0.871	0.2 (0.2, 0.3)	0.2 (0.2, 0.3)	0.2 (0.2, 0.3)	0.988
Fatty liver index, median (IQR)	2.2 (0.7, 6.3)	1.5 (0.5, 4.9)	1.6 (0.5, 5.0)	0.325	0.4 (0.1, 1.3)	0.3 (0.1, 1.4)	0.3 (0.1, 1.4)	0.963
Serum SHBG, nmol/L (median, IQR)	30.4 (23.5, 36.8)	30.8 (23.5, 39.9)	30.8 (23.5, 39.9)	0.546	49.3 (32.6, 71.9)	52.6 (36.9, 72.4)	52.5 (36.6, 72.4)	0.289
Serum total testosterone, nmol/L 46v, median (IQR)	16.1 (13.4, 19.6)	15.9 (12.4, 20.9)	16.0 (12.5, 20.8)	0.701	0.8 (0.6, 1.0)	0.8 (0.6, 1.0)	0.8 (0.6, 1.0)	0.760
Free testosterone concentration, nmol/L, median (IQR	2.1 (1.9, 2.4)	2.1 (1.9, 2.4)	2.1 (1.9, 2.4)	0.608	1.380 (1.040, 1.790)	1.310 (1.050, 1.650)	1.310 (1.042, 1.650)	0.289
Bioavailable testosterone, median (IQR)	8.5 (7.2, 10.3)	8.2 (6.8, 10.2)	8.2 (6.8, 10.2)	0.313	0.260 (0.190, 0.340)	0.240 (0.180, 0.320)	0.240 (0.180, 0.320)	0.189
Free androgen index, median (IQR)	52.2 (44.5, 64.4)	52.2 (43.0, 63.7)	52.2 (43.2, 63.8)	0.376	1.7 (1.2, 2.2)	1.5 (1.0, 2.1)	1.5 (1.0, 2.1)	0.138

Some data are missing because some study cases have denied the subsequent use of data.
Screen detected DM= no previous diabetes diagnoses.
FINRISK; estimates the 10-year risk of cardiovascular diseases and includes the diabetes in model (27).
OGTT; oral glucose tolerance test; IQR; interquartile range; AUC; area under curve; HOMA; Homeostasis Model Assessment; CRP; C-reactive protein; CVD score; cardiovascular disease score; SD: standard deviation.
p-values are based on the Benjamini-Hochberg corrections and that Q (20%) the false discovery rate value was used.

post-adolescent male acne patients), insulin resistance (IR) assessed by HOMA was significantly higher in acne cases than in controls (14). Similarly, the association between acne and IR was seen in a small Italian study in which young males ($n=22$, mean age 18.6 years) with acne were compared with controls (mean age 20.2 years) (10). Interestingly, the current study did not find any metabolic disturbances in the female subjects, even though some studies have reported IR to affect both sexes (7, 12), and a study ($n=219$) from Brazil reported females with acne to also have changes in their lipid profile (13). The aetiology of adult acne is multifactorial and it is speculated that, besides metabolic disturbances, different underlying factors, such as stress, hormones and diet, affect the development of the disease in females and males (2, 6, 19, 20). However, more studies are needed to explore the sex differences in the aetiology of adult acne.

Over half of the current cases had had symptoms of acne for more than 10 years. Unfortunately, due to the study design, it was not possible to separate post-adolescent acne from persistent and late-onset acne (2). Nevertheless, the majority of the current cases had a long history with acne. Chronic skin diseases, in particular acne, have a great impact on emotional state and everyday limitations (23). Of note is that adult acne, compared with adolescent acne, is known to cause even more diminished quality of life, more acne scars and more psychosocial symptoms (3) and thus, more attention should be focused on the patients with adult acne and the appropriate treatment of their disease.

Strength and limitations

The major strength of the present study is the general population of unselected subjects including both sexes. Many patients, especially males, do not easily seek medical advice for their skin diseases, and may be thus missing in hospital-based studies (5, 14). In the current study, all subjects were evaluated by experienced dermatologists instead of self-reporting or register-based data. It is not always easy to distinguish acne from other facial skin diseases, and dermatologists have the best ability to do this. Due to the unique birth cohort design, it was possible to study the metabolic and cardiovascular profile of the current subjects. The participation rate was satisfactory (>60%) and highly comparable with the participation rates in other cross-sectional European health examination surveys (15, 24). A limitation was that, since the current study population represented middle-aged Caucasian subjects, the current findings may not be generalized to other age groups or nationalities. Furthermore, since the study was not longitudinal it is not possible to exclude the possibility of a bidirectional association between acne and metabolic parameters. In addition, not all study subjects who were invited decided to participate, which may have led to bias; in the current study, participants were more often from higher social class, more often employed, and more likely to be married and with children compared with non-participants (15).

Conclusion

These findings indicate that adult acne is common in middle-aged subjects, and affects both sexes. Notably, its clinical picture differs slightly between males and females. The pathomechanism of adult acne is multifactorial, and even though it is still partly unclear, it seems that male subjects with adult acne have a higher risk of metabolic disturbances, especially in insulin secretion, than their acne-free controls. Disturbances of insulin metabolism may precede the development of prediabetes stage or type 2 diabetes (25), which highlights the need for comprehensive care for patients with adult acne, focusing not only on the skin findings.

ACKNOWLEDGEMENTS

We thank all cohort members and researchers who participated in the 46 years study. We also acknowledge the work of the NFBC project center.

Data referral: https://etsin.fairdata.fi/dataset/716939c3-7a2a-4b6a-91f3-92aca09bc52d.

NFBC data are available from the University of Oulu, Infrastructure for Population Studies. Permission to use the data for research purposes can be applied for via the electronic material request portal. In the use of data, we follow the EU General Data Protection Regulation (679/2016) and Finnish Data Protection Act. The use of personal data is based on cohort participant's written informed consent at his/her latest follow-up study, which may cause limitations to its use. Contact NFBC project center (NFBC projectcenter@oulu.fi) and visit the cohort website for more information.

The authors have no conflicts of interest to declare.

REFERENCES

1. Heng AHS, Chew FT. Systematic review of the epidemiology of acne vulgaris. Sci Rep 2020; 10: 5754.
2. Williams C, Layton AM. Persistent acne in women: implications for the patient and for therapy. Am J Clin Dermatol 2006; 7: 281–290.
3. Skroza N, Tolino E, Mambrin A, Zuber S, Balduzzi V, Marchesiello A, et al. Adult acne versus adolescent acne: a retrospective study of 1,167 patients. J Clin Aesthet Dermatol [2018; 11: 21–25.
4. Collier CN, Harper JC, Cantrell WC, Wang W, Foster KW, Elewski BE. The prevalence of acne in adults 20 years and older. J Am Acad Dermatol 2008; 58: 56–59.
5. Han XD, Oon HH, Goh CL. Epidemiology of post-adolescence acne and adolescence acne in Singapore: a 10-year retrospective and comparative study. J Eur Acad Dermatol Venereol 2016; 30: 1790–1793.
6. Albuquerque RGR, Rocha MAD, Bagatin E, Tufik S, Andersen ML. Could adult female acne be associated with modern life? Arch Dermatol Res 2014; 306: 683–688.
7. Sharma S, Goel A, Kaur J, Bassi R, Tayade A. Insulin resistance in adult Acne. IP Ind J Clin Exp Dermatol 2019; 5: 202–205.
8. Bagatin E, Freitas THP de, Rivitti Machado MC, Ribeiro BM, Nunes S, Rocha MAD da. Adult female acne: a guide to clinical practice. An Bras Dermatol 2019; 94: 62–75.

9. Poli F, Dreno B, Verschoore M. An epidemiological study of acne in female adults: results of a survey conducted in France. J Eur Acad Dermatol Venereol 2001; 15: 541–545.
10. del Prete M, Mauriello MC, Faggiano A, di Somma C, Monfrecola G, Fabbrocini G, et al. Insulin resistance and acne: a new risk factor for men? Endocrine 2012; 42: 555–560.
11. Melnik BC, John SM, Plewig G. Acne: risk indicator for increased body mass index and insulin resistance. Acta Derm Venereol 2013; 93: 644–649.
12. Chandak S, Singh A, Madke B, Jawade S, Khandelwal R. Acne vulgaris and metabolic syndrome: a possible association. Cureus 2022; 14: e24750.
13. da Cunha MG, Batista ALF, Macedo MS, Santos CD, Filho M, Fonseca FLA. Study of lipid profile in adult women with acne. Clin Cosmet Investig Dermatol 2015; 8: 449–454.
14. Nagpal M, De D, Handa S, Pal A, Sachdeva N. Insulin resistance and metabolic syndrome in young men with acne. JAMA Dermatol 2016; 152: 399–404.
15. Nordström T, Miettunen J, Auvinen J, Ala-Mursula L, Keinänen-Kiukaanniemi S, Veijola J, et al. Cohort profile: 46 years of follow-up of the Northern Finland Birth Cohort 1966 (NFBC1966). Int J Epidemiol 2021; 6: 1786–1787.
16. Sinikumpu SP, Huilaja L, Jokelainen J, Koiranen M, Auvinen J, Hägg PM, et al. High prevalence of skin diseases and need for treatment in a middle-aged population. a northern Finland birth cohort 1966 study. PLoS One 2014; 9: e99533.
17. White GM. Recent findings in the epidemiologic evidence, classification, and subtypes of acne vulgaris. J Am Acad Dermatol 1998; 39: 34.
18. Shen Y, Wang T, Zhou C, Wang X, Ding X, Tian S, et al. Prevalence of acne vulgaris in Chinese adolescents and adults: a community-based study of 17,345 subjects in six cities. Acta Derm Venereol 2012; 92: 40–44.
19. Rocha MA, Bagatin E. Adult-onset acne: prevalence, impact, and management challenges. Clin Cosmet Investig Dermatol 2018; 11: 59–69.
20. Knaggs HE, Wood EJ, Rizer RL, Mills OH. Post-adolescent acne. Int J Cosmet Sci 2004; 26: 129–138.
21. Briscoe ME. Why do people go to the doctor? Sex differences in the correlates of GP consultation. Soc Sci Med 1987; 25: 507–513.
22. Melnik BC, John SM, Plewig G. Acne: risk indicator for increased body mass index and insulin resistance. Acta Derm Venereol 2013; 93: 644–649.
23. Pärna E, Aluoja A, Kingo K. Quality of life and emotional state in chronic skin disease. Acta Derm Venereol 2015; 95: 312–316.
24. Mindell JS, Giampaoli S, Goesswald A, Kamtsiuris P, Mann C, Mannisto S, et al. Sample selection, recruitment and participation rates in health examination surveys in Europe – experience from seven national surveys. BMC Med Res Methodol 2015; 15: 74–78.
25. Hanson RL, Pratjey RE, Bogardus C, Narayan KMV, Roumain JML, Imperatore G, et al. Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. Am J Epidemiol 2000; 151: 190–198.
26. Sinikumpu S. Skin diseases and their association with systemic diseases in the Northern Finland Birth Cohort 1966. Tampere: Acta Universitatis Ouluensis, Juvenes Print; 2018.
27. Vartiainen E, Laatikainen T, Peltonen M, Puska P. Predicting coronary heart disease and stroke: The FINRISK Calculator. Glob Heart 2016; 11: 213–216.