Original article

Psychiatric disorders and compliance with prenatal care: A 10-year retrospective cohort compared to controls

Joseph Ben-Sheetrit[a,b,*,1], Liat Huller-Harari[a,1], Michal Rasner[a], Nehemia Magen[c], Nitsa Nacasch[a], Paz Toren[a,d]

[a] Tel-Aviv Brüll Community Mental Health Center, Clalit Health Services, Tel-Aviv, Israel
[b] Geha Mental Health Center, Petah Tikva, Israel
[c] Clalit Health Services, Tel-Aviv, Israel
[d] Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel

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ABSTRACT

Background: Inadequate prenatal care has been associated with adverse perinatal outcomes. We sought to compare compliance with prenatal care visits (PCV), oral glucose tolerance test (OGTT) and serum alfa-fetoprotein (aFP) in women with psychiatric disorders (PD) and healthy controls.
Methods: Subjects were 5395 women (1043 PD and 4352 controls), members of Clalit Health Services (Tel-Aviv district, Israel), who gave birth during 2004–2014. We used Generalized Estimating Equations with binary-logistic models, considering consecutive pregnancies as repeated measures with unbalanced design. The diagnostic subgroup was the main independent, assessed once with and once without age, socioeconomic status and multiple gestation variables.
Results: Risk for non-compliance with OGTT was increased in women with depression (aOR = 1.4, 95% CI = 1.1–1.7) and schizophrenia (aOR = 1.8, 95% CI = 1.1–2.9), but not anxiety. Risk for non-compliance with aFP was decreased in women with anxiety (aOR = 0.6, 95% CI = 0.5-0.8), but women with depression and schizophrenia did not differ from controls. PD were at risk for both absence of PCV (aOR = 4.6, 95% CI = 2.7–8.0) and high utilization of PCV (>20 visits, aOR = 2.8, 95% CI = 2.1–3.7). Psychopharmacological treatment during pregnancy was associated with high utilization of PCV (OR = 2.2, 95% CI = 1.7–2.9), increased compliance with aFP tests (OR = 1.4, 95% CI = 1.1–1.7) and marginally-significant increased compliance with OGTT (OR = 0.82, 95% CI = 0.67–1.01).
Conclusion: PD under-utilized tests perceived for the wellbeing of the mother (OGTT) and over-utilize tests for the wellbeing of the fetus (aFP). PD exhibited patterns of both very low and very high utilization of PCV. Psychopharmacological treatment during pregnancy may improve some measures of compliance with prenatal care.

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1. Introduction

Pregnancy is a normal physiological process, yet complications that increase morbidity and mortality for the mother and baby occur in up to 20% of pregnancies [1]. The purpose of prenatal care is to ensure a successful pregnancy outcome when possible, including the delivery of a live, healthy fetus [1]. Prenatal care includes history taking, physical examinations, laboratory tests and prenatal ultrasound tests [1]. Prenatal care is an important predictor of outcomes for both mothers and babies [2–4].

Women with psychiatric disorders are as likely as healthy mothers to become pregnant, and have an even higher rate of unplanned pregnancies [5,6]. Women with schizophrenia and affective disorders have increased risks for pregnancy complications [7]. Several studies examined utilization of prenatal care in women with psychiatric disorders. Although most of these studies have found inadequate utilization of prenatal care in women with psychiatric disorders [8,9], others have not [10]. Poor compliance with prenatal care in women with psychiatric disorders has been associated with adverse perinatal outcomes, including preterm births, low birth weight and small for gestational age babies compared to controls [9,10]. Most of the previous studies have focused on severe mental illness, specifically schizophrenia,

bipolar disorder and major depression. Although one study included a group of patients with non-psychotic mental illness [9], the group was too heterogenic (including 15 women with major depressive disorder.

5 women with anxiety disorders, 12 with emotionally unstable personality disorder, 3 with post-traumatic stress disorder, 2 with severe adjustment disorder and 1 with anorexia nervosa) to permit any clear conclusions regarding these disorders. In previous studies, prenatal care has largely been considered in terms of number of prenatal visits (NPV) and the time of initiation of prenatal care. Previous studies suggest that high NPV may be associated with increased risk for negative outcomes such as induction of labor and cesarean delivery possibly due to additional testing and unnecessary interventions [11]. However, the issue of high NPV in women with psychiatric disorders has not been previously addressed. None of the previous studies included mothers with multiple gestation pregnancies (MGP), a high-risk subgroup which deserve special monitoring and treatment as part of prenatal care [12]. Moreover, to the best of our knowledge, compliance with laboratory prenatal tests in women with psychiatric disorders has not been previously examined. As laboratory studies such as infectious and genetic screening and metabolic studies (e.g., oral glucose tolerance test) are necessary in order to achieve to primary goal of prenatal care of ensuring successful pregnancy outcomes, our lack of knowledge in this regard is of major clinical concern. Finally, it is unknown whether psychiatric treatment during pregnancy can moderate the risk for non-compliance with prenatal care. To further address these issues, we conducted a retrospective cohort analysis of utilization of prenatal care in women with psychiatric disorders and healthy controls in the Tel-Aviv district of Clalit Health Services (CHS), the largest HMO in Israel, using data from 2004 to 2014.

2. Method

2.1. Procedure

In this study we analyzed patient compliance with prenatal care using the computerized database of the CHS, the largest HMO in Israel. The Tel-Aviv district of the CHS includes about 310,000 members, which represent about 40% of the district's population. The computerized database contains demographic data, number of visits to general practitioners and specialists, medical and psychiatric diagnoses, medications, laboratory tests, and results of ultrasound and imaging studies. The CHS database has been previously used in several studies (e.g., [13–15]), and the validity of its diagnoses was found to be high [13,14]. Inclusions criteria were: (1) women, (2) at least 1 live birth from October 2004 to October 2014 (i.e., the study period). Exclusion criteria were: (1) Teenage mothers (<18 years-old), (2) women with intellectual disability, (3) women with substance use disorders.

The study was approved by the CHS Institutional Review Board (IRB). The information received by the authors did not include identifying personal information, and the IRB approved exemption from Informed Consent (retrospective data analysis).

2.2. Subjects

Included were 5395 women. The Study group consisted of 1043 women with psychiatric disorders of mean age 30.9 ± 5.2 years (range 18–41) who have had overall 1680 pregnancies (median 2.0 ± 0.9) during the study period. The Control group consisted of 4352 women without neurological or psychiatric disorders of mean age 27.8 ± 2.9 years (range 18–46), who have had overall 5765 pregnancies (median 1.0 ± 0.9) during the study period. The psychiatric diagnoses in the database were assigned by

psychiatrists, neurologists and general practitioners according to the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) based on patient examination, coded for statistical purposes according to the 9th edition of the International Classification of Diseases (ICD-9, this is common practice in Israel). Neurological disorders were assigned by neurologists and general practitioners according to ICD-9. Diagnoses are active until cancelled by a physician seeing the patient who determines that they are no longer active. Psychiatric disorders included in the study were depressive disorders (major depressive disorder, dysthymic disorder, depressive disorder NOS), anxiety disorder (generalized anxiety disorder, panic with or without agoraphobia, social phobia), bipolar disorder 1 and 2, schizophrenia, and other psychotic disorders (delusional disorder, brief psychotic disorder, psychotic disorder NOS), using the appropriate codes from ICD-9. Psychiatric disorders codes excluded were all recorded disorders encompassed by the "Mental Disorders" section in ICD-9 (codes 290–319). Neurological disorders codes excluded were all diagnoses encompassed by the "Disease of the Nervous System" (ICD-9 codes 320–359).

The distribution of diagnoses in the study group was as follows (percentages refer to the study group): Depressive disorders (without anxiety disorders, Depression-only group), N = 395 (37.9%); Anxiety disorders (without depressive disorders, Anxiety-only group), N = 241, (23.1%); Depressive and Anxiety disorders (Depression & Anxiety group), N = 225 (21.6%); Bipolar disorder, N = 19 (1.8%); Schizophrenia, N = 70 (6.7%); and Other Psychotic disorders, N = 93 (8.9%). Data of the study group were first analyzed under the broader categories of depressive and anxiety disorders vs. schizophrenia and psychotic disorders, and then as separate diagnostic subgroups. The bipolar disorder subgroup was too small to attain statistical significance and was therefore not included in the analyses. For demographic data of subjects, see Table 1.

2.3. Measures of compliance

The Israeli Ministry of Health (IMH) recommends, in addition to visits to the gynecologist (the ideal number of which is not specified in the IMH recommendations), that routine prenatal care should include the following: screening for genetic diseases (pre-conception or early during pregnancy); complete blood count, blood type, fasting glucose levels, screening for syphilis and a urine chemistry and culture (immediately after the first prenatal visit and before week 12); several ultrasound tests during pregnancy (during first weeks and at the 1st and 2nd trimester); maternal serum markers (e.g., alpha-fetoprotein, aFP); and an oral glucose tolerance test (OGTT, weeks 24–28) [16]. Utilization of prenatal care was assessed in our study with regard to the following: number of prenatal visits (NPV); OGTT and aFP. NPV is the main measure that was assessed in previous studies. Laboratory tests such as aFP and OGTT are part of prenatal care [1], but have not been previously assessed. Compliance with prenatal ultrasound and genetic tests was considered but not assessed in our study because undergoing these tests via private clinics has become very popular in Israel, so a crucial percentage of the data regarding ultrasound tests was unavailable to us. Compliance with prenatal laboratory tests (i.e. aFP, OGTT) was assessed using dichotomous variables (having done the test or not). We defined compliance with prenatal care visits as NPV within 4–10, considering 4 as the minimum adequate NPV for even extreme prematurity (22-weeks' gestation) according to the Kessner Index [17], and 10 as an adequate NPV above which negative outcomes have been described in the literature [11]. Because it is unclear what should be the minimal NPV for low risk women, we defined underutilization as absence of prenatal care visits (NPV = 0). Overutilization was examined using several criteria: (1) Exceeding 10 visits [11];

Table 1
Demographic data of the subjects in our sample[*] (N = 5395).

(a) Age distribution of the subjects in our sample							
Diagnostic group / Age (years)	Controls N (%)	Depression N (%)	Anxiety N (%)	Depression & Anxiety N (%)	Bipolar disorder N (%)	Schizophrenia N (%)	Other Psychotic disorders N (%)	Total N (% of entire sample)
18–24	199 (4.6)	42 (10.6)	32 (13.3)	26 (11.6)	2 (10.5)	16 (22.9)	16 (17.2)	333 (6.2)
25–29	3478 (79.9)	92 (23.3)	67 (27.8)	58 (25.8)	5 (26.3)	15 (21.4)	29 (31.2)	3744 (63.4)
30–34	499 (11.5)	136 (34.4)	81 (33.6)	92 (40.9)	8 (42.1)	15 (21.4)	33 (35.5)	864 (16.0)
≥ 35	176 (4.0)	125 (31.6)	61 (25.3)	49 (21.8)	4 (21.1)	24 (34.3)	15 (16.1)	454 (8.4)
Total	4352 (100)	395 (100)	241 (100)	225 (100)	19 (100)	70 (100)	93 (100)	5395 (100)
Mean age ± SD	27.8 ± 2.9	30.7 ± 5.1	29.8 ± 5.3	30.2 ± 4.9	30.5 ± 4.0	29.8 ± 5.9	28.7 ± 4.9	28.3 ± 3.7

(b) Socioeconomic status (SES) distribution of the subjects in our sample							
Diagnostic group / SES group	Controls N (%)	Depression N (%)	Anxiety N (%)	Depression & Anxiety N (%)	Bipolar disorder N (%)	Schizophrenia N (%)	Other Psychotic disorders N (%)	Total N (% of entire sample)
Low	66 (1.5)	48 (12.2)	16 (6.6)	22 (9.8)	5 (26.3)	43 (61.4)	11 (11.8)	211 (3.9)
Middle	1200 (27.6)	255 (64.6)	163 (67.6)	157 (69.8)	11 (64.7)	24 (33.3)	65 (69.9)	1875 (34.8)
High	3086 (70.9)	92 (23.3)	62 (25.7)	46 (20.4)	3 (17.6)	3 (4.2)	17 (18.3)	3309 (61.3)
Total	4352 (100)	395 (100)	241 (100)	225 (100)	19 (100)	70 (100)	93 (100)	5395 (100)

[*]Data refers to the first pregnancy of subjects in the database.

(2) Exceeding the standard 14-visit schedule [18]; and (3) Exceeding 20 visits (more than once every two weeks considering a 40-week gestation).

2.4. Age-group variable

The difference in mean age between the study and control groups was statistically significant (30.9 ± 5.2 vs. 27.8 ± 2.9, respectively, t = − 26.4, p < 0.001). Subjects' age was not normally distributed (Shapiro-Wilk tests' p < 0.001 for the study and control groups). Therefore, and based on the previous literature [19], we defined the age variable as categorical, assigning each subject to one the following groups: 18–24 years-old, 25–29 years-old, 30–34 years-old, and ≥35 years-old (see Table 1a), and considered 25–29 years-old mothers as the reference group. The categorical age-group variable was included in all further analyses in order to assure significance of findings beyond age differences.

2.5. Socioeconomic status (SES)-group variable

We defined a 3-level SES variable based on exemption from Social Security Tax (SST) and billing approval by the CHS. Exemption from payment of the SST in Israel is usually based on having a low income or documented disability, or otherwise belonging to specific populations of lower SES (e.g. new immigrants), and is considered a strong indication of a low SES. Additionally, the CHS allows some of its members to pay for healthcare services by means of direct billing of their bank account, which is usually an indication of higher SES. Based on these data, each patient was assigned to one of the following groups (Table 1b): High (no SST exemption, direct billing approved), Middle (no SST exemption, direct billing not approved) or Low SES (exemption of SST payment, regardless of billing approval). The modal category was middle SES (68.9%) for the study group and high SES for controls (71.3%), a statistically significant difference ($\chi^2_{(2)}$ = 1617.6, p < 0.001). The SES-group variable was included in all further analyses in order to assure significance of findings beyond SES differences.

2.6. Statistical analysis

SPSS ver. 22 (IBM Inc., Chicago, IL) was used for statistical analysis. Demographic data are presented as mean or median ± standard deviation as appropriate. Considering the nature of the data as repeated measures (pregnancies) with unbalanced design (the total number of pregnancies and the time intervals between them varies per subject), we conducted Generalized Estimating Equation (GEE) analyses of prenatal care utilization as criterion-derived dichotomous dependent variables (defined above). The diagnostic subgroup was the main independent, assessed once with and once without the effects of age, SES, and MGP, yielding crude and adjusted odds ratios compared to controls (cOR and aOR, respectively). The effects of diagnostically relevant psychopharmacological treatment (e.g. antipsychotics for schizophrenia) during pregnancy were analyzed separately. The models were conducted once with a broad 3-level diagnostic group variable (depressive and anxiety disorders, schizophrenia and psychotic disorders, and controls) and subsequently for specific diagnostic subgroups as appropriate.

3. Results

3.1. Oral glucose tolerance test (OGTT) (Table 2)

Women with depression and anxiety were more likely than controls to not comply with OGTT (cOR = 1.6, p < 0.0005, 95% CI = 1.4–1.8, aOR = 1.4, p < 0.0005, 95% CI = 1.1–1.6). The risk was higher for the depression-only group vs. controls (cOR = 1.6, p < 0.0005, 95% CI = 1.3–1.9, aOR = 1.4, p = 0.002, 95% CI = 1.1–1.7) than for the anxiety-only group vs. controls (cOR = 1.2, p=0.03, 95% CI = 1.0–1.6, aOR non-significant, p = 0.42). The depression & anxiety group had a nearly 2-fold increase in risk for non-compliance (cOR = 1.9, p=0.002, 95% CI = 1.3–3.2, aOR = 1.7, p < 0.0005, 95% CI = 1.3–2.1), similarly to women with schizophrenia (cOR = 2.0, p < 0.002, 95% CI = 1.3–3.2, aOR = 1.8, p=0.01, 95% CI = 1.1–2.9).

Age had no effect on the risk for non-compliance, except for a decreased risk in 30–34 years-old compared to 25–29 years-old (OR = 0.7, p=0.001, 95% CI = 0.5–0.8). Compared to women of high SES, women of middle SES were twice as likely to not comply with OGTT (aOR = 2.1, p < 0.0005, 95% CI = 1.9–2.4), with marginally-significant results for the low- vs. high-SES group (aOR = 1.3, p = 0.069, 95% CI = 1.0–1.8). The risk for non-compliance decreased in the second and third pregnancies of the subjects compared to their first (aOR = 0.3, p < 0.0005 for both). Women with MGP were 1.4 times more likely to not comply with OGTT (p < 0.0005, 95% CI = 1.2–1.6). Women who received psychopharmacological treatment during pregnancy were marginally less likely not to comply

Table 2
Compliance with Oral Glucose Tolerance Test (OGTT) in our sample (N = 5395).

(a) Compliance rates with Oral Glucose Tolerance Test (OGTT) in specific psychiatric subgroups*							
Diagnostic group / Compliance*	Controls (Pregnancies, N (%)	Depression (Pregnancies, N (%)	Anxiety (Pregnancies, N (%)	Depression & Anxiety (Pregnancies, N (%)	Bipolar disorder (Pregnancies, N (%)	Schizophrenia (Pregnancies, N (%)	Other Psychotic disorders (Pregnancies, N (%)	Total Pregnancies, N (% of entire sample)
No	1395 (33.6)	261 (41.8)	144 (36.4)	174 (45.4)	8 (28.6)	48 (49.5)	66 (43.7)	2636 (35.4)
Yes	3830 (66.4)	364 (58.2)	252 (63.6)	209 (54.6)	20 (71.4)	49 (50.5)	85 (56.3)	4809 (64.6)
Total	5765 (100)	625 (100)	396 (100)	383 (100)	28 (100)	97 (100)	139 (100)	7445 (100)

(b) Group comparison of compliance with Oral Glucose Tolerance Test (OGTT)								
Diagnostic group / Compliance	Controls (Pregnancies N (%)	Dep. & Anx. (Pregnancies N (%)	Scz. & Psy. (Pregnancies N (%)	Three-Group $\chi^2_{(2)}$	GEE Crude OR [95% CI]		GEE Adjusted* OR [95% CI]	
					Dep & Anx. vs. Controls	Scz & Psy. vs. Controls	Dep & Anx. vs. Controls	Scz & Psy. vs. Controls
No	2400 (45.1)	513 (40.0)	93 (41.7)	11.2 p = 0.004	0.8 [0.7–0.9] p = 0.003	0.8 [0.7–1.1] p = 0.32	0.8 [0.7–0.9] p = 0.002	0.9 [0.6–1.2] p = 0.31

GEE – Generalized Estimating Equation; OR – Odds Ratio; Dep. – Depression; Anx – Anxiety. Scz – Schizophrenia; Psy – Psychotic disorders.
*See text for specific subgroup comparisons.

with OGTT compared to women who did not receive treatment (GEE OR = 0.82, p = 0.068, 95% CI = 0.67–1.01).

3.2. Serum alpha feto-protein test (aFP) (Table 3)

Women with depressive and anxiety disorders had lower risk for non-compliance with serum aFP than controls (cOR = 0.8, p = 0.003, 95% CI = 0.7–0.9, aOR = 0.7, p = 0.001, 95% CI = 0.6–0.9). Women of the depression-only group did not differ from controls, whereas patients of the anxiety-only group had significantly lower risk for non-compliance compared to controls (aOR = 0.6, p = 0.001, 95% CI = 0.5–0.8). The lower risk compared to controls was attenuated in the depression & anxiety group (aOR = 0.7, p = 0.044, 95% CI = 0.6–1.0). Women with schizophrenia and psychotic disorders did not differ from controls. The risk for non-compliance was the same for the second and third pregnancies of the subjects compared to their first, but was significantly higher for the fourth (aOR = 3.1, p < 0.0005, 95% CI = 1.8–5.2) and fifth pregnancy (aOR = 4.8, p = 0.015, 95% CI = 1.4–17.2). Age, SES and MGP had no significant effect. Women who received psychopharmacological treatment during pregnancy were more

likely to comply with aFP compared to women who did not receive treatment (GEE OR = 1.4, p = 0.002, 95% CI = 1.1–1.7).

3.3. Number of prenatal visits (NPV) (Table 4)

Women with psychiatric disorders were more likely than controls to exhibit both under- and overutilization of prenatal care visits (Table 3). The risk for underutilization compared to controls was higher in the depression-only group (aOR = 4.8, p < 0.0005, 95% CI = 2.5–9.5) than in the anxiety-only group (aOR = 3.7, p < 0.0005, 95% CI = 1.9–7.4). The highest risk was found in the depression & anxiety group compared to controls (aOR = 6.5, p < 0.0005, 95% CI = 3.2–13.0), which was higher than that of women with other psychotic disorders compared to controls (aOR = 3.7, p < 0.0005, 95% CI = 1.9–7.4). The risk for underutilization in the schizophrenia group was marginally significant (cOR = 3.2, p=0.052, 95% CI = 1.0–10.3, aOR = 3.4, p = 0.07, 95% CI = 0.9-12.8). There was no statistically significant difference in the risk for underutilization in women who received psychopharmacological treatment during pregnancy (GEE OR p > 0.05).

The risk for over-utilization (NPV > 20) was higher in the anxiety-only group vs. controls (aOR = 3.2, p < 0.0005, 95% CI = 2.1–

Table 3
Compliance with alpha-fetoprotein (aFP) in our sample* (N = 4823).

(a) Compliance rates with alpha-fetoprotein (aFP) in specific psychiatric subgroups*							
Diagnostic subgroup / Compliance*	Controls (Pregnancies, N (%)	Depression (Pregnancies, N (%)	Anxiety (Pregnancies, N (%)	Depression & Anxiety (Pregnancies, N (%)	Bipolar disorder (Pregnancies, N (%)	Schizophrenia (Pregnancies, N (%)	Other Psychotic disorders (Pregnancies, N (%)	Total Pregnancies, N (% of entire sample)
No	2400 (45.1)	244 (42.4)	129 (36.0)	140 (40.2)	10 (38.5)	32 (38.1)	61 (43.9)	3016 (44.0)
Yes	2921 (54.9)	331 (57.6)	229 (64.0)	208 (59.8)	16 (61.5)	52 (61.9)	78 (56.1)	3835 (56.0)
Total	5321 (100)	575 (100)	358 (100)	348 (100)	26 (100)	84 (100)	139 (100)	6851 (100)

(b) Group comparison of compliance with alpha-fetoprotein (aFP)								
Diagnostic group / Compliance	Controls (Pregnancies N (%)	Dep. & Anx. (Pregnancies N (%)	Scz. & Psy. (Pregnancies N (%)	Three-Group $\chi^2_{(2)}$	GEE Crude OR [95% CI]		GEE Adjusted* OR [95% CI]	
					Dep & Anx. vs. Controls	Scz & Psy. vs. Controls	Dep & Anx. vs. Controls	Scz & Psy. vs. Controls
No	1395 (33.6)	579 (41.2)	114 (85.0)	41.5 p < 0.0005	1.6 [1.4–1.8] p < 0.0005	1.7 [1.3–2.2] p < 0.0005	1.4 [1.1–1.6] p < 0.0005	1.7 [1.3–2.2] p < 0.0005

GEE – Generalized Estimating Equation; OR – Odds Ratio; Dep. – Depression; Anx – Anxiety.Scz – Schizophrenia; Psy – Psychotic disorders.
*See text for specific subgroup comparisons.

Table 4
Utilization of Prenatal Visits in Our Sample.

Compliance Criterion (NPV) / Diagnostic Group	Controls (Pregnancies N (%))	Dep. & Anx. (Pregnancies N (%))	Scz. & Psy. (Pregnancies N (%))	Three-Group $\chi^2_{(2)}$	GEE Crude OR [95% CI] Dep & Anx. vs. Controls	Scz & Psy. vs. Controls	GEE Adjusted* OR [95% CI] Dep & Anx. vs. Controls	Scz & Psy. vs. Controls
Underutilization								
No visits during entire pregnancy (0)	58 (1.0)	78 (5.6)	9 (3.6)	125.7 p < 0.0005	5.8 [3.9-8.5] p < 0.0005	3.7 [1.7-8.0] p = 0.001	4.9 [2.8-8.5] p < 0.0005	3.5 [1.4-8.7] p = 0.006
Adequate Utilization†								
4 to10 visits during pregnancy (4–10)	2216 (43.6)	431 (30.7)	76 (30.6)	89.2 p < 0.0005	0.5 [0.5-0.6] p < 0.0005	0.6 [0.4-0.7] p < 0.0005	0.5 [0.4-0.6] p < 0.0005	0.5 [0.4-0.6] p < 0.0005
Over-utilization								
More than 10 visits during pregnancy (>10)	2375 (47.4)	835 (59.5)	152 (61.3)	78 p < 0.0005	1.6 [1.4-1.9] p < 0.0005	1.8 [1.3-2.5] p < 0.0005	2.0 [1.7-2.3] p < 0.0005	2.1 [1.5-2.8] p < 0.0005
Exceeding standard AACOG schedule (>14)	1160 (20.1)	461 (32.8)	87 (35.1)	123.5 p < 0.0005	1.9 [1.7-2.2] p < 0.0005	2.1 [1.6-3.0] p < 0.0005	2.3 [1.9-2.7] p < 0.0005	2.4 [1.7-3.3] p < 0.0005
Exceeding once every two weeks** (>20)	285 (5.0)	182 (13.0)	30 (12.1)	127.5 p < 0.0005	3.1 [2.5-3.9] p < 0.0005	2.8 [1.8-4.4] p < 0.0005	2.9 [2.1-3.9] p < 0.0005	2.4 [1.5-4.0] p < 0.0005

NPV – Number of prenatal visits; GEE – Generalized Estimating Equation; Dep. – Depression; Anx – Anxiety; Scz – Schizophrenia. Psy – Psychotic disorders.; AACOG – American Academy of Obstetrics and Gynecology (2002) [14]; * Adjusted for: Age, socioeconomic status. singleton/multiple gestation pregnancy; ** Considering a 40-week gestation length; † – See text for details.

4.8) than in the depression-only group (aOR = 2.4, p < 0.0005, 95% CI = 1.7–3.5). The highest risk compared to controls was in the depression & anxiety group (aOR = 3.5, p < 0.0005, 95% CI = 2.4–5.3), which was higher than the risk in patients with schizophrenia (aOR = 3.3, p = 0.002, 95% CI = 1.6–7.0) and other psychotic disorders (aOR = 1.9, p = 0.04, 95% CI = 1.0–3.5) compared to controls. The risk was higher in women who received psychopharmacological treatment during pregnancy (GEE OR = 2.2, p < 0.0005, 95% CI = 1.7–2.9).

In the analysis for adequate utilization, 18–24 year-old mothers were more likely than 25–29 years-old to adequately utilize prenatal care (aOR = 1.3, p = 0.017, 95% CI = 1.0–1.6). Regarding parity, the likelihood for adequate utilization increased with each consecutive pregnancy, rising from aOR = 1.6 in the second (p < 0.0005, 95% CI = 1.4–1.8) to aOR = 1.8 in the third (p < 0.0005, 95% CI = 1.5–2.3) and aOR = 3.1 (p < 0.0005, 95% CI = 1.9–5.0) in the fourth pregnancy. SES and MGP had no significant effect on NPV.

4. Discussion

4.1. Laboratory prenatal tests

In this study, we examined compliance with prenatal care in women with and without psychiatric disorders. After adjusting for age, socioeconomic status, parity and multiple gestations, we found that women with psychiatric disorders had an increased risk for non-compliance with OGTT compared to controls. The risk for non-compliance was slightly increased in the anxiety-only group, higher in the depression-only group, and reached a two-fold increase in the schizophrenia and the depression & anxiety groups. The increased risk for non-compliance with OGTT is consistent with previous studies showing inadequate utilization of prenatal care in women with schizophrenia [8,9] and poor compliance with medical care in general in depressed patients [20]. This may be due to higher prevalence of psychosocial risk factors such as lack of social support, unintended pregnancies, attitudes toward health professionals and financial difficulties [8]. In the current study we found that women of high SES were more likely to comply with OGTT than women of middle SES, with marginally significant results for low SES, but psychiatric disorders and SES contributed independently to the risk for non-compliance. In addition to psychosocial factors, psychiatric disorders may directly affect motivation for care [2], which may lead to inadequate utilization of prenatal care [21]. Anhedonia, a symptom of both depression and schizophrenia [22], seems particularly relevant in this regard. In a postpartum study of low-income women in New-York, the most common reasons given for inadequate utilization of prenatal care were: "feeling depressed and not up to going for care", and "needing time and energy to deal with other problems" [21].

Interestingly, in contrast to their lower compliance with OGTT, we found that women with schizophrenia and depression did not differ from controls in compliance with aFP. It may be that the difference in compliance between these tests lies in the mother's perception of their objective. Whereas oral glucose tolerance test may be perceived by mothers as merely concerning their own health (risk for diabetes), the term alpha-*fetoprotein* may alert mothers that the test is for the baby. The similar risk for non-compliance with aFP in women with schizophrenia and depression compared to controls may in fact represent an abnormally normal finding, stemming from increased anxiety for the fetus in women with psychiatric disorders. The fact that anxiety disorders were associated with greater compliance with aFP compared to controls further supports this hypothesis. In contrast, anxiety disorders contributed positively to the risk for non-compliance with OGTT. As discussed above, this may be understood in terms different behavioral responses of mothers to anxiety about their own health

and the health of the fetus. The existing literature suggests that both healthcare avoidance and over-seeking of healthcare can result from health-related anxiety [23], depending in part on the degree to which one is preoccupied with worries about the potential consequences of not seeking medical care [24]. If one manages to suppress such thoughts, one avoids; if one ruminates over catastrophic consequences, one over-seeks [24]. It is arguably easier to dismiss concerns about one's own health than to disregard such concerns about the wellbeing of one's future baby. Indeed, the "fear of having a physically or mentally handicapped child" was found to be a major factor of anxiety in pregnancy [25]. This may explain why anxiety may lead to a pattern of low utilization of OGTT but high utilization of aFP.

4.2. Prenatal visits

After adjusting for possible confounders, we found that women with psychiatric disorders were more likely to exhibit both absence and very high utilization of prenatal care visits. These patterns may stem from similar factors of motivational deficits and health anxiety discussed above. Although the complete absence of prenatal care visits during pregnancy is arguably abnormal for any pregnant woman, we acknowledge that over-utilization may in some cases be due to objective demands of high-risk pregnancies. For instance, depression and anxiety have been associated with fetal growth retardation [26] and preeclampsia [27], and schizophrenia has been associated with placental abnormalities, antepartum hemorrhages and fetal distress [7] –complications that may necessitate more frequent prenatal visits. High utilization is therefore best seen in terms of a combination of the overall morbidity of the individual and over-utilization of prenatal care visits.

4.3. Parity and multiple gestational pregnancies

Our study is the first to show that parity decreases the risk for non-compliance with OGTT. Further, our study is the first to show a significant increase in the likelihood for adequate utilization of prenatal care visits with each consecutive pregnancy of the mother. The fact that parity had no effect of aFP beyond the effects of age may be due to the greater emphasis that is put on the importance of aFP with increasing age. Regarding multiple gestation pregnancies, although we found an increased risk for non-compliance with regards to OGTT, but not to aFP and NPV. Further studies are needed in order to replicate and elucidate the effects of multiple gestation pregnancies on utilization of prenatal care.

4.4. Age and SES group differences

In our study, women with psychiatric disorders were on average 3.1 years older than controls, and were more likely to be assigned to middle or low SES categories. It should be noted that women with schizophrenia had also the highest rate of younger (18–24 years-old) mothers, which may point to unplanned pregnancies [5,6]. Age and SES variables were included in all analyses, and findings regarding compliance with prenatal care were significant beyond differences in these variables.

4.5. The effects of psychopharmacological treatment

Women who received psychopharmacological treatment were more likely to comply with aFP, and were marginally more compliant with OGTT. However, they were at risk for high utilization of prenatal visits. A possible explanation for these findings is that psychopharmacological treatment increases patient compliance, but also increases the likelihood that more rigorous prenatal visits will be requested either by the doctor or by the patient (or both) due to possible teratogenic risk that many psychiatric medications carry. Overall, it seems that psychiatric treatment during pregnancy increases patient compliance with prenatal care in women with psychiatric disorders, although more studies are clearly needed.

4.6. Strengths, limitations and conclusion

Our study adds to the existing literature in several ways. It is the first study to directly compare compliance with prenatal care in women suffering from several distinct groups of psychiatric disorders and controls in the same study, and the first to examine the effects of psychopharmacological treatment during pregnancy on compliance with prenatal care. Moreover, it is the first analysis of compliance with laboratory prenatal tests (i.e., OGTT and aFP) in women with psychiatric disorders. Unlike previous studies that either randomly selected one of the pregnancies or simply analyzed the first pregnancy, we employed GEE analysis with consecutive pregnancies as repeated measures. Unlike previous studies, multiple gestation pregnancies were taken into account in our analysis. Moreover, our study is the first to address the issue of both absent and very high utilization of prenatal care visits.

The current study has several limitations. First, the retrospective nature of our analysis precludes any definite conclusions regarding causality. Second, although some possible confounders and mediators were taken into account, such as age, socioeconomic status, multiple gestation pregnancies and previous pregnancies, data regarding other factors were not available to us and were thus not taken into account. These include partner support, maternal medical comorbidities obstetric and neonatal outcomes of previous pregnancies. These factors may limit the generalizability of our findings, and other studies are needed in order to confirm them. Moreover, our data sample did not include maternal and neonatal outcomes that would allow to directly correlate inadequate compliance and obstetric complications; however, this has been previously established in the previous literature. Finally, as in previous studies, the severity of psychiatric disorders and the differential impact of disorder onset (e.g. chronic prenatal morbidity versus perinatal exacerbation) were not available to us due to the retrospective nature of the data.

In conclusion, our finding suggest that women with psychiatric disorders exhibit low utilization of tests perceived for the wellbeing of the mother (i.e., OGTT) but high utilization of tests for the wellbeing of the fetus (i.e., aFP), and exhibit patterns of both absence and very high utilization of prenatal care visits. There is an increased risk for non-compliance with OGTT in women with depression and schizophrenia, but not anxiety. Women with anxiety are more compliant with aFP than controls, whereas women with depression and schizophrenia do not differ from controls in compliance with aFP. Women who receive psychopharmacological treatment during pregnancy are more likely to comply with aFP and may be more compliant with OGTT, and exhibit high utilization of prenatal visits. Healthcare professionals should be aware of the risks of both unusually-low and unusually-high utilization of prenatal care in women with psychiatric disorders and strive to improve compliance with psychiatric treatment in order to improve prenatal care utilization. Further studies are indicated.

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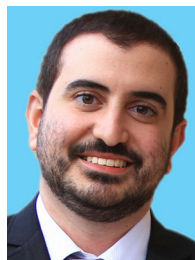
Dr. Joseph Ben-Sheetrit obtained his MD degree from the Sackler Faculty of Medicine at the Tel-Aviv University in Israel. He is a psychiatry resident at Clalit Health Services, Israel. He is a member of the Israel Society of Biological Psychiatry. He has focused so far on ADHD and psychopharmacology and has published studies about ADHD-related impairment and persistent side effects of Selective Serotonin Reuptake Inhibitors (SSRIs).

Dr. Liat Huller-Harari is a psychiatrist and psychotherapist specializing in perinatal and women's psychiatry. She is a team director at the Tel-Aviv Brüll Community Mental Health Center in Tel-Aviv, Israel, where she founded the Women's Mental Health Clinic. She has graduated lactation consulting and Gender studies, and encompasses those themes in her work with women with perinatal psychiatric disorders. Dr. Huller-Harari has published several studies about post-traumatic stress disorder (PTSD) following childbirth and other topics of perinatal psychiatry.

Dr. Michal Rasner has obtained her MD degree at the Semmelweis University of Budapest, Hungary. She is a psychiatry resident at the Brüll Tel-Aviv Community Mental Health Center, Tel-Aviv, Israel. She focuses on gender psychiatry.

Mr. Nehemia Magen obtained his MBA degree from the Open University in Tel-Aviv, Israel. He specializes in data mining and analysis. He works at the Tel-Aviv district of Clalit Health Services in Israel.

Dr. Nitsa Nacasch is a psychiatrist and psychotherapist specializing in post-traumatic stress disorder (PTSD) and obsessive-compulsive disorder (OCD). She is the director of the Adult Outpatient Clinic at the Brüll Tel-Aviv Community Mental Health Center and the Cognitive-Behavioral Therapy (CBT) program of the School of Continuing Medical Education at the Sackler Faculty of Medicine, in Tel-Aviv, Israel. She is a certified trainer of Prolonged Exposure (PE) therapy and has conducted many PE workshops for mental health professionals in Israel and abroad. Dr. Nacasch has published several studies on PTSD and OCD and has co-authored several books on PTSD.

Prof. Paz Toren, MD, MHA, is an Associate Professor of Psychiatry at the Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel. She is the director of the Tel-Aviv Brüll Community Mental Health Center and its Child and Adolescent Outpatient Clinic in Tel-Aviv, Israel. Prof. Toren is the chairman of postgraduate studies in child and adolescent psychiatry at the Sackler Faculty of Medicine, Tel-Aviv University, Israel. Her research interests include psychopharmacology, child psychiatry and psychopathology.