

Research Aricle Open Access

Prodromal Symptoms and Signs of First Episode Schizophrenia in Iraq

Al-Abbudi SJR*

FIBMS, Consultant Psychiatrist, Section of Psychiatry, Department of Medicine, Al-Imamein Al-Kadhimein Medical City, Baghdad, Iraq

*Corresponding author: Al-Abbudi SJR, FIBMS, Consultant Psychiatrist, Section of Psychiatry, Department of Medicine, Al-Imamein Al-Kadhimein Medical City, Baghdad, Iraq, 70131, Tel: +9647810705221, E-mail: shalanjoodah@yahoo.com

Citation: Al-Abbudi SJR (2018) Prodromal Symptoms and Signs of First Episode Schizophrenia in Iraq. J Psychiatry Ment Illn 1(1): 102

Received Date: February 17, 2018 Accepted Date: April 19, 2018 Published Date: April 23, 2018

Abstract

Background: Onset of schizophrenia is often preceded by other symptoms and types of behaviour, usually referred to as prodromal symptoms.

Objectives: Identify the main prodromal symptoms and signs preceding the full blown picture of first episode schizophrenia.

Methods: This is a cross-section study. 328 Iraqi first episode schizophrenic inpatients admitted to Ibn-Rushed psychiatric mental hospital were examined during the period June, 1st, 2009 to June, 1st, 2011. Diagnosis confirmed through a Structured Clinical Interview for DSM-IV-TR. List of sociodemographic and clinical data was used. Detailed psychiatric history taking and mental state examination were applied. Supplemental information was obtained from patients and family members.

Results: The main frequent prodromal signs and symptoms preceding the development of a full blown picture of first episode schizophrenia were; lack of sleep, aggression, restlessness, disorganized speech, anxiety, suspiciousness, social withdrawal, odd behavior, somatic complaints.

Conclusion: The study explores the symptoms preceding the full blown picture of first episodes schizophrenia. Psycho-educational approach to patients and families may be mandatory to increase the awareness about schizophrenic prodromal symptoms to reduce the duration of untreated psychosis.

Keywords: Schizophrenia; Prodromal; First Episode; Symptom; Iraq

List of Abbreviations: DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, fourth edition, American Psychiatric Association

Introduction

Schizophrenia is a severe mental disorder that has significant, long-lasting negative effects on the patients as well as the entire society [1]. Schizophrenia is a debilitating mental illness that affects 1% of the population in all cultures. It affects equal numbers of men and women, but the onset is often later in women than in men [2]. The term schizophrenia was introduced by Bleuler over a hundred year ago to describe the breaking up or splitting of psychic functioning he observed in these patients and the diagnosis of this disorder is still based exclusively on clinical symptoms [1]. Schizophrenia is the most common functional psychotic disorder, and individuals with the disorder can present with a variety of manifestations [3]. Patients with schizophrenia present clinically with psychotic, negative and cognitive symptoms, which can become evident late in adolescence or in early adulthood [4]. No single sign or symptom is pathognomonic of schizophrenia [5]. We can describe at least three stages in the development of a schizophrenic illness: the prodrome, the first episode and chronic phase [6]. It is generally believed that the onset and recurrence of psychotic symptoms in schizophrenia are often preceded by other symptoms and types of behaviour, usually referred to as prodromal symptoms [7]. Most individuals with schizophrenia retrospectively report a prodromal period characterized by increasing problems in thinking, feeling, and behaving [8]. It is now recognized that in the majority (68%) of cases, the index psychotic episode is preceded by a prodromal stage [9]. In recent years there has been more research designed to identify any such prodromal symptoms and assess their relationship to the psychotic process in schizophrenia [7]. It is not always possible to differentiate between a prodromal symptom and the true onset of psychosis [10]. During these prodromal or residual periods, the signs of disturbance may manifest through only negative symptoms, or by two or more symptoms listed in DSM-IV Criterion A which are present in an attenuated form, e.g. odd beliefs and unusual perceptual experiences [11].

The prodrome indicates a period before the full manifestation of a psychotic illness, during which patients first experience changes in their emotions, cognition or behaviour which may indicate a deviation from the normal level of functioning [4]. The onset of psychotic symptoms observed in schizophrenia is frequently preceded by nonspecific changes in behavior, emotional state, and/ or cognitive state, with common signs and symptoms of the prepsychotic stage of schizophrenia including sleep disturbance, anxiety, anger/irritability, depressed mood, deterioration in functioning, social withdrawal, poor concentration, suspiciousness, loss of motivation, and low energy [12,13]. The psychotic prodrome is potentially important for early diagnosis and management of psychotic disorders, early detection of relapse, prospective studies of high-risk individuals, and prognosis [14]. There has been increasing interest in the potential for early detection and intervention during the prodromal phase of a psychotic disorder, i.e., the period of functional decline before full-blown psychotic symptoms first appear [15].

Patients and Methods

Design and setting

A cross-sectional study was conducted in Ibn-Rushed psychiatric mental hospital, Baghdad, Iraq. The data collection was done during the period June, 1st, 2008 to June, 1st, 2010.

Study Population and Sampling

First episode schizophrenic inpatients diagnosed by a senior psychiatrist, of any age, sex, residence and educational level were assessed.

Inclusion criteria

All patients included in the study were; Iraqi, first episode schizophrenic inpatients, fulfilling the DSM-IV diagnostic criteria of schizophrenia, agreed to participate, and free of any neuroleptic medications during the prodromal phase.

Exclusion criteria

Patients with a history of organic brain disease, head injury, seizure disorder, pregnant, and drug or alcohol dependence were excluded.

Data collection Tools

The subjects had all been diagnosed as first episode schizophrenic, confirmed through a Structured Clinical Interview for DSM-IV-TR. List of sociodemographic and clinical data was used. Detailed psychiatric history taking and mental state examination were applied. Supplemental information was obtained from patients and family members. Patients and their family members were asked when the patient (or the family member) first experienced (or noticed) behavioral changes which, in retrospect, appear to have been related to the patient's becoming ill. These sign and symptoms of behavioral changes were reported in the special list prepared for this study. Definitions: prodrome is the period between the most valid estimates of the onset of a change in the person and the onset of psychosis. The onset of the prodromal phase was defined by the appearance of the first noticeable symptom or symptoms considered to indicate the appearance of the disease. The onset of the psychotic phase was defined as the appearance of active phase symptoms (American Psychiatric Association 1994) [16].

Definition of variables

The independent variables evaluated to explain prodromal symptoms were socio-demographics (age, gender, marital status, occupation, education level, economic status, and living circumstances), and patient characteristics (religion, the source of referral, the reaction of the family, and family history).

Statistical Analysis

Statistical package of social sciences (SPSS) version 19 for windows was used for data entry and analysis

Ethical Issues

Informed consent was obtained from the patients' families after clarifying the objectives of the study. Names were kept anonymous and all paper files and electronic records were kept in full privacy.

Results

A total of 345 patients were approached; 328 completed the interviews, with age range (17-60) years, mean age (33.25±10.02) years. Male 57.3%, about 80% of sample age below 40 years, more than half were singles, two third not working, two third of low education, half satisfied their economic status, more than 90% lives within their families, 94% Muslims, 70% family referral, 72%

of the family accepted the illness, and half of positive family history of mental illness (Table 1).

		No.	%
	16 - 25 Years	89	27.1%
	26 - 35 Years	123	37.5%
AGE GROUP	36 - 45 Years	66	20.1%
	46 - 55 Years	38	11.6%
	56 Years +	12	3.7%
	Male	188	57.3%
SEX	Female	140	42.7%
	Single	189	57.6%
	Married	68	20.8%
MARITAL STATUS	Separated	34	10.3%
	Divorced	30	9.2%
	Widowed	7	2.1%
	Student	23	7.0%
	Employed	46	14.0%
O COMPATION.	Housewife	77	23.5%
OCCUPATION	Free work	61	18.6%
	Retired	6	1.8%
	Unemployed	115	35.1%
	Illiterate	20	6.1%
	Primary	99	30.2%
EDUCATION LEVEL	Intermediate	94	28.7%
	Secondary	46	14%
	University	69	21%
	Poor	115	35.1%
ECONOMIC STATUS	Satisfied	186	56.7%
	Rich	27	8.2%
	With Family	299	91.1%
LIVING CIRCUMSTANCES	With relatives	11	3.4%
	Alone	18	5.5%
	Muslim	311	94.8%
RELIGION	Christian	14	4.3%
	Other	3	0.9%
	Family	231	70.4%
	Relative	49	14.9%
SOURCE OF REFERRAL	Physician	27	8.2%
	Faith healar	15	4.57%
	Court	6	1.8%
	Accepted	239	72.9%
REACTION OF FAMILY	Denil	22	6.7%
	Rejected	67	20.4%
F. 1 M. 1	Negative	177	54.0%
FAMILY HISTORY	Positive	151	46.0%
Table 1. Distribution of the study of	roup by sociadomographic	1 1: 1	1

 Table 1: Distribution of the study group by sociodemographic and clinical characteristics

The main frequent prodromal signs and symptoms preceding the development of full blown picture of first episode schizophrenia were; lack of sleep 57%, aggression 48.1%, restlessness 36.8%, disorganized speech 30.4%, anxiety 20.7%, suspiciousness 19.5%, social withdrawal 16.7%, odd behavior 16.1% somatic complaints 15.5%, (Table 2).

Statistical significance was assessed for each of the prodromal signs and symptoms with sociodemographic and clinical variables (Table 3).

PRODROMAL SYMPTOMS	No.(328)	%
Sleep	188	57.3%
Aggression	158	48.1%
Restless	121	36.8%
Speech	100	30.4%
Anxiety	68	20.7%
Suspiciousness	64	19.5%
Social Withdrawal	55	16.7%
Odd Behavior	53	16.1%
Somatic Complaints	51	15.5%

Table 2: Prodromal symptoms and signs in first-episode schizo-phrenia in descending order of frequency and percentages

		SLEEP		SLEEP AGGRES SION		RESTLESS		SPEECH		SUSPI- CIOUS- NESS		SOCIAL WITH- DRAWAL		SOMATIC COM- PLAINTS		ANXIETY		ODD BE- HAVIOR	
		No.	P	No.	P	No.	P	No.	P	No.	P	No.	P	No.	P	No.	P	No.	P
	16 – 25 Years	55	0.0	51		35		26		23	0.0	12	0.0	7		21		14	
AGE GROUP	26 - 35 Years	69		58		50	0.0	41		19		30		22	0.0	21	0.2	6	0.0
	36 - 45 Years	31		23	0.0 52	4.5		16	0.7	22		6		19		16		16	
GROUP	46 - 55 Years	29	10	18	32			13		0		3		3		10		9	
·	56 Years +	4		8			4		0		4		0		0		8		
CEW	Male	98	0.0	103	0.0	49	0.0	59	06	43	0.0	34	0.4	34	0.1	33	0.1	32	0.6
SEX	Female	90	32	55	05	72 00	00	41	83	21	75	21	59	17	42	35	00	21	23
	Single	99		90		76		52		48		34		32		43		30	
MARI-	Married	38		32		14 9 0.0 00	25		7		12		16		11		17		
TAL	Separated	28	0.0	9	0.0			9	0.3	6	0.0	9	0.0	3	0.0	10	0.2	0	0.0
STATUS	Divorced	23	- 00	20	01			10	11	3		0		0		4		6	
	Widowed	0		7		7		4		0		0		0		0		0	
	Student	13		16		4 17 41 0.0 15 0 44		3		7		0		3		3		14	0.0
OCCU- PATION	Employed	27	0.0	17				7		19		9		9	0.0	11		9	
	Housewife	50		24	0.0		0.0	22	0.0	11	0.0	12	0.2	14		21	0.1	7	
	Free work	27		36	00		27	03	6	00	12	20	16	26	7	50	7	00	
	Retired	6		6			0		0		0		0		0				
	Unemployed	65		59			41		21		22		9		26		13		
	Illiterate	10		7			0.1	11		3	0.0	3	0.0	4	0.1	6	0.0	4	0.0
EDUCA-	Primary School	53	0.0	57	0.0			37	00	13		18		17		15		9	
TION LEVEL	Intermediate	53	0.0	43	19			19	06	16		25		9		9		24	
EEVEE	Secondary	20		14		20		10		19		3		12		20		10	
	University	52		37		17		23		13		6		9		18		6	
ECO-	Poor	68		62		38		44		25		18	22	22		19		16	0.6
NOMIC	Satisfied	107	0.5 81	79	0.0	69	0.1 89	46	0.0	36	0.4	34	0.5 99	29	0.0 47	35	0.0	33	
STATUS	Rich	13	01	17		14		10	33	3		3		0 47	1,	14		4	
LIVING	Live with Family	172		149		105		87	0.1 58	57		55		47		60		47	
CIRCUM- STANCES	Live with Relatives	7	0.7 49	0	0.0 05	7 78		4		4	0.3 46	0	0.0 41	4	0.0 31	8	.0 00	0	0.0 48
	Alone	9		9		9		9		3		0		0		0		6	
	Muslim	181		151		118		94		61		51	0.3	48		65		49	
RELI- GION	Christian	4	0.0 29	4	0.0 67	3	3 01 88	3	0.0 25	3	0.6	4		3	0.6 30	3	0.6 72	4	0.3
GIOIT	Other	3		3		0		3		0		0		0		0		0	

		SLEEP		AGGRES- SION		RESTLESS		SPEECH		SUSPI- CIOUS- NESS		SOCIAL WITH- DRAWAL		SOMATIC COM- PLAINTS		ANXIETY		ODE HAV	BE- IOR
		No.	P	No.	P	No.	P	No.	P	No.	P	No.	P	No.	P	No.	P	No.	P
SOURCE OF RE- FERRAL	Family Referral	149		127		95	0.0	77		35	0.0	28	0.0	28	0.0	41		34	
	Relative	13		7		9		7		17		15		20		17		13	
	Physician	11	0.0	18	0.0	17 0.0 00			0.0 29	3		6		3		10	0.0	0	0.0
	Faith healar	12		3			6	6		6	01	0		0		3			
	Court Refer- ral	3		3		0	0	0		3		0		0		0		3	
REAC-	Accepted	134		118		83	77		47	0.2	37		35		60		30	0.0	
TION OF	Denil	3	0.0	16	0.0	9	0.4	6 0.5	7		6	0.3 52	6	0.2	0	0.0	10		
FAMILY	Rejected	51		24	00	29		17		10		12		10		8	03	13	
FAMILY HISTORY	Negative	93	0.0	84	0.7	67	06	43	0.0	35	0.8	31	0.6	31	0.2	47	0.0	32	0.3
	Positive	95	58	74	80	54	54 96	57	08	29	97	24	95	20	88	21	05	21	06

Table 3: The correlation between the prodromal symptoms and signs and the sociodemographic and clinical variables of the study group

Discussion

One of the methodologies employed in the past to investigate the prodromal phase of schizophrenia is the detailed, retrospective reconstruction from patient and information interviews and other information sources of changes from the patient's previous personality, through the first prodromal symptoms to frank psychosis. This method was used by Bleuler (1950) [17], Kraepelin (1921) [18], Conrad (1958) [19], Meares (1959) [20], Bowers and Freedman (1966) [21], Bowers (1968) [22], Stein (1967) [23], Fish (1976) [24], Docherty Pocherty *et al.* (1978) [25], Huber *et al.* (1980) [26], and more recently Harness groups (Hafner *et al.* 1992a, 1992b, 1993, 1994; Hambrecht *et al.* 1994) [27-31], and Beiser *et al.* (1993) [32]. The main prodromal signs and symptoms founded by this study that preceding the development of a full blown picture of the first episode schizophrenia were; lack of sleep, aggression, restlessness, disorganized speech, anxiety, suspiciousness, social withdrawal, odd behavior, and somatic complaints.

Lack of sleep (57.3%)

Significantly correlated with; age, gender, marital status, education level, religion, the source of referral, and the reaction of the family. Sleep disturbance was described by; Cameron (1938) [33], Bowers and Freedman (1966) [21], Bowers (1968) [22], Donlon and Blacker (1973) [34], Huber *et al.* (1980) [26], Heinrichs and Carpenter (1985) [35], Birchwood *et al.* (1989) [36], Hafner *et al.* (1992a) [27], Hambrecht *et al.* (1994) [31], Yung and McGorry (1996) [37], Ferrarelli (2015) [1].

Aggression (48.1%)

Significantly correlated with gender, marital status, occupation, education level, economic status, living circumstances, the source of referral, and the reaction of the family. Aggressive, disruptive behavior was described by; Cameron (1938) [33], Meares (1959) [20], Varsamis and Adamson (1971) [38], Heinrichs and Carpenter (1985) [35], Subotnik and Nuechterlein (1988) [39], Birchwood *et al.* (1989) [36], Hafner *et al.* (1992a) [27], Hambrecht *et al.* (1994) [31], Yung and McGorry (1996) [37], Gourzis *et al* (2002) [10], Pompili and Fiorillo (2015) [40].

Restlessness (36.8%)

Significantly correlated with gender, marital status, occupation, living circumstances, and source of referral. Restlessness was described by; Chapman (1966) [41], Fish (1976) [24], Birchwood *et al.* (1989) [36], Hafner *et al.* (1992a) [27], Hambrecht *et al.* (1994) [31], Yung and McGorry (1996) [37].

Disorganised speech (30.4%)

Significantly correlated with the occupation, education level, economic status, religion, the source of referral, and family history of mental illness. Speech abnormalities was described by; Chapman (1966) [41], Cutting (1985) [42], Hafner *et al.* (1992a) [27], Hambrecht *et al.* (1994) [31] Yung and McGorry (1996) [37], Gourzis *et al.* (2002) [10].

Anxiety (20.7%)

Significantly correlated with education level, economic status, living circumstances, the source of referral, the reaction of the family, and family history of mental illness. Anxiety was described by; Cameron (1938) [33], Meares (1959) [20], Bowers and Freedman (1966) [21], Chapman (1966) [41], Varsamis and Adamson (1971) [38], Donlon and Blacker (1973) [34], Fish (1976) [24], Docherty *et al.* (1978) [25], Herz and Melville (1980) [43], Huber *et al.* (1980) [26], Heinrichs and Carpenter (1985) [35],

Subotnik and Nuechteriein (1988) [39], Birchwood et al. (1989) [36], Hafner et al. (1992a) [27], Hambrecht et al. (1994) [31], Yung and McGorry (1996) [37], Gourzis et al. (2002) [10].

Suspiciousness (19.5%)

Significantly correlated with age, marital status, occupation, education level, and source of referral. Suspiciousness was described by; Conrad (1958) [19], Stein (1967) [23], Varsamis and Adamson (1971) [38], Heinrichs and Carpenter (1985) [35], Subotnik and Nuechterlein (1988) [39], Birchwood *et al.* (1989) [36], Hafner *et al.* (1992a) [27], Hambrecht *et al.* (1994) [31], Yung and McGorry (1996) [37], Gourzis *et al.* (2002) [10].

Social withdrawal (16.7%)

Significantly correlated with age, marital status, education level, living circumstances, and source of referral. Social withdrawal was described by Cameron (1938) [33], Meares (1959) [20], Chapman (1966) [41], Donlon and Blacker (1973) [34], Docherty *et al.* (1978) [25], Birchwood *et al.* (1989) [36], Hafner *et al.* (1992a) [27], Hambrecht *et al.* (1994) [31] Yung and McGorry (1996) [37], Gourzis *et al.* (2002) [10].

Odd behavior (16.1%)

Significantly correlated with age, marital status, occupation, education level, living circumstances, the source of referral, and the reaction of the family. Odd behavior was described by; Conrad (1958) [19], Meares (1959) [20], Birchwood *et al.* (1989) [36], Yung and McGorry (1996) [37], Gourzis *et al.* (2002) [10].

Somatic complaints (15.5%)

Significantly correlated with age, marital status, occupation, economic status, living circumstances, and source of referral. Physical symptoms and somatic complaints was described by; Bleuler (1950) [17], Cameron (1938) [33], Meares (1959) [20], Offenkrantz (1962) [44], Chapman (1966) [41], Varsamis and Adamson (1971) [38], Donlon and Blacker (1973) [34], Fish (1976) [24], Herz and Melville (1980) [43], Huber *et al.* (1980) [26], Heinrichs and Carpenter (1985) [35], Subotnik and Nuechterlein (1988) [39], Hafner *et al.* (1992a) [27], Hambrecht *et al.* (1994) [31], Yung and McGorry (1996) [37], Gourzis *et al.* (2002) [10].

This study explores the importance of the prodromal signs and symptoms preceding the development of full blown first schizophrenic episode. It is important for developing country like ours to educate the patients' families about prodromal symptoms of schizophrenia since most patients live within their families, hope this study take part in raising the awareness of these symptoms. Psycho-educational approach to the patient and family throughout available media may be mandatory to increase the awareness about schizophrenic prodromal symptoms to reduce the duration of untreated psychosis and allow therapeutic intervention to prevent the development of a full blown picture of a schizophrenic episode. Further studies on the mode of onset, presentation, the early course of schizophrenia were recommended.

Limitations

Selection bias cannot be excluded as the study was conducted in a specialized center.

Acknowledgements

Thanks and appreciation to Professor Dr. Mohammed Al-Samarrai (God rest his soul) to support the idea of this research

Reference

 $2. Al-Abbudi\ Sh\ J.\ Causal\ Beliefs\ of\ Schizophrenia\ among\ a\ sample\ of\ Iraqi\ Schizophrenic\ Inpatients'\ Families\ in\ Iraq.\ Iraqi\ JMS\ 2016;\ Vol.\ 14(3)\ 237-242$

3.Patel K R, Cherian J, Gohil K, Atkinson D. Schizophrenia: Overview and Treatment Options, P& T. 2014 Sep; 39(9): 638-645. PMCID: PMC4159061

4.Khamker N. First episode schizophrenia, South African Family Practice 2015; 57(5):29-33. http://hdl.handle.net/10520/EJC179965

5.Schultz S H, North S W, Shields C G. Schizophrenia: A Review. American Family Physician: 2007 Vol. 76 No. 12. PMID: 17619525

6.Wójciak P, Molenda A R, Rybakowski J, Stages of the clinical course of schizophrenia – staging concept. Psychiatr. Pol. 2016; 50(4): 717–730 DOI: http://dx.doi.org/10.12740/PP/58723

7.Malla A K, Norman R M G. Prodromal Symptoms in Schizophrenia, British Journal of Psychiatry Apr 1994, 164 (4) 487-493; DOI: 10.1192/bjp.164.4.487 8.Addington J, Heinssen R. Prediction and Prevention of Psychosis in Youth at Clinical High Risk, Annu. Rev. Clin. Psychol. 2012.8:269-289. doi: 10.1146/annurev-clinpsys.032511.143146

9.Hafner H, Maurer K. Early detection of schizophrenia: current evidence and future perspectives. World Psychiatry 2006;5(3):130-8. PMCID: PMC1636122 10.Gourzis P, Katrivanou A, Beratis S. Symptomatology of the initial prodromal phase in schizophrenia. Schizophr Bull 2002; 28: 415-29. DOI: https://doi.org/10.1093/oxfordjournals.schbul.a006950

11. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th edition) (DSM-V) Arlington: American Psychiatric Association, 2013.

12.Yung AR, Phillips LJ, Yuen HP, McGorry PD. Risk factors for psychosis in an ultra high-risk group: psychopathology and clinical features. Schizophr Res 2004; 67: 131-42. DOI: 10.1016/S0920-9964(03)00192-0

13. Choi J S, Chon M W, Kang D H, Jung M H, Kwon J S. Gender Difference in the Prodromal Symptoms of First-episode Schizophrenia, J Korean Med Sci 2009; 24: 1083-8. DOI: 10.3346/jkms.2009.24.6.1083

14.Alison R. Yung A R, McGorry P D. The Prodromal Phase of First-Episode Psychosis: Past and Current Conceptualizations, Schizophr Bull 1996;22, NO.2:353-370. DOI: https://doi.org/10.1093/schbul/22.2.353

15.Addington J et al. North American Prodrome Longitudinal Study: A Collaborative Multisite Approach to Prodromal Schizophrenia Research, Schizophr Bull (2007) 33 (3): 665-672. DOI: https://doi.org/10.1093/schbul/sbl075

16. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. Washington, DC: American Psychiatric Association; 1994.

17.Bleuler, E. Dementia Praecox or the Group of Schizophrenias. [1911] Translated by J. Zinkin. New York, NY: International Universities Press, 1950.

18.Kraepelin, E. Manic Depressive Insanity and Paranoia. [1919] Translated by R.M. Barclay. Edinburgh, Scotland: E. and S. Livingstone, 1921.

19. Conrad, K., ed. Die beginnende Schizophrenic. Stuttgart, Germany: Georg Thieme Verlag, 1958.

20. Meares, A. The diagnosis of prepsychotic schizophrenia. Lancet, (1959)1:55-59,.

21. Bowers, M.B., and Freedman, D.X. "Psychedelic" experiences in acute psychoses. Archives of General Psychiatry, (1966) 15:240-248,.

22.Bowers, M.B. Pathogenesis of acute schizophrenic psychosis. Archives of General Psychiatry, (1968)19:348 355.

23. Stein, W.J. The sense of becoming psychotic. Psychiatry, (1967)30:262-275.

24. Fish, F.J. Fish's Schizophrenia. Bristol, England: Wright and Sons, 1976.

25.Docherty, J.P.; van Kammen, D.P.; Siris, S.G.; and Marder, S.R. Stages of onset of schizophrenic psychosis. American Journal of Psychiatry, (1978)135:420-426. DOI: 10.1176/ajp.135.4.420

26. Huber, G.; Gross, G.; Schiittler, R; and Linz, M. Longitudinal studies of schizophrenic patients. Schizophrenia Bulletin, (1980)6(4)592-605.

27.Hafner, H.; Riecher-Rossler, A.; Hambrecht, M.; Maurer, K.; Meissner, S.; Schmidtke, A.; Fatkenheuer, B.; Loffler, W.; and van der Heiden, W. IRAOS: An instrument for the assessment of onset and early course of schizophrenia. Schizophrenia Research, 1992a 6:209-223.

28. Hafner, H.; Riecher-Rossler, A.; Maurer, K.; Fatkenheuer, B.; and Loffler, W. First onset and early symptomatology of schizophrenia: A chapter of epidemiological and neurobiological research into age and sex differences. European Archives of Psychiatry and Clinical Neurosciences, 1992b, 242:109-118.

29.Hafner, H.; Maurer, K.; Loffler, W.; and Riecher-Rossler, A. The influence of age and sex on the onset and early course of schizophrenia. British Journal of Psychiatry, (1993)162:80-86.

30.Hafner, H.; Maurer, K.; Loffler, W.; Fatkenheuer, B.; van der Heiden, W.; Riecher-Rossler, A.; Behrens, S.; and Gattaz, W.F. The epidemiology of early schizophrenia: Influence of age and gender on onset and early course. British Journal of Psychiatry, (1994)164(Suppl. 23):29-38,.

31.Hambrecht, M.; Hafner, H.; and Loffler, W. Beginning schizophrenia observed by significant others. Social Psychiatry and Psychiatric Epidemiology, (1994)29:53-60.

32.Beiser, M.; Erickson, D.; Fleming, J.A.E.; and Iacono, W.G. Establishing the onset of psychotic illness. American journal of Psychiatry, (1993)150:1349-1354.

33. Cameron, D.E. Early schizophrenia. American Journal of Psychiatry, (1938) 95:567-578.

34.Donlon, P.T.; and Blacker, K.H. Stages of schizophrenic decompensation and reintegration. Journal of Nervous and Mental Disease, (1973)157:200-209.

35.Heirtrichs, D.W., and Carpenter, W.T., Jr. Prospective study of prodromal symptoms in schizophrenic relapse. American Journal of Psychiatry, (1985) 142:371^373.

36.Birchwood, M.; Smith, J.; MacMillan, J.F.; Hogg, B.; Prasad, R.; Harvey, C; and Bering, S. Predicting relapse in schizophrenia: The development and implementation of an early signs monitoring system using patients and families as observers: A preliminary investigation. Psychological Medicine, (1989) 19:649-656.

37.Yung, A.R.; McGorry, P.D.; McFarlane, C.A.; and Patton, G. The PACE Clinic: Development of a clinical service for young people at high risk of psychosis. Australasian Psychiatry, (1995) 3:345-349.

38. Varsamis, J., and Adamson, J.D. Early schizophrenia. Canadian Psychiatric Association Journal (1971)16:487-497.

39. Subotnik, K.L., and Nuechterlein, K.H. Prodromal signs and symptoms of schizophrenic relapse. Journal of Abnormal Psychology, (1988) 97:405-412.

 $40. PompiliM, Fiorillo\ A, Aggression\ and\ Impulsivity\ in\ Schizophrenia.\ Psychiatric\ Times\ 2015: 1-4\ (http://www.psychiatrictimes.com)$

41. Chapman, J.P. The early symptoms of schizophrenia. British Journal of Psychiatry, (1966) 112:225-251.

 $42. Cutting, J.\ The\ Psychology\ of\ Schizophrenia.\ London,\ England:\ Churchill\ Livingstone,\ 1985.$

 $43. Herz, M.I., and Melville, C. Relapse in schizophrenia. American Journal of Psychiatry, (1980) \\ 137:801-805, DOI: \\ 10.1176/ajp.137.7.801$

44.Offenkrantz, W. Multiple somatic complaints as a precursor of schizophrenia. American Journal of Psychiatry, (1962) 119:258-259,.

Submit your next manuscript to Annex Publishers and benefit from:

- **Easy online submission process**
- > Rapid peer review process
- > Online article availability soon after acceptance for Publication
- ➤ Open access: articles available free online
- ➤ More accessibility of the articles to the readers/researchers within the field
- > Better discount on subsequent article submission

Submit your manuscript at http://www.annexpublishers.com/paper-submission.php