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ACUTE PORPHYRIA AMONGST PSYCHIATRIC PATIENTS

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SUMMARY

A total of 519 consecutive patients, admitted to psychiatric wards of two different hospitals, were screened for evidence of increased excretion of porphobilinogen in the urine by original Watson Schwartz test and modified Watson Schwartz test supported with quantitative estimation of porphobilinogen by Remington's method in search of cases of acute porphyria amongst psychiatric patients. An additional 273 normal healthy volunteers were also screened as controls. Two cases (0.38%) were found which could be unequivocally diagnosed to be suffering from acute intermittent porphyria amongst psychiatric patients. These cases belonged to the category of missed diagnosis being labelled as hysterical. Seven more cases were positive by modified Watson Schwartz test but the test was only transiently positive and the Ehrlichaldehyde reactor substance was unstable. In the absence of detailed enzymatic and family studies, these cases have been kept under the categery of suspected prophyria. A significant number of psychiatric patients (12.9%) gave positive original Watson-Schwartz test but were negative for modified test. Similar reaction was seen in 2.6% of healthy controls. The significance of this finding needs to be evaluated.

Psychiatric symptoms constitute an important manifestation of acute porphyria (Cashman, 1961; Holmberg, 1961; Myres 1961; Pryce, 1961; Ruth, 1968; Gibsey, Jones & Merk, 1972; Carney, 1972). These symptoms are reported to be present in 55-80% of patients diagnosed to be suffering with acute porphyria (Markovitz, 1954; Waldenstrom, 1957; Goldberg, 1959; Eales, 1962; Jeffery *et al.*, 1970). At times, the psychiatric symptoms may be the sole presentation of the disease, and at others, the abdominal and neurological symptoms may be erroneously considered to be functional (Macalpine and Hunter, 1966; Scully *et al.*, 1975; Chatterjee & Baghiana, 1975). It is said that Waldenstorm, the pioneer investigator in the field of porphyria, found most of the subjects for his studies by survey of patients from Swedish mental hospitals (Kark, 1955). However, systematic studies to find out the prevalence of this disorder amongst psychiatric patients have been few (Kallbling *et al.*, 1961; McEwin *et al.*, 1972). Our earlier observations have indicated that the occurrence of acute porphyria is not uncommon in the psychiatric units in India (Golecha, 1979). Therefore, a systematic study on the prevalence of porphyria amongst psychiatric patients was carried out and the results are reported in this paper. In addition, the results of urinary prophobilinogen (PBG) detection with and without butanol extraction and quantitative determination of urinary PBG by Remington's method are also compared.

MATERIAL AND METHODS

A total of 519 patients, admitted to the psychiatric wards of G.M. & Associated Hospitals, Lucknow and Command Hospital, Lucknow, were studied. The command hospital sample included out-patients as well as those who could not be submitted to the hospital due to administrative reasons. These subjects were included irrespective of age-sex and diagnostic category. Only two subjects could not be studied because they

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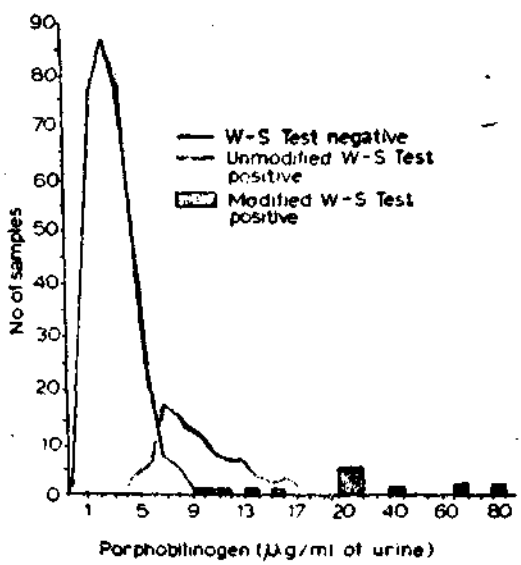
supplied tap water repeatedly, instead of urine. Clinical evaluation was done independently of the biochemical findings in the urine. The psychiatric diagnosis was based on the guidelines of ICD-9.

In addition, a control sample of 273 normal healthy volunteers from the two institutions was also screened.

The male female ratio in the test sample was 2.8 : 1 and in controls 2.98 : 1. The age range of psychiatric patients was 5—65 years with mean age of 29.0 ±8.6 years in males and 25.8±9.4 years in females. Corresponding ages amongst controls were 23±9.2 yrs in males and 24.0±9.4 yrs in females. Majority of the individuals, both amongst the test group (59.3%) & controls (64.1%), belonged to the state of Uttar Pradesh.

The urine sample was collected on the first day of admission in all the individuals, except in 33 cases who were very violent or uncooperative on admission. In the later group, the sample was collected at the earliest possible opportunity. History of drug intake during previous 7 days was carefully recorded in all cases. A fresh, random urine sample was collected and tested within 1 hour of collection.



The qualitative test for urinary porphobilinogen was carried out as described by Watson *et al.* (1961) with the modification that chloroform extraction was repeated till no more colour was extracted. The volumes recommended were strictly adhered. The quantitative estimation was carried out according to the method described by Remington (1971).

RESULTS

The results of the unmodified & modified Watson-Schwartz (W-S) test for qualitative detection of urinary porphobilinogen in psychiatric patients and control subjects are summarised in Table No. 1. Unmodified W-S test, as originally

TABLE No. 1—*Results of Quantitative detection Urinary porphobilinogen.*

	Watson-Schwartz test			
	Unmodified		Modified	
	No. positive	% positive	No. positive	% positive
I *Psychiatric* patients*				
Male (383) ..	62	..	6	..
Female (136)..	14	..	3	..
Total (519) ..	96	..	9	1.7
II *Normal healthy control*				
Male (206) ..	4	..	..	..
Female (67) ..	3	..	..	..
Total (273) ..	7	2.6	..	..

*2 Samples gave a false positive reaction where the acid control itself produced a purple colour.

described by Watson & Schwartz (1941), was found to be positive in 14.6% of the psychiatric patients compared to 2.6% in healthy controls. On the other hand modified W-S test, which includes butanol-extraction, was positive in only 1.7% of the psychiatric patients and in none of the controls. The psychiatric diagnosis of the patients and the results of Watson-Schwartz test are given in Table No. 2.

TABLE No. 2—*Psychiatric diagnosis in Watson-Schwartz test positive cases.*

ICD-9 category	Diagnosis	Watson Unmodified	Schwartz test modified (including butanol extraction)
290.4	Arteriosclerotic dementia (n=1) ..	1	..
293	Transient organic psychotic condition (n=6) ..	2	..
294	Other organic psychotic condition (n=7)	2	..
295	Schizophrenic psychosis (n=214) ..	33	1
296.0	Mania & Hypomania (n=41) ..	9	4
296.1	Psychotic depression (n=26) ..	9	..
300.0	Anxiety state (n=1) ..	4	..
300.1	Hysteria (n=68) ..	10	4
300.4	Neutotic depression (n=43) ..	6	3

Only those cases which were positive with modified W-S test are taken to be suffering with porphyria. Out of 9 such patients; 4 had a diagonosis of hysteria, 3 of neurotic depression and 1 each of organic psychosis (epileptic) and schizophrenia respectively. Even amongst this group, there were two categories. In two patients the test was persistently positive, even during remission, while in other seven the test was only transiently positive, and the chromogen was partially extractable in butanol. The aldehyde reactor in the urine, in later cases, was often unstable. Both the cases with persistent porphobilinoginuria were initially admitted as cases of acute abdomen. When the clinical examination and investigations failed to establish a diagnosis, the associated abnormal behaviour and preoccupation with their suffering prompted the treating surgeons to take psychiatric opinion and the patients were transferred to psychiatric service. As the present study was in progress, both the patients were promptly diagnosed to be suffering from prophyria. Out of 519 patients, 345 (66.5%) have recieved some drug in 7 days prior to collection of urine sample for the test. The drugs included; phenothiazines, benzodiapenes, tricyclic antidepressants, lithium carbonate, vitamins, phenobarb & antibiotics. There was no relationship between the history of drug intake & the result of W-S test.

Since in the present study a large number of urine samples were found to have Ehrlich aldehyde reacting chromogens, which extracted with butanol, a semi-quantitative assay of urinary porphobilinogen by Remington's method was also carried out. The results are given in figure. This shows that in all the urine samples, which were classified as W-S test negative, the PBG was less than 9 μg/ml. Average excretion of PBG in these samples was 3.3 ± 1.58 μg/ml (N=353). In urine samples which were positive by unmodified W-S test but were negative for modified W-S test (N=92), the urinary PBG varied between 4-17 μg/ml (9.4 ± 2.8 μg/ml). On the other hand, in urine samples classified as positive with modified W-S test (N=15), the urinary PBG was always above 9 & ranged even upto 80 μg/ml (37.6 μg/ml ± 27.2 μg/ml).

DISCUSSION

In the present study, out of 519 patients with psychiatric disorders, 2 patients were unequivocally found to be suffering with acute intermittent porphyria. This gives an overall prevalence of 0.38% which is comparable with the finding of 0.45% prevalence by Mc Ewin *et al.* (1972) from Australia. An additional 7 patients (1.36%) could be suffering with acute porphyria of variegate or coproporphyria type since the modified Watson-Schwartz test was only transiently positive such patients need to be investigated further.

The original W-S test only, without butanol extraction, was positive in 12.6% of psychiatric patients compared to 2.56% of normal healthy controls. This supports the use of butanol extraction as recommended by Watson *et al.* (1961), to exclude non-PBG Ehrlich aldehyde reactors. It is interesting to note that such chromogens were seen in a higher percentage of psychiatric patients compared to controls. The biological significance of non-PBG chromogens in psychiatric patients remains to be evaluated (Watson, *et al.*, 1964).

In the present study two patients were found to give a false positive reaction. In these cases, acid control gave a colour similar to that obtained with Ehrlich reagent. This reinforces the need for using a control in screening programmes (McEwenk Patterson, 1972).

The semiquantitative estimate of PBG by Remington's method could provide an useful ancillary evidence. The average excretion of PBG in W-S negative samples was 3.3±1.58 ug/ml. The upper limit of normal excretion has been reported to be 2.5 μg/ml (Waldenstrom, 1963) and the range of daily excretion as 100-1700 μg/24 hrs (Doss, 1979). In two cases,which were unequivocally suffering with acute intermittent porphyria, the urinary PBG by Rimington's method was consistently above 25 μg/ml. However, there was significant overlap between W-S negative, W-S positive & modified W-S test positive cases with respect to urinary PBG values measured by this method. Hence, this test can not be recommended to be a satisfactory screening procedure.

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