

## DISCUSSION

Having a chronic disease during childhood confers a large risk of developing a psychiatric disorder, and chronic renal disease is not an exception, it is a significant stressor with a psychological and social impact on children and their family.<sup>(1)</sup> In the last decades there was a striking improvement in survival of children with chronic kidney disease. As life expectancy has increased in children with CRF, concern has risen about its physical, psychological consequences.<sup>(83)</sup>

In the current study, self assessment reports were used for depression (Children's Depression Inventory, CDI) and anxiety symptoms (Children's Manifest Anxiety Scale, CMAS) to describe the psychological problems in children with CRF on regular HD. The study also investigated some of the risk factors for depression and anxiety in children with CRF.

To our knowledge this is the first study addressing psychiatric disorders in pediatric patients having CRF at Alexandria University Children's Hospital, aiming to discover the magnitude of this problem among those patients and paving the way to provide them with mental and psychological welfare.

Anxiety disorders are one of the most common emotional disorders in the general population especially in children having CRF.<sup>(84)</sup> Regarding the estimation of the prevalence of anxiety among CRF patients undergoing (HD) in our study: all studied patients who had CRF have been diagnosed as having anxiety on CMAS: 20% of cases had score of mild anxiety on CMAS, 40% had moderate anxiety, and 40% had significantly severe anxiety on CMAS.

Consistent with these results, another cross sectional study included 20 children with CRF selected from HD unit and psychiatric department of AL-zahraa hospital, Al-Azher University, (Cairo). Anxiety scores were assessed for all the participated groups using CMAS. Anxiety score showed that 100% of patients with CRF had anxiety disorder.<sup>(13)</sup> Similarly, study done by Abdel Salam et al<sup>(85)</sup> from el Zagazig University, Egypt revealing that the prevalence of mild to severe anxiety in children on HD was 100% also. Squalli et al<sup>(86, 87)</sup> reported that the level of anxiety in maintenance HD patients has been observed to be as high as 69.3%. Fukunishi et al<sup>(11)</sup> noted separation anxiety to be as much as 65% of patients treated for continuous ambulatory peritoneal dialysis (CAPD) and HD. Also in another study, 22 cases of children with CRF on HD, 20 cases on peritoneal dialysis and 95 cases on conservative treatment were enrolled in study using State-Trait Anxiety Inventory (STAI). There was a significantly higher level of anxiety-state among HD children (8-12 years) and adolescents group (13-18 years) compared with other groups of participants of the same age.<sup>(88)</sup>

The presence of high prevalence of anxiety in the studied sample can be explained by negative body image in CRF patients due to growth retardation and bone deformity, stigmata of HD therapy which is particularly devastating (multiple scars, needle puncture marks, and disfiguring fistula or arteriovenous shunts). These problems are often exacerbated by the delay in the emergence of secondary sex characteristics especially in adolescents that often accompanies uremia. These negative changes in body image exacerbate the child feelings of being different

and result in alienation of the peer group.<sup>(89-91)</sup> The associated psychological and sociological factors add to the stress in addition to the underlying chronic disease.

A number of psychosocial problems like loss of freedom due to dependency on machine.<sup>(92)</sup> Social adjustment problems, deterioration in psychomotor performances, mental functions and perceptual performances lead to an anxiety state.<sup>(93-96, 63)</sup> Anxiety influences the quality of the patient's life<sup>(19, 63, 64)</sup>, and may negatively affect the course of the disease.<sup>(64)</sup>

According to the studies by Feroze et al,<sup>(19)</sup> anxiety among hemodialyzed patients was triggered when patients arrived for HD treatment, when they heard alarm and machine sound or when new staff connected the patient to dialysis machine. On the other hand, the lower percentage of psychiatric disorders in the predialysis group could be explained by the extensive use of the denial, which acts as a protective psychological mechanism against overwhelming anxiety.<sup>(97)</sup>

In contrast to the current study, psychiatric assessment was done in study done by Bakr et al<sup>(20,9)</sup> according to the DSM-IV TR criteria in 19 children in the predialysis period and 19 children with CRF on regular HD. The prevalence rate of psychiatric disorders in all the studied patients was 52.6%. Anxiety was reported in 5.1 %. The variation between the prevalence of anxiety of the current study and the study carried by Bakr et al could be due to small size of the sample studied by Bakr et al also the heterogeneity of the patients in their study.

As regard the prevalence of depression among CRF children in this study, there were 40 patients 72.7 % of the 55 children with CRF had depression on CDI scale, 15 patients 27.3% had no depression. This observation may be explained by the fact that children on dialysis experience more distressing physical symptoms, more medications and investigations and more dependence on machines that could possibly malfunction at any time. Also, they receive more attention from their physicians and parents, meaning more dependency, which decreases the functionality of these children. Accordingly, they realize that their physical health and life are in danger, augmenting their psychological resources to cope with these stresses. Denial of the illness or its dreadful complications is one of the coping mechanisms of patients with a chronic illness. It serves to reject feelings associated with severe events or thoughts, thus protecting patients against severe anxiety and depression.<sup>(98)</sup> Sometimes the impact of biological factors such as the exposure to dialysis and medications as well as the dependency of patients on others at a time when they should be more independent may exceed the capacity of the child to adjust, which dooms such denial mechanisms and leads to the development of many maladaptive behavior patterns exhibited by the dialysis patients.<sup>(99)</sup>

In contrast to the result of our study, Hernandez et al found that 53.73% of children and adolescents with CRF undergoing (HD) in Lima had depression.<sup>(8)</sup> Also another cross-sectional study in which the Child Depression Inventory (CDI), was administered to 44 patients aged 9–18 years with CRF living in the USA; 13 cases 30 % met criteria for depression, representing 18 % of patients aged <13 years and 34 % of those aged ≥13 years.<sup>(100)</sup>

The variations between the results of the present study and the results of the other studies could be explained that our socioeconomic distribution is vastly different from other developed countries like for example USA which may affect the prevalence rate of psychological disorders.

Bakr et al <sup>(9)</sup> found that depression was as high as 15.8% in children with terminal chronic renal insufficiency using the semi-structural clinical interview for children and adolescents (SCICA); the variation between the prevalence of depression of the current study and the study carried by Bakr et al could be explained by numbers of limitations in their study. First, they did not comment on clinical and demographic factors associated with psychological disease, specifically with the depressed patients. Second: They also mentioned that the presence of psychiatric disorders among their study cohort was not significantly correlated with age, sex, severity of anemia, duration of disease, or the efficacy of HD, but did not show the results on which they based this observation, also the heterogeneity of the studied patients in their study and the small size of the sample was observed. Also the differences in the used tool of psychiatric assessment have affected the consistency of prevalence rates. This was illustrated well also in a study completed by Amr et al <sup>(101)</sup> showed significantly higher results on the anxiety and depression scale of CBCL (the child behavior checklist) in the group of dialyzed and pre-dialyzed children than in the control group. However, using another tool (SCICA), it was noted, on the contrary, higher results in the reference group than in groups of sick patients.

As regard the gender difference, It was found that 53.3% of males patients had moderate anxiety compared to 24% of females patients, but there was no significant relationship between gender and anxiety among CRF patients. Similar to our results, there was no significant relation documented in the study done by Alzhar University where they found 60% of CRF patients affected with anxiety were males. <sup>(13)</sup>

As regard depression, it was found that 80% of males patients had depression compared to 64% of female patients but it was not statistically significant. Also, it was found that in group of children aged (7-12 yrs) , 66.7% of males had depression in comparison to 44, 4% of females patients in the same age group, 88. 9% of males in the group of adolescents aged (13-18 yrs) had depression compared to 75% of females adolescents.

It is well known that prior to puberty, the prevalence of depression is roughly equal in both sexes, but from puberty onwards, depression is more common in females <sup>(102)</sup>, indicating a gender difference in pediatric depression but in contrast to this suggestion ,in the current study ,it was found that anxiety and depression are more common in males than female patients with CRF.Consistent with our results , Sasaki et al <sup>(103)</sup> did not find any difference of serum Brain-Derived Neurotrophic Factor (BDNF) levels between female pediatric patients with depression and female control subjects, unlike in male subjects .It was suggested that decreased levels of (BDNF) in male pediatric depressed patients and not in female may play a role in the pathophysiology of depression .

But in contrast to our study, Kogon et al <sup>(100)</sup> found that the boys had a lower prevalence of depression than the girls also another Study using birlescon score, found that 100% of the children with high depressive symptomatology were females. <sup>(8,104,1)</sup>Previous studies have explain this result indicating that stress, inflammatory responses, and depressive symptoms are more common and more intense in females than in males;

perhaps these responses are mediated by estradiol and differential activation of components of the hypothalamic pituitary adrenal (HPA) system.<sup>(105-107)</sup> A further detailed study will be needed to delineate more clearly the relation between anxiety, depression and gender.

As regard the relationship between the prevalence of anxiety, depression, and the age of our patients, most of our patients affected by anxiety and depression were adolescents (13 -18 yrs) but it was found that there was no significant relationship between the age and anxiety. Similarly, El Sadek et al<sup>(13)</sup> from El Azhar University reported that there was no significant correlation between age and anxiety. But in contrast to the result of the present study, study done by Kiliś-Pstrusińska K et al<sup>(88)</sup>, in which 22 cases with CRF children on HD were enrolled in a study using (STAI) for adolescents and STAI-C for children, they documented that the level of anxiety among adolescents was significantly higher in the HD group compared with other groups. Perhaps the result of the current study was different from other studies because it was suggested that the way of stress management of the patient is of great importance regardless of the age.

As regard depression, we found that (82.4%) of adolescents had depression in comparison to 57.1% of children aged (7-12 yrs) and it was statistically significant (p value =0.041). Result of this study was consistent with the study done by Kogan<sup>(100)</sup> who found that younger children had a lower prevalence of depression. This can be explained that adolescence is a particularly important phase in life; a critical time of rapid physical, psychological and social development. It is a time of transition that varies across individuals and cultures.<sup>(108)</sup> During the transition from childhood to adulthood, adolescents establish patterns of behavior and make lifestyle choices that affect both their current and future health<sup>(109)</sup>, and they may be aware of their limitations connected with the disease.<sup>(17,84)</sup>

Residence, a key factor of socioeconomic status, as well as the location of the dialysis unit, might contribute to outcome of patients with CRF. In our study, we found that 40.6% of those coming from rural areas suffered from severe as well as moderate anxiety in comparison to 39.1% of those coming from urban areas. Also we found that of those who came from urban areas, there were 82.6% having depression compared to 65.6 % of those who came from rural areas. These results document that there was higher percentage of anxiety in patients coming from rural areas in comparison to those coming from urban areas but it was not statistically significant. This result was similar to the result of another study in which CRF children on hemodialysis were enrolled in a study using (STAI) for adolescents and (STAI-C) for children.<sup>(88)</sup> Perhaps this can be explained that patients living in rural areas found difficulty in accessing medical care and can't attend their dialysis sessions regularly which exposed them to more complications related to the disease. A further study using a large sample size will be needed to document this association.

In the present study, we didn't find any significant relationship between anxiety, depression and school attendance. Regarding anxiety, it was found that 40.8% of those who attend school had severe anxiety in comparison to 33.3% of those who didn't attend. Perhaps, like children treated with peritoneal dialysis and had daily contact with healthy peers at school, they discern their otherness in many ways, and therefore they underestimate their abilities and this explain why anxiety increased in those children who

attended school.<sup>(88)</sup> Children with CRF undergoing HD with a schedule including 3 dialysis sessions per week, may have trouble fitting in with children of their own age because of their small stature, their delayed cognitive development, or the physical effects of immunosuppressive drugs. Such children find it impossible to continue their formal studies and the impossibility of socio-professional insertion.<sup>(110)</sup>

This result can be supported by study done in which CRF children on HD ,peritoneal dialysis and on conservative treatment were enrolled in one study using (STAI) and (STAI-C) for children, there was higher level of anxiety among PD adolescents who attended school and had more time for contacts with peers compared with those who didn't attend school.<sup>(88)</sup>

But in contrast to this result, it was found that 50% of those who didn't attend school had moderate anxiety compared to 38.8% of those who attended. Similar result as regard depression was found, as 83.3% of those who didn't attend school had depression compared to 71.4 % of those who attended. Perhaps this can be explained that children who are more likely to attend school regularly, have the chance to continue regular social interaction at school as well as their education with fewer interruptions. Having a normal life as much as possible can help a child feel more like other children. Further studies are needed to delineate the association between anxiety, depression and school attendance.

As regard family structure, Children of single parent homes are especially vulnerable to anxiety and depression. Lack of a two-parent household, in which it is typically the father who is absent, combined with the emotional stress by the mother, who has to fill both roles. She doesn't have time to supervise and interact with their children. This could not be supported by the current study, as it was found that 54.5% of patients who had one parent home had moderate anxiety compared to 36.4% of patients who had complete family structure but no significant relationship was found between anxiety, depression and family structure. Similarly, Kiliś-Pstrusińska K et al<sup>(88)</sup> documented the same result as the present study. Perhaps this result was due to the presence of many other risk factors other than family structure that can affect the emotional status of those children including biological, social, demographical risk factors compared to other children of general population without such risk factors. Also, another possible explanation is that the cause of depression in those children may be the parental depression itself which can be transmitted to children in the home regardless is the family structure. The result of the present study paves the way for future studies on wider scale using tool for assessment of anxiety and depression in children and their parents at same time.<sup>(111)</sup>

Factors related to family conditions have been found to be an important associated factor for anxiety and depression. This could not be supported by the current study, as it was found that 50% of patients who had family history of renal disease had moderate anxiety compared to 37.2 % of patients who didn't have family history. Also, 91.7% of those who had family history had depression compared to 67. 4% of those who didn't had but no significant relationship was found between anxiety, depression and the presence of family history of renal disease. Perhaps this contradictory result can be due to the absence of renal disease in the family of studied patients, which was severe enough to have an impact on the psychological well being of their children except in a small number of cases.

Presence of close friend to confide in is an important predictive factor for anxiety and depression in CRF patients. This is because Social support contributes to the patient quality of life and decrease the number of hospitalizations in children with chronic renal insufficiency. <sup>(112)</sup>Children with kidney disease may have trouble in making friends. The physical activity restrictions and sometimes the smaller stature, the drug treatment or the dialysis program, the food and drinks restriction could limit them for socializing. <sup>(113)</sup>This could not be supported by the current study as we didn't find any significant relationship between anxiety, depression and the presence of close friend to confide in. In contrast to the current study, it was found that among 67 patients with a mean age of 14 years, duration of illness  $\geq 3$  months, none of the children with high depressive symptomatology, had a friend to confide in ( $p=0.03$ ).<sup>(8)</sup>

Although, it was not statistically significant but it was found also that 45.5% of those who had a close friend, had severe anxiety compared to 18.2% of those who didn't have one. The variation in the result of the current study than other studies could be explained that in our hospital, we have noticed that most of the children were choosing friends among those who were hospitalized for the same medical condition (peritoneal or HD) who suffered nearly from the same psychological illness which may increase the chance of having anxiety and depression in those children.

Investigations were done on the relationship between level of serum hemoglobin, anxiety and depression among patients with CRF as a possible risk factor. In our study; we didn't detect any significant relationship between anxiety and HB level. But there was a negative correlation between haemoglobin level and anxiety (low hemoglobin was associated with increased anxiety scores). Similarly, study done by Abdel Salam et al <sup>(85)</sup> from el Zagazig University, Egypt revealing the same result as the current study. This negative correlation with respect to hemoglobin level may be related to malnutrition in anxious children. In contrast to our result, study carried in AL-Azhar university shows that a highly statistically significant ( $p$  value=0.01) decrease in the mean hemoglobin level in CRF compared to the controls.<sup>(13)</sup>

As regard depression, the mean haemoglobin level in depressed patients was ( $8.78 \pm 1.66$ ) in comparison to the mean in non depressed patients ( $9.93 \pm 1.46$ ) and it was statistically significant ( $p$  value= 0.022). As we know that anemia can develop during any stage of CRF in children and remains widely prevalent among the pediatric CRF population.<sup>(114)</sup>It is associated with significant morbidity and mortality in patients with CRF. Complications related to anemia include kidney disease progression, cardiovascular disease, hospitalization, mortality, and an impaired quality of life <sup>(115)</sup>.The correction of anemia has been associated with an improvement in exercise capacity and quality of life. Also an increase in hemoglobin level was associated with an improvement in exercise tolerance, physical performance and school attendance.<sup>(116)</sup>

We studied the relationship between adequacy of dialysis (KtV), anxiety and depression in children with CRF as a possible risk factor; we found that there was no significant relationship between decline of adequacy of dialysis and anxiety.83% of those who had inadequate dialysis, had severe anxiety in comparison to 34.7% of those who had adequate dialysis. Also there was no significant relationship between depression and adequacy of dialysis in children with CRF. Similarly, Bakr et al <sup>(9)</sup> did not found any relationship between depression, anxiety and Adequacy of dialysis. However, we found

that 83.3% of those who had inadequate dialysis, had depression in comparison to 71.4% of those who had adequate dialysis. Number of studies have demonstrated that the occurrence of depressive symptomatology in patients with chronic dialysis was associated with a lower weekly Kt/V compared to those absence of depressive symptomatology ( $p=0.01$ ).<sup>(8)</sup> They explain their result that there is evidence that suboptimal dialysis increase mortality in patients undergoing peritoneal dialysis and HD with cardiac, cerebral and other co-morbidities. A Kt/V that diminishes by 0, 1 weekly is associated with a 5 % increase in relative death risk<sup>(117,118)</sup> and suboptimal dialysis contributes to the risk of depression.<sup>(119,120-122)</sup>, but this relation couldn't be supported by the current study, may be a larger sample is needed to delineate this association or perhaps, depression in CRF children is a multifactorial disorder that could be influenced by many factors, not only the adequacy of dialysis.

The duration since start of dialysis is another proposed risk factor for anxiety and depression in patients with CRF. In our study, we found a significant relationship between anxiety and the duration of dialysis ( $p$  value =0.045) and also there was a positive correlation ( $r=0.272$ ). Similarly, Kiliš-Pstrusińska et al<sup>(87)</sup> found that there was a significant relationship between anxiety-state and the duration of the disease in children with CRF on HD. Consistent with the result of the present study, EL Sadek et al<sup>(13)</sup> (AL-Azhar university) found that there was a significant positive correlation between the presence of psychiatric disorders and the duration of HD. This result confirms that the extended duration of disease will not make it easier for the patients to adjust to the situation, but it will lead to the further enhancement of anxiety.<sup>(123)</sup> Anxiety may be exacerbated by the social isolation arising from the necessity of arriving to HD sessions and from frequent hospitalizations.<sup>(13)</sup>

As regard depression, our study showed no significant relationship between depression and duration of dialysis as the mean duration of dialysis among CRF children with depression was ( $3.36\pm 3.6$ ) years which was not significantly different from the mean duration in non depressed patients which was ( $4.25 \pm 3.71$ ). Similarly, a number of studies investigating depression in other pediatric chronic illnesses have, however, failed to find an association between depression and duration of illness.<sup>(124)</sup> Also Soliday et al,<sup>(125)</sup> found that depression and anxiety among patients are the strongest at the beginning of the disease. This was explained that after about one year following the diagnosis, the life of the family and the patients stabilizes. One of the concepts clarifying this condition is the so called adaption to the stressor (the stressing factor).<sup>(126)</sup>

As regard the effect of the number of dialysis session per week on the occurrence of depression and anxiety in children with CRF. We didn't found any significant relationship. This could be explained that the disease itself and not the number of dialysis sessions, which has an impact on the psychological well being of those children.

Finally, we found that there was a significant relationship between anxiety ( $p$  value=0.047) and socioeconomic status. As regard depression, we didn't found significant relationship between it and socioeconomic status but we found that 62.5%, 87.5% of those classified as having low, moderate socioeconomic status respectively had depression in comparison to 57.1% of those classified as having high socioeconomic status. Similarly, Fielding et al<sup>(127)</sup> found that lower socioeconomic status was associated with more behavioral disturbances in the children, and increased depression and anxiety in their

parents. These findings are supported by a review of the literature that suggested that low income households may have fewer resources to pay for medications, access a pharmacy or clinic, or pay for insurance. Individuals of lower socioeconomic status (SES) have a higher risk for mortality and morbidity compared with those of higher SES. <sup>(128,129)</sup> The association of CRF with SES in various studies could be related to the effect of the characteristics of the area. <sup>(130)</sup> Differences across regions and countries on the population access and quality of health care and even lifestyle may have a different impact on the relationship between SES and CRF.

## SUMMARY

Chronic renal failure (CRF) during childhood is a significant stressor with a psychological and social impact on the children and their family. Children with CRF suffer from an illness that has no known cure and requires daily life-style modification. They often experience growth retardation and altered body image and frequently miss school and other normative activities. These obstacles likely affect the psychological well-being of those children.

The aim of the current study was to estimate the prevalence of anxiety and depression among chronic renal failure patients on dialysis and to study some of the multifactorial risk factors, which may affect the prevalence of anxiety and depression among those patients.

This study was conducted on 55 children. All children were aged (7-18) years and had no other chronic medical or surgical conditions; to exclude the impact of other illness.

For the assessment of anxiety and depression symptoms among the studied children, self reporting scales were used including; children manifest anxiety scale (CMAS) and children depression inventory scale (CDI)

In this study, of the 55 children, all patients were being diagnosed as having anxiety. 11 patients (20%) with mild anxiety, 22 patients (40%) with moderate anxiety, 22 patients (40%) with severe anxiety. As regard depression, there were 17 patients (30, 9%) with mild depression, 18 patients (32, 7 %,) with moderate depression, 5 patients (9, 1%) with severe depression.

We found a significant relationship between prevalence of anxiety and duration of dialysis (0,045) and socioeconomic status (p value =0,047).

As regard depression, we found a significant relationship between the prevalence of depression and age (p value=0, 04), hemoglobin level (p value=0, 02), however we didn't find a statistically significant relationship between anxiety, depression and others risk factors including: gender, residency, school attendance, complete family structure, family history of renal disease, presence of close friend, adequacy of dialysis and number of dialysis session per week.

It is concluded that there is significant increase in the prevalence of anxiety or depression among CRF children on haemodialysis in comparison to others studies in foreign countries and here appear the rule of socioeconomic standard in Egypt and his great impact on the psychological well-being of those children. As regard anxiety, there is a relationship between it and duration of dialysis and socioeconomic status among those children .Also there is a significant relationship between age, haemoglobin level and depression, while no statistically significant relationship was found between depression, anxiety and other risk factors like; gender, residency, school attendance, complete family structure ,family history of renal disease, presence of close friend , adequacy of dialysis and number of dialysis session per week.

## *Summary*

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We recommend regular monitoring for detection of anxiety and depression among chronic renal failure children on dialysis using screening self reporting scales. We recommend also training of pediatric psychologists to use screening scales on regular basis during the follow up sessions, especially among school aged children and adolescents. Clinicians should educate and counsel families of patients about anxiety and depression and options for dealing with these disorders. It is also recommended to update new screening scales and modifying it to Arabic forms to suit our Egyptian children; to ensure proper assessment. At the same time, we recommend to study larger numbers of children on dialysis in Egypt. Finally there must be an academic support for those children at schools to improve their performance and, therefore, decrease their psychiatric comorbidities.

## CONCLUSIONS

### **From the current study, we concluded that:**

- 1) There is significant increase in the prevalence of anxiety and depression among CRF children on haemodialysis in comparison to others studies in foreign countries and here appear the rule of socioeconomic standard in Egypt and its great impact on the psychological well-being of those children.
- 2) The psychiatric co-morbidity among CRF children on haemodialysis is not uncommon among children aged (6-18) years. There was a prevalence rate of (20%) mild anxiety, (40%) of moderate anxiety and (40%) of high anxiety
- 3) As regard depression, there was a prevalence rate of (30.9%) of mild depression, (32.7%) moderate depression, (9.1%) severe depression.
- 4) As regard anxiety, there was a relationship between duration since start of dialysis, socioeconomic status and anxiety among those children.
- 5) There was a significant relationship between age, hemoglobin level and depression.
- 6) There is no statistically significant relationship between prevalence of depression, anxiety and other risk factors like: gender, residency, school attendance, complete family structure ,family history of renal disease, presence of close friend ,adequacy of dialysis , number of dialysis session per week.